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Via Electronic Submission and UPS Overnight

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Division of Dockets Management
Department of Health and Human Services
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

This petition is submitted under 21 C.F.R. § 10.30 on behalf of the Organic and Natural Health Association ("ONHA") to request the Commissioner of Food and Drugs to amend 21 C.F.R. Part 111, the current good manufacturing practice ("CGMP") regulations governing dietary supplements ("Part 111"), to include persons who manufacture, process, package, or hold finished dietary ingredients ("dietary ingredient suppliers").[1] We also request that the Food and Drug Administration ("FDA" or the "Agency") clarify the regulatory responsibilities of private label distributors[2] under Part 111.

ONHA is a Section 501(c)(6) trade association founded in October 2014. ONHA is dedicated to creating and promoting transparent business practices that safeguard access to organic and natural food, products, and services. Our overarching goal is to advance and grow a robust organic and natural marketplace in partnership with business and consumer organizations committed to the following guiding principles:

> (1) sustainability of food, farm, and goods production and distribution practices and processes that are restorative to nature, give the utmost consideration to animal welfare,

[1] ONHA believes that, consistent with the existing CGMP regulations, a person engaged solely in activities related to the harvesting, storage, or distribution of "raw agricultural commodities" that will be incorporated into a dietary ingredient should not be subject to the CGMPs. Under Section 201(r) of the FDCA, the term "raw agricultural commodity" means any food in its raw or natural state, including all fruits that are washed, colored, or otherwise treated in their unpeeled natural form prior to marketing. *See* 21 U.S.C. § 321(r).

[2] A private label distributor is a company that markets a dietary supplement product under its own brand name but does not perform any manufacturing, processing, or packaging operations; rather, a private label distributor relies on contract manufacturers to perform such operations.

are socially responsible, and demonstrate our commitment to a resilient environment by altering the current resource consumption paradigm;

(2) transparency and honest relationships between consumers and corporations and our commitment to instill business and marketing practices that value disclosure and unambiguous knowledge as well as empower and inform consumer purchasing;

(3) accessibility to organic and natural food, products and services as part of our commitment to the health and wellness of all individuals, communities and cultures; and

(4) traceability in the ongoing and consistent practice of holding suppliers, manufacturers and distributors accountable for a clearly-defined, quality-controlled production process based on our commitment to ensure products are accurately labeled, undergo appropriate testing, and reflect consumers' desire for wholesome goods and services.

To uphold these principles, as it relates to dietary supplements, we believe it is necessary to ensure that dietary ingredient suppliers are subject to Part 111.

FDA's efforts to ensure the quality of dietary supplements in the food supply can only be fully realized by requiring suppliers of dietary ingredients—the building blocks of any finished dietary supplement—to (1) adhere to the Part 111 standards of quality that help ensure authentic and safe finished dietary supplement product and (2) ensure that the products they produce are not adulterated in violation of Section 402 of the Federal Food, Drug, and Cosmetic Act (the "FDCA") and meet the requirements of Section 403 of the FDCA. Under the existing regulations, dietary ingredient suppliers have no regulatory obligation to manufacture or hold dietary ingredients in accordance with the specific production and process controls that are necessary to ensure finished product quality, and absent contractual obligations, dietary supplement manufacturers and consumers have no recourse against such suppliers that fail to manufacture quality product.

Such a regulatory framework falls short of Congress's intent that FDA establish regulations to oversee the quality of dietary supplements. Moreover, this omission of dietary ingredient suppliers from the CGMP regulations has permitted the introduction of dietary ingredients with questionable quality at significantly lower price points than dietary ingredients that are manufactured pursuant to GMPs. Indeed, legitimate suppliers are under pressure to compete with these low-cost options but cannot do so, allowing the marketplace to be flooded with low-cost, low-quality options from ingredient manufacturers that produce ingredients of questionable quality, thereby threatening the very existence of the legitimate supply chain.

FDA has the statutory authority pursuant to the Dietary Supplement Health and Education Act of 1994 ("DSHEA") to require dietary ingredient suppliers to comply with Part 111, and only by so doing can FDA fulfill its public health mandate and help restore consumer confidence in the quality of dietary supplements. As ONHA discusses below, neither the existing regulations governing dietary ingredients and finished dietary supplements nor the proposed rules under the Food Safety Modernization Act ("FSMA") adequately address the quality manufacturing of

dietary ingredients, and neither justifies the exclusion of dietary ingredient suppliers from the responsibility to manufacture product in accordance with quality standards.

Finally, ONHA believes that Part 111 must clearly state the roles and responsibilities of each person subject to the regulations in order to promote an effective and efficient process to produce quality dietary supplements free of adulteration and misbranding. To that end, we request that FDA clarify its position regarding the obligations of private label distributors of dietary supplements, including the extent of obligations to oversee contract manufacturers' compliance with Part 111, as well as any obligation to conduct finished product testing of the dietary supplement sold under the private labeler's brand name. This issue has become more acute in recent FDA warning letters to some private labelers.

I. ACTIONS REQUESTED

ONHA requests that FDA amend Part 111, as follows:

(1) include dietary ingredient suppliers within the scope of Part 111, as outlined in the Appendix to this Citizen Petition; and

(2) clarify the Part 111 obligations imposed on private label distributors of finished dietary supplements.

II. STATEMENT OF GROUNDS

ONHA firmly believes that Part 111 has indeed helped to significantly improve the quality of dietary supplements in our food supply. Nevertheless, the ability of dietary supplement finished product manufacturers to ensure the quality of finished products is significantly hindered by the lack of regulation of the suppliers of dietary ingredients used in finished dietary supplement products. Indeed, adulterants may be added before or during the manufacturing stage of the ingredient or prior to shipment of the ingredient to the finished product manufacturer; however, unless the finished product manufacturer knows what adulterants to look and test for, identifying adulterants is often similar to looking for a needle a haystack. Moreover, the finished product manufacturer may know very little about the ingredient and how it was processed (as is frequently the case with branded ingredients protected by patents, or for certain extracts, for example), adding further difficulty in ensuring that quality ingredients make it into finished products. Indeed, FDA's decision to exempt those responsible for producing dietary ingredients from the regulatory mandate to abide by quality manufacturing processes has created an unnecessary and in some ways insurmountable burden on finished dietary supplement manufacturers.

This Statement of Grounds is organized to first explain why quality standards require inclusion of dietary ingredient suppliers within the scope of Part 111. Specifically, we articulate why the existing regulations governing dietary ingredients, as well as the proposed rules under FSMA, provide no justifiable grounds for excluding dietary ingredient suppliers from Part 111. Second, we also outline FDA's clear regulatory authority to include dietary ingredient suppliers under Part 111. Finally, we explain why the Agency should further clarify the applicability of Part 111 to private label distributors.

A. Quality Manufacturing Requires Responsibility at the Ingredient Level

As stated in the preamble to the June 25, 2007 dietary supplement CGMP final rule (the "2007 Final Rule")[3]:

> "Well-established principles of CGMP require process controls at each step of the manufacturing process ***as early in the production process as possible***. Quality cannot be tested into the product only at the end. . . [i]nstead, the quality of the dietary supplement must be built into the product throughout the manufacturing process; ***quality begins with the starting material***. . . ."[4] (emphasis added).

Consistent with FDA's views that quality must be built into the production process as early as possible, it is perplexing why the agency excluded dietary ingredient suppliers, the first parties involved in the process of manufacturing dietary supplements, from the CGMP requirements necessary to achieve product quality. ONHA believes that the Agency must require dietary ingredient suppliers (who are the only parties able to provide quality early in the production process) to comply with Part 111, and that FDA should do so in a manner generally consistent with the Agency's approach taken in the 2003 proposed rule regarding dietary supplement CGMPs (the "2003 Proposed Rule").[5] This regulatory action is essential to achieve control over the identity, purity, quality, strength and composition of the dietary supplements distributed in our food supply, an industry that produces a global product supply to a market of well over $100 billion dollars a year.[6]

1. <u>Dietary Ingredient Suppliers Must have Regulatory Responsibility for Manufacturing Quality Ingredients</u>

Recognizing the importance of imposing quality at an early stage in the manufacturing process, FDA's 2003 Proposed Rule indeed included dietary ingredient suppliers within the scope of the Part 111 requirements.[7] Throughout FDA's regulatory framework, the Agency emphasizes the importance of food, drug, medical device, and cosmetic suppliers serving as responsible actors and taking steps to safeguard against adulterated and misbranded product. Accordingly, the exclusion of dietary ingredient suppliers, the first parties in the process of manufacturing dietary supplements, is a glaring omission.

Including dietary ingredient suppliers within Part 111 is essential from a product quality and production standpoint. In many instances, dietary ingredient suppliers are best equipped with the skill and expertise to evaluate the quality and identity of a raw material. For example, certain botanicals must be harvested from a certain geographic region or at a certain time of the year to ensure their optimal effectiveness, or certain parts of the plant must be used to ensure effectiveness.

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[3] FDA "Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling and Holding Operations for Dietary Supplements" Final Rule, 72 Fed. Reg. 34752 (June 25, 2007) (hereinafter "Final Rule").
[4] *Id.* at (Ref 9) 72 Fed. Reg. 34762.
[5] FDA "Current Good Manufacturing Practice in Manufacturing, Packaging, or Holding Dietary Ingredients and Dietary Supplements," Proposed Rule, 68 Fed. Reg. 12158 (March 13, 2003) (hereinafter "Proposed Rule").
[6] We recognize that there has been a lot of discussion recently concerning whether certain testing is appropriate to effectuate identity testing for dietary ingredients. This petition is not intended to address that issue.
[7] *See* Proposed Rule at 12175.

The dietary ingredient supplier is the party in the best position to determine whether these factors have been met. Indeed, the finished supplement manufacturer likely cannot control for these important botanical attributes via identity or in-process testing. While much has been made over the use of DNA testing to help establish the identity of botanicals, such testing does not provide any information as to the quality of the botanical used to manufacture the dietary ingredient. As emphasized by industry comments submitted in response to the 2003 Proposed Rule, "the difficulty to test in-process, or in the finished product, some botanical and other dietary ingredients, makes it necessary to include raw ingredient manufacturers in the rule to ensure consistent high quality from the beginning."[8] Exempting dietary ingredient suppliers has and will continue to undermine FDA goals of establishing a reliable system of production and process controls that is performed by those persons best equipped to assess the quality of dietary ingredients.

2. Existing Regulations Governing Dietary Ingredient Suppliers Do Not Negate the Need for Quality Controls in the Manufacturing Process

FDA's stated rationale for excluding dietary ingredient suppliers from Part 111 fails to appreciate that the existing requirements for ingredient safety are distinct from the regulatory obligations for building quality into the manufacturing process. The 2007 Final Rule explains that the Agency's reason for exempting dietary ingredient suppliers was due, at least in part, to FDA's belief that the safety of dietary ingredients is sufficiently governed by other provisions of the FDCA (specifically, Section 402(f) related to preventing dietary supplement adulteration) and existing regulations (namely, the CGMP regulations applicable to foods, 21 C.F.R. Part 110, and regulations governing the review and approval of any new dietary ingredient, 21 C.F.R. Part 190).[9] However, that thought process appears to use safety and quality interchangeably, when they are two different (but admittedly somewhat dependent) endpoints. Moreover, as explained below, FDA's existing rules and regulations do not address the unique characteristics of dietary ingredients that must be evaluated in order to ensure the integrity of such ingredients and finished supplements and that they are produced in a manner so as to prevent adulteration, including economic adulteration.

First, FDA's general food CGMPs are not detailed enough to ensure that dietary ingredients are produced under adequate quality standards. Under FDA's current framework, dietary ingredients are subject to the so-called "umbrella" food CGMPs, which are a broad set of regulations generally-applicable to all food products to promote a safe and sanitary food supply. However, both Congress and FDA recognized that these umbrella food CGMPs are not sufficient to address the unique characteristics of dietary supplements because, unlike most foods, dietary supplements "may contain bioactive ingredients," such as "botanicals, often very complex mixtures that can vary depending on factors such as the part of the plant used, the location of harvesting, and the growing conditions . . ." for which the methods of testing can vary in nature and specificity.[10] Unfortunately, the "umbrella" food CGMPs do not account for these types of unique factors that are essential to dietary ingredient quality. In short, it is *the unique*

[8] *See* National Nutritional Foods Association, Comments re: Dietary Supplement CGMP Proposed Rule, Docket No. 96N-0416.
[9] *See* Final Rule, 72 Fed. Red. at 34763.
[10] *Id.* at 34762-63; *see also* S. Rep. No 140, 103rd Cong., 2d Sess. at 131(1994) (emphasizing that "dietary supplements may require a different manufacturing and quality controls" compared to food CGMPs).

characteristics of the dietary ingredients contained in the finished supplement that render the general food CGMPs inadequate to ensure the quality, purity, identity and strength of dietary supplements.

In deciding to amend the 2003 Proposed Rule and to exempt dietary ingredient suppliers from the Part 111 regulations, FDA appears to have ultimately agreed with comments suggesting that FDA had not demonstrated (1) a compelling need to create a set of CGMP regulations specific to dietary ingredient suppliers separate and apart from the food CGMPs or (2) a failure of the umbrella food CGMPs to address concerns over dietary ingredient quality.[11] Yet, to the extent that FDA recognized the importance of establishing specific dietary supplement CGMPs due to the unique composition and processing of the ingredients contained therein, ONHA believes that the manufacturing controls applicable to dietary ingredients must also necessarily be specific, and not general, to the characteristics and nature of dietary ingredients. For example, botanical dietary ingredients are frequently standardized to contain a specific percentage of a particular bioactive ingredient. Contrary to conventional foods, the effectiveness of a dietary supplement often depends on the amount of that particular standardized ingredient in the finished product. Likewise, contrary to conventional foods, the part of the plant used in a dietary supplement can make a large difference in the bioactivity of the ingredient (and thus, the effectiveness of the finished product). The general food CGMPs are insufficiently detailed to account for factors such as these that affect the identity, purity, strength and composition of dietary ingredients. Specifically, the general food CGMPs do not contemplate that the timing of harvest, the geographical growing location, or the part of the plant must be controlled. This creates a compelling need to include dietary ingredient suppliers within Part 111.

Second, the blanket prohibition on the commercial distribution of adulterated foods under Section 402 of the FDCA does not obviate the need for FDA to establish a clear set of rules and regulations to ensure that dietary ingredients are produced in a quality, unadulterated manner. The 2007 Final Rule provides that "CGMP is achieving *control over manufacturing processes* [. . .] to ensure that you manufacture what you intend so that the characteristics of and/or attributes desired in a final product will be consistently and reliably achieved."[12] The CGMP manufacturing controls establish a system to produce "quality"[13] products in order to prevent adulteration. In other words, quality production is the means that allows manufacturers to accomplish the ends of supplying quality, unadulterated dietary supplements.

FDA, however, cannot reasonably expect that dietary ingredients will be consistently produced in a reliable and quality manner so as to prevent adulteration in violation of the FDCA, while at the same time concluding that dietary ingredient suppliers need not abide by a system of manufacturing controls that establish the framework needed to produce quality dietary supplement products. Likewise, FDA's New Dietary Ingredient Notification ("NDIN") process intended to establish that an ingredient is safe for consumption does not help guarantee that the ingredient is

[11] *Id.* at 34791.
[12] *Id.* at 34762.
[13] As defined in the dietary supplement CGMPs "quality means that the dietary supplement consistently meets the established specifications for identity, purity, strength, and composition, and limits on contaminants, and has been manufactured, packaged, labeled, and held under conditions to prevent adulteration under section 402(a)(1), (a)(2), (a)(3), and (a)(4) of the [FDCA]." 21 C.F.R. § 111.3.

manufactured consistent with quality standards or consistently supplied free of accidental contamination or intentional economic adulteration. (Interestingly, though, FDA does expect the notifier to provide basic manufacturing information on the ingredient in its NDIN.) For example, the requirement to submit an NDIN does not ensure that a botanical is harvested at the correct time to provide bioactive constituents.

ONHA believes that under the current regulatory framework, dietary ingredient suppliers lack the necessary responsibility for their manufacturing processes. Indeed, absent possible contractual obligations with customers, dietary ingredient suppliers are largely free to produce ingredients without responsibility for testing the quality, purity, strength and identity of the products that are ultimately released into the food supply.

3. Identity Testing by Finished Supplement Manufacturers Is Not Sufficient To Ensure Quality

In response to industry pushback regarding the inclusion of dietary ingredient suppliers within Part 111,[14] FDA agreed to exclude dietary ingredient suppliers from the scope of regulations, and, instead, shift the burden of assessing the quality of dietary ingredients to dietary supplement manufacturers.[15] The Agency believed doing so would established "adequate controls" for the use of dietary ingredients.[16] Specifically, the final Part 111 requirements governing production and process controls require finished supplement manufacturers to conduct 100 % identity testing for dietary ingredients and to establish specifications for ingredients and finished supplements. However, for the reasons set forth below, ONHA believes it is clear that identity testing, while one sufficient step in ensuring quality, is not sophisticated enough at this point in time to sufficiently demonstrate ingredient quality on its own. Rather, quality must be built into the manufacturing and processing of dietary ingredients from the earliest stages.

First, as explained in Section II.A.1 above, dietary ingredient suppliers are, in many cases, the only persons with the expertise to evaluate the quality of the dietary ingredient from the beginning stages of the manufacturing process. For example, the potency of botanicals may significantly differ based upon the specific part of the plant used or the time of harvesting. The only party able to ensure that a specific part of the plant was used or that a plant was harvested at the correct time is the ingredient supplier. Neither identity testing of the raw materials by the finished product manufacturer nor in-process testing by the finished product manufacturer can accurately assess these factors. Finished product manufacturers must rely on the ingredient suppliers, who are currently not subject to the CGMP requirements.

Second, adulteration is more likely to occur at the ingredient manufacturing level, but to the extent that it occurs earlier in the supply chain, it can also be more easily identified and contained by the ingredient suppliers. For example, as emphasized by results from a 1998 survey of members of the American Herbal Products Association evaluating botanical adulteration, 81 citations of contamination were found across 45 different herbs, often based on contamination

[14] *See* Final Rule, 72 Fed. Reg. at 34791.
[15] *Id.* at 34792.
[16] *Id.*

rather than complete substitution.[17] The survey results also concluded that adulteration is more easily identified early when herbs are purchased in their whole form—an aspect that the final dietary supplement manufacturer would not be involved in from a process perspective.

It is an unfortunate fact that economic adulteration of dietary ingredients continues to occur in certain sectors of the industry. As FDA is likely aware, dietary ingredient suppliers have in the past sold, and in some cases continue to sell, ingredients to finished dietary supplement manufacturers that are not what they are purported to be. While ONHA recognizes the regulatory obligation on the part of finished supplement manufacturers to test the identity of the dietary ingredient received from a supplier, importantly, identity testing by finished dietary supplement manufacturers may not detect contamination or economic adulteration if an ingredient is not wholly replaced but is only partially so. Moreover, a finished dietary supplement manufacturer can only test for those contaminants / adulterants of which it is aware. Accordingly, the finished dietary supplement manufacturer is not in the best position to identify potential contamination or economic adulteration of dietary ingredients. While it cannot be expected that all contamination will be identified and prevented at the ingredient level, it is more feasible to mitigate against contamination at the early stages of ingredient manufacturing than it is at later stages in the production process.

To be clear, ONHA does not advocate for eliminating the regulatory responsibility of finished supplement manufacturers to conduct identity testing; rather, ONHA believes that FDA should take additional measures to help protect against the production and distribution of adulterated dietary ingredients by requiring dietary ingredient suppliers to test for the identity, purity, composition, and strength of the products they produce; requiring the dietary ingredient suppliers to provide such quality assurances to the finished supplement supplier in the form of a Certificate of Analysis ("COA"); and by holding the ingredient suppliers responsible from a regulatory standpoint. Indeed, ONHA is hopeful that by subjecting dietary ingredient suppliers to the CGMP regulations, more finished dietary supplement manufacturers may be able to avail themselves of the process to petition FDA to request exemption from 100 percent identity testing of dietary ingredients, providing a significant economic benefit to finished product manufacturers.

B. FDA has the Legal Authority to Require Dietary Ingredient Suppliers to Comply with the CGMPs

As stated by Congress, DSHEA requires that "[a] dietary supplement must have the identity and strength that it is represented to have and must meet the quality (including tablet and capsule disintegration), purity or compositional specifications . . . that it is represented to meet . . ."[18] However, DSHEA's mandate cannot be achieved if the regulations fail to ensure the quality of the starting ingredients at the earliest practical point in the supply chain. In this regard, the dietary ingredient supplier is the most logical place in the supply chain to assess the quality of any particular dietary ingredient. Indeed, the dietary ingredient manufacturer knows more about the starting material and the ingredient manufacturing process than any other party in the supply chain.

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[17] *See* "Survey on Botanical Adulteration," American Herbal Products Association, March 4, 1998 (cited in Proposed Rule at Ref. 11, 68 Fed. Reg. 12162).

[18] S. Rep. 103-410 to Accompany S. 784, Dietary Supplemental Health and Education Act of 1994, 103rd Congress, pp. 5 (Oct. 8, 1994).

Thus, it is nonsensical to exempt dietary ingredient suppliers from Part 111. Moreover, although DSHEA mandates that the dietary supplement CGMPs shall be "modeled after" the food CGMPs, nothing in DSHEA restricts the authority of FDA to impose the Part 111 requirements on dietary ingredient suppliers.

In response to the 2003 Proposed Rule, which would have included dietary ingredient suppliers within the scope of Part 111, FDA received comments that the Agency lacked legal authority and precedent to include ingredient suppliers within the scope of the CGMPs because DSHEA mandates that the Part 111 dietary supplement CGMPs be modeled after the food CGMPs, and neither the food CGMPs nor the drug CGMPs offer precedent or guidance concerning the regulation of ingredients.[19] For the reasons discussed below, ONHA believes that this argument lacks merit and that the FDA indeed has robust statutory authority to subject dietary ingredient suppliers to Part 111 because (1) the purpose of the dietary supplement CGMPs is to ensure the quality of the dietary ingredients contained therein, and (2) the dietary supplement CGMPs are not required to be identical to the food CGMPs.

In the preamble to the 2003 Proposed Rule, FDA recognized that "Congress sought to ensure in DSHEA that dietary supplements would provide accurate information to the consumer on the identity of the dietary ingredient, and if an herb or botanical, the source from which it is derived [and ensure that] dietary ingredients do not present an unreasonable risk of illness or injury."[20] It defies logic to reason that Congress provided broad, independent authority to FDA to issue CGMP regulations governing dietary supplements, under Part 402(g) of the FDCA, while expecting FDA to have no oversight over the manufacturing controls used to produce dietary ingredients contained in such finished supplements. As stated in Section II.A.2 above, Congress recognized in DSHEA that the unique characteristics of dietary supplements require special manufacturing control regulations that are not addressed by the food CGMPs.

Additionally, ONHA agrees with, and reemphasizes today, FDA's stated position in the preamble to the 2007 Final Rule that Congress's requirement that the dietary supplement CGMPs be "modeled after" the food CGMPs does not mandate Part 111 to mirror Part 110. The term "modeled after" suggests use as a pattern or plan, while contemplating that the Part 111 regulations would differ somewhat from the Part 110 regulations. We agree with FDA's position in the 2007 Final Rule; had Congress intended the dietary supplement CGMPs to be identical to the food CGMPs, there would have been no reason for Congress to address dietary supplements CGMPs whatsoever.[21]

It is clear that Congress intended FDA to have independent authority and flexibility to impose CGMP requirements that would provide consumers the assurance that the dietary supplements they consume do not contain dietary ingredients (or other ingredients) that were manufactured in such a way that the final product is adulterated or misbranded. In light of

[19] *See* Final Rule, 72 Fed. Reg. at 34791.
[20] *See* Proposed Rule, 68 Fed. Reg. at 12167.
[21] *See* Final Rule, 72 Fed. Reg. at 34777 (explaining that such an interpretation would "frustrate the success of the regulation undertaken by Congress" because it would not take into consideration the unique characteristics and risks associated with dietary supplements) (quoting *American Trucking Assn's v. U.S.*, 344 U.S. 298, 311 (1953)).

Congress's intent, FDA would not exceed its authority, or run afoul to the purpose of DSHEA, if the Agency took appropriate and necessary measures to require dietary ingredient suppliers to abide by the manufacturing control standards under Part 111 that are designed to ensure the quality of dietary supplements. To the contrary, mandating compliance of dietary ingredient suppliers with CGMPs is entirely consistent with Congressional intent to ensure the quality of finished dietary supplement products.

C. FSMA's Proposed Rules are not Sufficient to Ensure the Quality of Dietary Ingredients

While FDA may indeed have the legal authority to include dietary ingredient suppliers within the scope of Part 111, and the failure of existing regulations to ensure the quality of dietary ingredients may necessitate a change to Part 111, ONHA recognizes that it is critical to consider whether FDA's proposed rules under FSMA will address the concerns identified above regarding the quality of dietary ingredients. Specifically, FDA recently published two proposed rules applicable to the manufacturing and import of dietary ingredients; on September 29, 2014, FDA issued a revised proposed rule, *Foreign Supplier Verification Programs (FSVP) for Importers of Foods for Humans and Animals*,[22] as well as a revised proposed rule entitled, *Current Good Manufacturing Practice and Hazard Analysis and Risk Based Preventive Controls for Human Food*.[23] While each of these proposed rules is intended to enhance regulatory oversight to ensure that foods, including dietary ingredients, are safe and free of adulteration or misbranding, neither directly addresses the need for quality manufacturing controls of dietary ingredient suppliers. Indeed, as discussed above, safety and quality are not interchangeable; rather, they are two different (but admittedly somewhat dependent) endpoints.

First, the FSVP proposed rule, which mandates that those who import human foods use approved foreign suppliers, would do little, if anything, to enhance the manufacturing controls of dietary ingredient suppliers. This is because the proposed rule generally exempts those persons who are subject to Part 111 or whose ***customers*** are subject to Part 111 requirements.[24] Because dietary ingredient suppliers' customers (*i.e.,* manufacturers of finished dietary supplement products) are subject to Part 111, then to the extent that a dietary ingredient supplier imported a raw ingredient for further manufacturing into a processed dietary ingredient to be used in a finished supplement, the dietary ingredient supplier would not be required to abide by the FSVP requirements to establish written procedures for use of approved foreign suppliers (should the proposed rule be adopted as proposed). Thus, the critical element of FSVP does not apply to many, if not most, dietary ingredient suppliers. Moreover, the provision, by definition, is applicable only to foreign suppliers and not to domestic dietary ingredient suppliers.

Second, while the proposed rule amending the food CGMPs (which applies to food facilities required to register with FDA, including dietary ingredient suppliers) includes a

[22] *See* 79 Fed. Reg. 58574 (Sept. 29, 2014).
[23] *Id.* at 58524.
[24] *See* 79 Fed. Reg. 58589 (revising the proposed rule "to specify that importers of dietary supplements and dietary supplement components that are subject to certain dietary supplement CGMP regulations in part 111 (21 CFR part 111) (or whose customers are subject to those regulations)" would not be required to comply with requirements to ensure the use of approved suppliers).

requirement that manufacturers of food ingredients conduct a hazard analysis and implement preventive control measures (to evaluate and reduce the risk of contamination), the purpose of the proposed rule is to impose a regulatory framework to address hazards in the food supply; its focus is not on the methods and means to instill quality from the outset. Further, as with the existing umbrella food CGMPs discussed above, the proposed rule to revise the food CGMPs does not address the unique characteristics or specific adulteration concerns associated with the manufacturing of dietary ingredients (*e.g.*, the importance of the time of harvest on the effectiveness of a botanical dietary ingredient). Rather, the proposed rule is intended as a broad and flexible rule that allows each firm, as appropriate, to establish testing to verify the implementation of preventive control measures.

It is not ONHA's intent to comment on FSMA's proposed rules through this Citizen Petition. Rather, we emphasize that regardless of the regulations implemented under FSMA, FDA would most effectively achieve its goal of ensuring that the quality of dietary supplements by requiring dietary ingredient suppliers to comply with Part 111.

D. The CGMPs Do Not Clearly Explain the Responsibilities of Private Label Distributors

Although Part 111 provides that the CGMPs apply to the specific manufacturing activities in which a person is engaged as it relates to the manufacturing, packaging, and distribution of dietary supplements, the regulations fail to clarify the scope of obligations of private labelers whose names appear on the finished product labels but who rely on contract manufacturers to manufacture, package, and label finished dietary supplements, and frequently rely on fulfillment houses to distribute the finished dietary supplement products. For example, the CGMP regulations, on their face, suggest that finished product testing applies only to those who manufacture dietary supplements. We understand, however, through FDA warning letters and Agency statements, that FDA considers private labelers to be subject to finished product testing obligations.

For instance, FDA takes the position in these warning letters that the private label distributor cannot delegate final release of the product to the contract manufacturer. However, this position does not take into account that many manufacturers are hesitant to share master manufacturing records, deviation reports, and batch records with the private labeler. These tensions between contract manufacturer and private labeler could be dealt with through appropriate Quality Agreements. However, the lack of regulatory certainty leaves private labelers unclear of their regulatory responsibilities. We request that FDA issue binding regulations to clarify the Part 111 obligations applicable to private label distributors of dietary supplements.

E. Conclusion

ONHA continues to believe that Part 111 has resulted in significant steps toward improving the quality of dietary supplements in our food supply. The importance of quality standards for dietary supplements, and the ingredients contained therein, is becoming ever more critical as the supplement industry continues to grow not only in the United States, but globally. Nevertheless, ONHA believes that based on over ten years of industry and Agency reflection on Part 111, it is

clear that more needs to be done to ensure the quality of dietary ingredients and finished dietary supplement products.

To that end, ONHA believes that the inclusion of dietary ingredient suppliers within the scope of Part 111 would effectively help ensure that quality is both expected and required from those at the beginning of the manufacturing process through the final distribution stage of dietary supplements. Existing regulations governing dietary ingredient suppliers do not effectively impose an obligation to produce quality product, and ONHA does not believe that FSMA's proposed rules, once finalized, will provide as robust a quality standard requirement as imposed by the Part 111 CGMPs.

Finally, the CGMP requirements applicable to private label distributors under Part 111 should be clarified by FDA. The absence of regulatory certainly may result in the failure of a private label distributor, or a contract manufacturer hired by such distributor, to understand and effectively fulfill its Part 111 obligations. Accordingly, ONHA requests that Part 111 be further revised to clarify FDA's position regarding private label distributors' obligations.

III. OTHER REQUIRED INFORMATION FOR FILING OF CITIZEN PETITION

A. ENVIRONMENTAL IMPACT

The actions requested in this petition are subject to categorical exclusion under 21 C.F.R. § 25.31.

B. ECONOMIC IMPACT

Pursuant to 21 C.F.R. § 10.30(b), an economic impact statement will be submitted upon request of the Commissioner.

C. CERTIFICATION

The undersigned certifies that, to the best of his knowledge and belief, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioners which are unfavorable to the petition.

Signed:

Todd A. Harrison
Counsel to ONHA

May 14, 2015

Appendix A

SUBPART A—GENERAL PROVISIONS

§111.1 Who is subject to this part?

(a) Except as provided by paragraph (b) of this section, you are subject to this part if you manufacture, package, label, or hold a dietary ingredient or dietary supplement, including:

(1) A dietary ingredient or dietary supplement you manufacture but that is packaged or labeled by another person; and

(2) A dietary ingredient or dietary supplement imported or offered for import in any State or territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico.

(b) The requirements pertaining to holding dietary supplements do not apply to you if you are holding those dietary supplements at a retail establishment for the sole purpose of direct retail sale to individual consumers. A retail establishment does not include a warehouse or other storage facility for a retailer or a warehouse or other storage facility that sells directly to individual consumers.

§111.3 What definitions apply to this part?

The definitions and interpretations of terms in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) apply to such terms when used in this part. For the purpose of this part, the following definitions also apply:

Actual yield means the quantity that is actually produced at any appropriate step of manufacture or packaging of a particular dietary ingredient or dietary supplement.

Batch means a specific quantity of a dietary ingredient or dietary supplement that is uniform, that is intended to meet specifications for identity, purity, strength, and composition, and that is produced during a specified time period according to a single manufacturing record during the same cycle of manufacture.

Batch number, lot number, or control number means any distinctive group of letters, numbers, or symbols, or any combination of them, from which the complete history of the manufacturing, packaging, labeling, and/or holding of a batch or lot of dietary ingredients or dietary supplements can be determined.

Component means any substance intended for use in the manufacture of a dietary supplement, including those that may not appear in the finished batch of the dietary supplement. Component includes dietary ingredients (as described in section 201(ff) of the act) and other ingredients.

Contact surface means any surface that contacts a component or dietary supplement, and those surfaces from which drainage onto the component or dietary supplement, or onto surfaces that contact the component or dietary supplement, occurs during the normal course of operations. Examples of contact surfaces include containers, utensils, tables, contact surfaces of equipment, and packaging.

Ingredient means any substance that is used in the manufacture of a dietary supplement and that is intended to be present in the finished batch of the dietary supplement. An ingredient includes, but is not necessarily limited to, a dietary ingredient as defined in section 201(ff) of the act.

In-process material means any material that is fabricated, compounded, blended, ground, extracted, sifted, sterilized, derived by chemical reaction, or processed in any other way for use in the manufacture of a dietary ingredient or dietary supplement.

Lot means a batch, or a specific identified portion of a batch, that is uniform and that is intended to meet specifications for identity, purity, strength, and composition; or, in the case of a dietary ingredient or dietary supplement produced by continuous process, a specific identified amount produced in a specified unit of time or quantity in a manner that is uniform and that is intended to meet specifications for identity, purity, strength, and composition.

Microorganisms means yeasts, molds, bacteria, viruses, and other similar microscopic organisms having public health or sanitary concern. This definition includes species that:

(1) May have public health significance;

(2) May cause a component or dietary supplement to decompose;

(3) Indicate that the component or dietary supplement is contaminated with filth; or

(4) Otherwise may cause the component or dietary supplement to be adulterated.

Must is used to state a requirement.

Pest means any objectionable insect or other animal including birds, rodents, flies, mites, and larvae.

Physical plant means all or any part of a building or facility used for or in connection with manufacturing, packaging, labeling, or holding a dietary ingredient or dietary supplement.

Product complaint means any communication that contains any allegation, written, electronic, or oral, expressing concern, for any reason, with the quality of a dietary ingredient or dietary supplement, that could be related to current good manufacturing practice. Examples of product complaints are: Foul odor, off taste, illness or injury, disintegration time, color variation, tablet size or size variation, under-filled container, foreign material in a dietary ingredient or dietary supplement container, improper packaging, mislabeling, or dietary ingredients or dietary supplements that are superpotent, subpotent, or contain the wrong ingredient, or contain a drug or other contaminant (e.g., bacteria, pesticide, mycotoxin, glass, lead).

Quality means that the dietary ingredient or dietary supplement consistently meets the established specifications for identity, purity, strength, and composition, and limits on contaminants, and has been manufactured, packaged, labeled, and held under conditions to prevent adulteration under section 402(a)(1), (a)(2), (a)(3), and (a)(4) of the act.

Quality control means a planned and systematic operation or procedure for ensuring the quality of a dietary ingredient or dietary supplement.

Quality control personnel means any person, persons, or group, within or outside of your organization, who you designate to be responsible for your quality control operations.

Representative sample means a sample that consists of an adequate number of units that are drawn based on rational criteria, such as random sampling, and that are intended to ensure that the sample accurately portrays the material being sampled.

Reprocessing means using, in the manufacture of a dietary ingredient or dietary supplement, clean, uncontaminated components or dietary supplements that have been previously removed from manufacturing and that have been made suitable for use in the manufacture of a dietary ingredient or dietary supplement.

Reserve sample means a representative sample of product that is held for a designated period of time.

Sanitize means to adequately treat cleaned equipment, containers, utensils, or any other cleaned contact surface by a process that is effective in destroying vegetative cells of microorganisms of public health significance, and in substantially reducing numbers of other microorganisms, but without adversely affecting the product or its safety for the consumer.

Theoretical yield means the quantity that would be produced at any appropriate step of manufacture or packaging of a particular dietary ingredient or dietary supplement, based upon the quantity of components or packaging to be used, in the absence of any loss or error in actual production.

Water activity (a_w) is a measure of the free moisture in a component or dietary supplement and is the quotient of the water vapor pressure of the substance divided by the vapor pressure of pure water at the same temperature.

We means the U.S. Food and Drug Administration (FDA).

You means a person who manufactures, packages, labels, or holds dietary ingredients or dietary supplements.

§111.5 Do other statutory provisions and regulations apply?

In addition to this part, you must comply with other applicable statutory provisions and regulations under the act related to dietary ingredients and dietary supplements.

Subpart B—Personnel

§111.8 What are the requirements under this subpart B for written procedures?

You must establish and follow written procedures for fulfilling the requirements of this subpart.

§111.10 What requirements apply for preventing microbial contamination from sick or infected personnel and for hygienic practices?

(a) *Preventing microbial contamination.* You must take measures to exclude from any operations any person who might be a source of microbial contamination, due to a health condition, where such contamination may occur, of any material, including components, dietary supplements, and contact surfaces used in the manufacture, packaging, labeling, or holding of a dietary ingredient or dietary supplement. Such measures include the following:

(1) Excluding from working in any operations that may result in contamination any person who, by medical examination, the person's acknowledgement, or supervisory observation, is shown to have, or appears to have, an illness, infection, open lesion, or any other abnormal source of microbial contamination, that could result in microbial contamination of components, dietary supplements, or contact surfaces, until the health condition no longer exists; and

(2) Instructing your employees to notify their supervisor(s) if they have or if there is a reasonable possibility that they have a health condition described in paragraph (a)(1) of this section that could result in microbial contamination of any components, dietary supplements, or any contact surface.

(b) *Hygienic practices.* If you work in an operation during which adulteration of the component, dietary supplement, or contact surface could occur, you must use hygienic practices to the extent

necessary to protect against such contamination of components, dietary supplements, or contact surfaces. These hygienic practices include the following:

(1) Wearing outer garments in a manner that protects against the contamination of components, dietary supplements, or any contact surface;

(2) Maintaining adequate personal cleanliness;

(3) Washing hands thoroughly (and sanitizing if necessary to protect against contamination with microorganisms) in an adequate hand-washing facility:

(i) Before starting work; and

(ii) At any time when the hands may have become soiled or contaminated;

(4) Removing all unsecured jewelry and other objects that might fall into components, dietary supplements, equipment, or packaging, and removing hand jewelry that cannot be adequately sanitized during periods in which components or dietary supplements are manipulated by hand. If hand jewelry cannot be removed, it must be covered by material that is maintained in an intact, clean, and sanitary condition and that effectively protects against contamination of components, dietary supplements, or contact surfaces;

(5) Maintaining gloves used in handling components or dietary supplements in an intact, clean, and sanitary condition. The gloves must be of an impermeable material;

(6) Wearing, where appropriate, in an effective manner, hair nets, caps, beard covers, or other effective hair restraints;

(7) Not storing clothing or other personal belongings in areas where components, dietary supplements, or any contact surfaces are exposed or where contact surfaces are washed;

(8) Not eating food, chewing gum, drinking beverages, or using tobacco products in areas where components, dietary supplements, or any contact surfaces are exposed, or where contact surfaces are washed; and

(9) Taking any other precautions necessary to protect against the contamination of components, dietary supplements, or contact surfaces with microorganisms, filth, or any other extraneous materials, including perspiration, hair, cosmetics, tobacco, chemicals, and medicines applied to the skin.

§111.12 What personnel qualification requirements apply?

(a) You must have qualified employees who manufacture, package, label, or hold dietary ingredients or dietary supplements.

(b) You must identify who is responsible for your quality control operations. Each person who is identified to perform quality control operations must be qualified to do so and have distinct and separate responsibilities related to performing such operations from those responsibilities that the person otherwise has when not performing such operations.

(c) Each person engaged in manufacturing, packaging, labeling, or holding, or in performing any quality control operations, must have the education, training, or experience to perform the person's assigned functions.

§111.13 What supervisor requirements apply?

(a) You must assign qualified personnel to supervise the manufacturing, packaging, labeling, or holding of dietary ingredients and dietary supplements.

(b) Each supervisor whom you use must be qualified by education, training, or experience to supervise.

§111.14 Under this subpart B, what records must you make and keep?

(a) You must make and keep records required under this subpart B in accordance with subpart P of this part.

(b) You must make and keep the following records:

(1) Written procedures for fulfilling the requirements of this subpart B; and

(2) Documentation of training, including the date of the training, the type of training, and the person(s) trained.

Subpart C—Physical Plant and Grounds

§111.15 What sanitation requirements apply to your physical plant and grounds?

(a) *Grounds.* You must keep the grounds of your physical plant in a condition that protects against the contamination of components, dietary supplements, or contact surfaces. The methods for adequate ground maintenance include:

(1) Properly storing equipment, removing litter and waste, and cutting weeds or grass within the immediate vicinity of the physical plant so that it does not attract pests, harbor pests, or provide pests a place for breeding;

(2) Maintaining roads, yards, and parking lots so that they do not constitute a source of contamination in areas where components, dietary supplements, or contact surfaces are exposed;

(3) Adequately draining areas that may contribute to the contamination of components, dietary supplements, or contact surfaces by seepage, filth or any other extraneous materials, or by providing a breeding place for pests;

(4) Adequately operating systems for waste treatment and disposal so that they do not constitute a source of contamination in areas where components, dietary supplements, or contact surfaces are exposed; and

(5) If your plant grounds are bordered by grounds not under your control, and if those other grounds are not maintained in the manner described in this section, you must exercise care in the plant by inspection, extermination, or other means to exclude pests, dirt, and filth or any other extraneous materials that may be a source of contamination.

(b) *Physical plant facilities.* (1) You must maintain your physical plant in a clean and sanitary condition; and

(2) You must maintain your physical plant in repair sufficient to prevent components, dietary supplements, or contact surfaces from becoming contaminated.

(c) *Cleaning compounds, sanitizing agents, pesticides, and other toxic materials.* (1) You must use cleaning compounds and sanitizing agents that are free from microorganisms of public health significance and that are safe and adequate under the conditions of use.

(2) You must not use or hold toxic materials in a physical plant in which components, dietary supplements, or contact surfaces are manufactured or exposed, unless those materials are necessary as follows:

(i) To maintain clean and sanitary conditions;

(ii) For use in laboratory testing procedures;

(iii) For maintaining or operating the physical plant or equipment; or

(iv) For use in the plant's operations.

(3) You must identify and hold cleaning compounds, sanitizing agents, pesticides, pesticide chemicals, and other toxic materials in a manner that protects against contamination of components, dietary supplements, or contact surfaces.

(d) *Pest control.* (1) You must not allow animals or pests in any area of your physical plant. Guard or guide dogs are allowed in some areas of your physical plant if the presence of the dogs will not result in contamination of components, dietary supplements, or contact surfaces;

(2) You must take effective measures to exclude pests from the physical plant and to protect against contamination of components, dietary supplements, and contact surfaces on the premises by pests; and

(3) You must not use insecticides, fumigants, fungicides, or rodenticides, unless you take precautions to protect against the contamination of components, dietary supplements, or contact surfaces.

(e) *Water supply.* (1) You must provide water that is safe and sanitary, at suitable temperatures, and under pressure as needed, for all uses where water does not become a component of the dietary ingredient or dietary supplement.

(2) Water that is used in a manner such that the water may become a component of the dietary ingredient or dietary supplement, e.g., when such water contacts components, dietary supplements, or any contact surface, must, at a minimum, comply with applicable Federal, State, and local requirements and not contaminate the dietary ingredient or dietary supplement.

(f) *Plumbing.* The plumbing in your physical plant must be of an adequate size and design and be adequately installed and maintained to:

(1) Carry sufficient amounts of water to required locations throughout the physical plant;

(2) Properly convey sewage and liquid disposable waste from your physical plant;

(3) Avoid being a source of contamination to components, dietary supplements, water supplies, or any contact surface, or creating an unsanitary condition;

(4) Provide adequate floor drainage in all areas where floors are subject to flooding-type cleaning or where normal operations release or discharge water or other liquid waste on the floor; and

(5) Not allow backflow from, or cross connection between, piping systems that discharge waste water or sewage and piping systems that carry water used for manufacturing dietary ingredients or dietary supplements, for cleaning contact surfaces, or for use in bathrooms or hand-washing facilities.

(g) *Sewage disposal.* You must dispose of sewage into an adequate sewage system or through other adequate means.

(h) *Bathrooms.* You must provide your employees with adequate, readily accessible bathrooms. The bathrooms must be kept clean and must not be a potential source of contamination to components, dietary supplements, or contact surfaces.

(i) *Hand-washing facilities.* You must provide hand-washing facilities that are designed to ensure that an employee's hands are not a source of contamination of components, dietary supplements, or any contact surface, by providing facilities that are adequate, convenient, and furnish running water at a suitable temperature.

(j) *Trash disposal.* You must convey, store, and dispose of trash to:

(1) Minimize the development of odors;

(2) Minimize the potential for the trash to attract, harbor, or become a breeding place for pests;

(3) Protect against contamination of components, dietary supplements, any contact surface, water supplies, and grounds surrounding your physical plant; and

(4) Control hazardous waste to prevent contamination of components, dietary supplements, and contact surfaces.

(k) *Sanitation supervisors.* You must assign one or more employees to supervise overall sanitation. Each of these supervisors must be qualified by education, training, or experience to develop and supervise sanitation procedures.

§111.16 What are the requirements under this subpart C for written procedures?

You must establish and follow written procedures for cleaning the physical plant and for pest control.

§111.20 What design and construction requirements apply to your physical plant?

Any physical plant you use in the manufacture, packaging, labeling, or holding of dietary ingredients or dietary supplements must:

(a) Be suitable in size, construction, and design to facilitate maintenance, cleaning, and sanitizing operations;

(b) Have adequate space for the orderly placement of equipment and holding of materials as is necessary for maintenance, cleaning, and sanitizing operations and to prevent contamination and mixups of components and dietary supplements during manufacturing, packaging, labeling, or holding;

(c) Permit the use of proper precautions to reduce the potential for mixups or contamination of components, dietary supplements, or contact surfaces, with microorganisms, chemicals, filth, or other extraneous material. Your physical plant must have, and you must use, separate or defined areas of adequate size or other control systems, such as computerized inventory controls or automated systems of separation, to prevent contamination and mixups of components and dietary supplements during the following operations:

(1) Receiving, identifying, holding, and withholding from use, components, dietary supplements, packaging, and labels that will be used in or during the manufacturing, packaging, labeling, or holding of dietary ingredients or dietary supplements;

(2) Separating, as necessary, components, dietary supplements, packaging, and labels that are to be used in manufacturing from components, dietary supplements, packaging, or labels that are awaiting material review and disposition decision, reprocessing, or are awaiting disposal after rejection;

(3) Separating the manufacturing, packaging, labeling, and holding of different product types including different types of dietary ingredients, dietary supplements and other foods, cosmetics, and pharmaceutical products;

(4) Performing laboratory analyses and holding laboratory supplies and samples;

(5) Cleaning and sanitizing contact surfaces;

(6) Packaging and label operations; and

(7) Holding components or dietary supplements.

(d) Be designed and constructed in a manner that prevents contamination of components, dietary supplements, or contact surfaces.

(1) The design and construction must include:

(i) Floors, walls, and ceilings that can be adequately cleaned and kept clean and in good repair;

(ii) Fixtures, ducts, and pipes that do not contaminate components, dietary supplements, or contact surfaces by dripping or other leakage, or condensate;

(iii) Adequate ventilation or environmental control equipment such as airflow systems, including filters, fans, and other air-blowing equipment, that minimize odors and vapors (including steam and noxious fumes) in areas where they may contaminate components, dietary supplements, or contact surfaces;

(iv) Equipment that controls temperature and humidity, when such equipment is necessary to ensure the quality of the dietary ingredient or dietary supplement; and

(v) Aisles or working spaces between equipment and walls that are adequately unobstructed and of adequate width to permit all persons to perform their duties and to protect against contamination of components, dietary supplements, or contact surfaces with clothing or personal contact.

(2) When fans and other air-blowing equipment are used, such fans and equipment must be located and operated in a manner that minimizes the potential for microorganisms and particulate matter to contaminate components, dietary supplements, or contact surfaces;

(e) Provide adequate light in:

(1) All areas where components or dietary supplements are examined, processed, or held;

(2) All areas where contact surfaces are cleaned; and

(3) Hand-washing areas, dressing and locker rooms, and bathrooms.

(f) Use safety-type light bulbs, fixtures, skylights, or other glass or glass-like materials when the light bulbs, fixtures, skylights or other glass or glass-like materials are suspended over exposed components or dietary supplements in any step of preparation, unless your physical plant is otherwise constructed in a manner that will protect against contamination of components or dietary supplements in case of breakage of glass or glass-like materials.

(g) Provide effective protection against contamination of components and dietary supplements in bulk fermentation vessels, by, for example:

(1) Use of protective coverings;

(2) Placement in areas where you can eliminate harborages for pests over and around the vessels;

(3) Placement in areas where you can check regularly for pests, pest infestation, filth or any other extraneous materials; and

(4) Use of skimming equipment.

(h) Use adequate screening or other protection against pests, where necessary.

§111.23 Under this subpart C, what records must you make and keep?

(a) You must make and keep records required under this subpart C in accordance with subpart P of this part.

(b) You must make and keep records of the written procedures for cleaning the physical plant and for pest control.

(c) You must make and keep records that show that water, when used in a manner such that the water may become a component of the dietary ingredient or dietary supplement, meets the requirements of §111.15(e)(2).

Subpart D—Equipment and Utensils

§111.25 What are the requirements under this subpart D for written procedures?

You must establish and follow written procedures for fulfilling the requirements of this subpart D, including written procedures for:

(a) Calibrating instruments and controls that you use in manufacturing or testing a component or dietary supplement;

(b) Calibrating, inspecting, and checking automated, mechanical, and electronic equipment; and

(c) Maintaining, cleaning, and sanitizing, as necessary, all equipment, utensils, and any other contact surfaces that are used to manufacture, package, label, or hold components or dietary supplements.

§111.27 What requirements apply to the equipment and utensils that you use?

(a) You must use equipment and utensils that are of appropriate design, construction, and workmanship to enable them to be suitable for their intended use and to be adequately cleaned and properly maintained.

(1) Equipment and utensils include the following:

(i) Equipment used to hold or convey;

(ii) Equipment used to measure;

(iii) Equipment using compressed air or gas;

(iv) Equipment used to carry out processes in closed pipes and vessels; and

(v) Equipment used in automated, mechanical, or electronic systems.

(2) You must use equipment and utensils of appropriate design and construction so that use will not result in the contamination of components or dietary supplements with:

(i) Lubricants;

(ii) Fuel;

(iii) Coolants;

(iv) Metal or glass fragments;

(v) Filth or any other extraneous material;

(vi) Contaminated water; or

(vii) Any other contaminants.

(3) All equipment and utensils you use must be:

(i) Installed and maintained to facilitate cleaning the equipment, utensils, and all adjacent spaces;

(ii) Corrosion-resistant if the equipment or utensils contact components or dietary supplements;

(iii) Made of nontoxic materials;

(iv) Designed and constructed to withstand the environment in which they are used, the action of components or dietary supplements, and, if applicable, cleaning compounds and sanitizing agents; and

(v) Maintained to protect components and dietary supplements from being contaminated by any source.

(4) Equipment and utensils you use must have seams that are smoothly bonded or maintained to minimize accumulation of dirt, filth, organic material, particles of components or dietary supplements, or any other extraneous materials or contaminants.

(5) Each freezer, refrigerator, and other cold storage compartment you use to hold components or dietary supplements:

(i) Must be fitted with an indicating thermometer, temperature-measuring device, or temperature-recording device that indicates and records, or allows for recording by hand, the temperature accurately within the compartment; and

(ii) Must have an automated device for regulating temperature or an automated alarm system to indicate a significant temperature change in a manual operation.

(6) Instruments or controls used in the manufacturing, packaging, labeling, or holding of a dietary ingredient or dietary supplement, and instruments or controls that you use to measure, regulate, or record temperatures, hydrogen-ion concentration (pH), water activity, or other conditions, to control or prevent the growth of microorganisms or other contamination must be:

(i) Accurate and precise;

(ii) Adequately maintained; and

(iii) Adequate in number for their designated uses.

(7) Compressed air or other gases you introduce mechanically into or onto a component, dietary supplement, or contact surface or that you use to clean any contact surface must be treated in such a way that the component, dietary supplement, or contact surface is not contaminated.

(b) You must calibrate instruments and controls you use in manufacturing or testing a component or dietary supplement. You must calibrate:

(1) Before first use; and

(2) At the frequency specified in writing by the manufacturer of the instrument and control; or

(3) At routine intervals or as otherwise necessary to ensure the accuracy and precision of the instrument and control.

(c) You must repair or replace instruments or controls that cannot be adjusted to agree with the reference standard.

(d) You must maintain, clean, and sanitize, as necessary, all equipment, utensils, and any other contact surfaces used to manufacture, package, label, or hold components or dietary supplements.

(1) Equipment and utensils must be taken apart as necessary for thorough maintenance, cleaning, and sanitizing.

(2) You must ensure that all contact surfaces, used for manufacturing or holding low-moisture components or dietary supplements, are in a dry and sanitary condition when in use. When the surfaces are wet-cleaned, they must be sanitized, when necessary, and thoroughly dried before subsequent use.

(3) If you use wet processing during manufacturing, you must clean and sanitize all contact surfaces, as necessary, to protect against the introduction of microorganisms into components or dietary supplements. When cleaning and sanitizing is necessary, you must clean and sanitize all contact surfaces before use and after any interruption during which the contact surface may have become contaminated. If you use contact surfaces in a continuous production operation or in consecutive operations involving different batches of the same dietary ingredient or dietary supplement, you must adequately clean and sanitize the contact surfaces, as necessary.

(4) You must clean surfaces that do not come into direct contact with components or dietary supplements as frequently as necessary to protect against contaminating components or dietary supplements.

(5) Single-service articles (such as utensils intended for one-time use, paper cups, and paper towels) must be:

(i) Stored in appropriate containers; and

(ii) Handled, dispensed, used, and disposed of in a manner that protects against contamination of components, dietary supplements, or any contact surface.

(6) Cleaning compounds and sanitizing agents must be adequate for their intended use and safe under their conditions of use;

(7) You must store cleaned and sanitized portable equipment and utensils that have contact surfaces in a location and manner that protects them from contamination.

[72 FR 34942, June 25, 2007, as amended at 73 FR 13124, Mar. 12, 2008]

§111.30 What requirements apply to automated, mechanical, or electronic equipment?

For any automated, mechanical, or electronic equipment that you use to manufacture, package, label, or hold a dietary ingredient or dietary supplement, you must:

(a) Design or select equipment to ensure that dietary ingredient or dietary supplement specifications are consistently met;

(b) Determine the suitability of the equipment by ensuring that your equipment is capable of operating satisfactorily within the operating limits required by the process;

(c) Routinely calibrate, inspect, or check the equipment to ensure proper performance. Your quality control personnel must periodically review these calibrations, inspections, or checks;

(d) Establish and use appropriate controls for automated, mechanical, and electronic equipment (including software for a computer controlled process) to ensure that any changes to the manufacturing, packaging, labeling, holding, or other operations are approved by quality control personnel and instituted only by authorized personnel; and

(e) Establish and use appropriate controls to ensure that the equipment functions in accordance with its intended use. These controls must be approved by quality control personnel.

§111.35 Under this subpart D, what records must you make and keep?

(a) You must make and keep records required under this subpart D in accordance with subpart P of this part.

(b) You must make and keep the following records:

(1) Written procedures for fulfilling the requirements of this subpart, including written procedures for:

(i) Calibrating instruments and controls that you use in manufacturing or testing a component or dietary supplement;

(ii) Calibrating, inspecting, and checking automated, mechanical, and electronic equipment; and

(iii) Maintaining, cleaning, and sanitizing, as necessary, all equipment, utensils, and any other contact surfaces that are used to manufacture, package, label, or hold components or dietary supplements;

(2) Documentation, in individual equipment logs, of the date of the use, maintenance, cleaning, and sanitizing of equipment, unless such documentation is kept with the batch record;

(3) Documentation of any calibration, each time the calibration is performed, for instruments and controls that you use in manufacturing or testing a component or dietary supplement. In your documentation, you must:

(i) Identify the instrument or control calibrated;

(ii) Provide the date of calibration;

(iii) Identify the reference standard used including the certification of accuracy of the known reference standard and a history of recertification of accuracy;

(iv) Identify the calibration method used, including appropriate limits for accuracy and precision of instruments and controls when calibrating;

(v) Provide the calibration reading or readings found;

(vi) Identify the recalibration method used, and reading or readings found, if accuracy or precision or both accuracy and precision limits for instruments and controls were not met; and

(vii) Include the initials of the person who performed the calibration and any recalibration.

(4) Written records of calibrations, inspections, and checks of automated, mechanical, and electronic equipment;

(5) Backup file(s) of current software programs (and of outdated software that is necessary to retrieve records that you are required to keep in accordance with subpart P of this part, when current software is not able to retrieve such records) and of data entered into computer systems that you use to manufacture, package, label, or hold dietary ingredients or dietary supplements.

(i) Your backup file (e.g., a hard copy of data you have entered, diskettes, tapes, microfilm, or compact disks) must be an exact and complete record of the data you entered.

(ii) You must keep your backup software programs and data secure from alterations, inadvertent erasures, or loss; and

(6) Documentation of the controls that you use to ensure that equipment functions in accordance with its intended use.

Subpart E—Requirement to Establish a Production and Process Control System

§111.55 What are the requirements to implement a production and process control system?

You must implement a system of production and process controls that covers all stages of manufacturing, packaging, labeling, and holding of the dietary ingredient or dietary supplement to ensure the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record.

§111.60 What are the design requirements for the production and process control system?

(a) Your production and in-process control system must be designed to ensure that the dietary ingredient or dietary supplement is manufactured, packaged, labeled, and held in a manner that will ensure the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record; and

(b) The production and in-process control system must include all requirements of subparts E through L of this part and must be reviewed and approved by quality control personnel.

§111.65 What are the requirements for quality control operations?

You must implement quality control operations in your manufacturing, packaging, labeling, and holding operations for producing the dietary ingredient or dietary supplement to ensure the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record.

§111.70 What specifications must you establish?

(a) You must establish a specification for any point, step, or stage in the manufacturing process where control is necessary to ensure the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record.

(b) For each component that you use in the manufacture of a dietary ingredient or dietary supplement, you must establish component specifications as follows:

(1) You must establish an identity specification;

(2) You must establish component specifications that are necessary to ensure that specifications for the purity, strength and composition of dietary ingredients or dietary supplements manufactured using the components are met; and

(3) You must establish limits on those types of contamination that may adulterate or may lead to adulteration of the finished batch of the dietary ingredient or dietary supplement to ensure the quality of the dietary ingredient or dietary supplement.

(c) For the in-process production:

(1) You must establish in-process specifications for any point, step, or stage in the master manufacturing record where control is necessary to help ensure that specifications are met for the identity, purity, strength, and composition of the dietary ingredients or dietary supplements and, as necessary, for limits on those types of contamination that may adulterate or may lead to adulteration of the finished batch of the dietary ingredient or dietary supplement;

(2) You must provide adequate documentation of your basis for why meeting the in-process specifications, in combination with meeting component specifications, will help ensure that the specifications are met for the identity, purity, strength, and composition of the dietary ingredients or dietary supplements and for limits on those types of contamination that may adulterate or may lead to adulteration of the finished batch of the dietary ingredient or dietary supplement; and

(3) Quality control personnel must review and approve the documentation that you provide under paragraph (c)(2) of this section.

(d) You must establish specifications for dietary ingredient or dietary supplement labels (label specifications) and for packaging that may come in contact with dietary ingredients or dietary supplements (packaging specifications). Packaging that may come into contact with dietary ingredients or dietary supplements must be safe and suitable for its intended use and must not be reactive or absorptive or otherwise affect the safety or quality of the dietary ingredient or dietary supplement.

(e) For each dietary ingredient or dietary supplement that you manufacture you must establish product specifications for the identity, purity, strength, and composition of the finished batch of the dietary ingredient or dietary supplement, and for limits on those types of contamination that may adulterate, or that may lead to adulteration of, the finished batch of the dietary ingredient or dietary supplement to ensure the quality of the dietary ingredient or dietary supplement.

(f) If you receive a product from a supplier for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier), you must establish specifications to provide sufficient assurance that the product you receive is adequately identified and is consistent with your purchase order.

(g) You must establish specifications for the packaging and labeling of the dietary ingredients or finished packaged and labeled dietary supplements, including specifications that ensure that you used the specified packaging and that you applied the specified label.

§111.73 What is your responsibility for determining whether established specifications are met?

You must determine whether the specifications you establish under §111.70 are met.

§111.75 What must you do to determine whether specifications are met?

(a) Before you use a component, you must:

(1)(i) Conduct at least one appropriate test or examination to verify the identity of any component that is a dietary ingredient, unless you are a finished dietary supplement manufacturer and you petition the agency under paragraph (a)(1)(ii) of this section and the agency exempts you from such testing;

(ii) If you are a finished dietary supplement manufacturer, ~~Y~~you may submit a petition, under 21 CFR 10.30, to request an exemption from the testing requirements in paragraph (a)(1)(i) of this section. The petition must set forth the scientific rationale, and must be accompanied by the supporting data and information, for proposed alternative testing that will demonstrate that there is no material diminution of assurance, compared to the assurance provided by 100 percent identity testing, of the identity of the dietary ingredient before use when the dietary ingredient is obtained from one or more suppliers identified in the petition. If FDA grants the petition, you must conduct the tests and examinations for the dietary ingredient, otherwise required under §111.75(a)(1)(i), under the terms specified by FDA when the petition is granted; and

(2) Confirm the identity of other components and determine whether other applicable component specifications established in accordance with §111.70(b) are met. To do so, you must either:

(i) Conduct appropriate tests or examinations; or

(ii) Rely on a certificate of analysis from the supplier of the component that you receive, provided that:

(A) You first qualify the supplier by establishing the reliability of the supplier's certificate of analysis through confirmation of the results of the supplier's tests or examinations;

(B) The certificate of analysis includes a description of the test or examination method(s) used, limits of the test or examinations, and actual results of the tests or examinations;

(C) You maintain documentation of how you qualified the supplier;

(D) You periodically re-confirm the supplier's certificate of analysis; and

(E) Your quality control personnel review and approve the documentation setting forth the basis for qualification (and re-qualification) of any supplier.

(b) You must monitor the in-process points, steps, or stages where control is necessary to ensure the quality of the finished batch of dietary ingredient or dietary supplement to:

(1) Determine whether the in-process specifications are met; and

(2) Detect any deviation or unanticipated occurrence that may result in a failure to meet specifications.

(c) For a subset of finished dietary ingredient or dietary supplement batches that you identify through a sound statistical sampling plan (or for every finished batch), you must verify that your finished batch of the dietary ingredient or dietary supplement meets product specifications for identity, purity, strength, composition, and for limits on those types of contamination that may adulterate or that may lead to adulteration of the finished batch of the dietary ingredient or dietary supplement. To do so:

(1) You must select one or more established specifications for identity, purity, strength, composition, and the limits on those types of contamination that may adulterate or that may lead to adulteration of the dietary ingredient or dietary supplement that, if tested or examined on the finished batches of the dietary ingredient or dietary supplement, would verify that the production and process control system is

producing a dietary ingredient or dietary supplement that meets all product specifications (or only those product specifications not otherwise exempted from this provision by quality control personnel under paragraph (d) of this section);

(2) You must conduct appropriate tests or examinations to determine compliance with the specifications selected in paragraph (c)(1) of this section;

(3) You must provide adequate documentation of your basis for determining that compliance with the specification(s) selected under paragraph (c)(1) of this section, through the use of appropriate tests or examinations conducted under paragraph (c)(2) of this section, will ensure that your finished batch of the dietary ingredient or dietary supplement meets all product specifications for identity, purity, strength, and composition, and the limits on those types of contamination that may adulterate, or that may lead to the adulteration of, the dietary ingredient or dietary supplement; and

(4) Your quality control personnel must review and approve the documentation that you provide under paragraph (c)(3) of this section.

(d)(1) You may exempt one or more product specifications from verification requirements in paragraph (c)(1) of this section if you determine and document that the specifications you select under paragraph (c)(1) of this section for determination of compliance with specifications are not able to verify that the production and process control system is producing a dietary ingredient or dietary supplement that meets the exempted product specification and there is no scientifically valid method for testing or examining such exempted product specification at the finished batch stage. In such a case, you must document why, for example, any component and in-process testing, examination, or monitoring, and any other information, will ensure that such exempted product specification is met without verification through periodic testing of the finished batch; and

(2) Your quality control personnel must review and approve the documentation that you provide under paragraph (d)(1) of this section.

(e) Before you package or label a product that you receive for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier), you must visually examine the product and have documentation to determine whether the specifications that you established under §111.70 (f) are met.

(f)(1) Before you use packaging, you must, at a minimum, conduct a visual identification of the containers and closures and review the supplier's invoice, guarantee, or certification to determine whether the packaging specifications are met; and

(2) Before you use labels, you must, at a minimum, conduct a visual examination of the label and review the supplier's invoice, guarantee, or certification to determine whether label specifications are met.

(g) You must, at a minimum, conduct a visual examination of the packaging and labeling of the finished packaged and labeled dietary ingredient or dietary supplements to determine whether you used the specified packaging and applied the specified label.

(h)(1) You must ensure that the tests and examinations that you use to determine whether the specifications are met are appropriate, scientifically valid methods.

(2) The tests and examinations that you use must include at least one of the following:

(i) Gross organoleptic analysis;

(ii) Macroscopic analysis;

(iii) Microscopic analysis;

(iv) Chemical analysis; or

(v) Other scientifically valid methods.

(i) You must establish corrective action plans for use when an established specification is not met.

[72 FR 34942, June 25, 2007, as amended at 72 FR 34968, June 25, 2007; 73 FR 27727, May 14, 2008]

§111.77 What must you do if established specifications are not met?

(a) For specifications established under §111.70(a), (b)(2), (b)(3), (c), (d), (e), and (g) that you do not meet, quality control personnel, in accordance with the requirements in subpart F of this part, must reject the component, dietary supplement, package or label unless such personnel approve a treatment, an in-process adjustment, or reprocessing that will ensure the quality of the finished dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record. No finished batch of dietary ingredients or dietary supplements may be released for distribution unless it complies with §111.123(b).

(b) For specifications established under §111.70(b)(1) that you do not meet, quality control personnel must reject the component and the component must not be used in manufacturing the dietary ingredient or dietary supplement.

(c) For specifications established under §111.70(f) that you do not meet, quality control personnel must reject the product and the product may not be packaged or labeled for distribution as a dietary ingredient or dietary supplement.

§111.80 What representative samples must you collect?

The representative samples that you must collect include:

(a) Representative samples of each unique lot of components, packaging, and labels that you use to determine whether the components, packaging, and labels meet specifications established in accordance with §111.70(b) and (d), and as applicable, §111.70(a) (and, when you receive components, packaging, or labels from a supplier, representative samples of each unique shipment, and of each unique lot within each unique shipment);

(b) Representative samples of in-process materials for each manufactured batch at points, steps, or stages, in the manufacturing process as specified in the master manufacturing record where control is necessary to ensure the identity, purity, strength, and composition of dietary ingredients or dietary supplements to determine whether the in-process materials meet specifications established in accordance with §111.70(c), and as applicable, §111.70(a);

(c) Representative samples of a subset of finished batches of each dietary ingredient or dietary supplement that you manufacture, which you identify through a sound statistical sampling plan (or otherwise every finished batch), before releasing for distribution to verify that the finished batch of dietary ingredient or dietary supplement meets product specifications established in accordance with §111.70(e), and as applicable, §111.70(a);

(d) Representative samples of each unique shipment, and of each unique lot within each unique shipment, of product that you receive for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier) to determine whether the received product meets specifications established in accordance with §111.70(f), and as applicable, §111.70(a); and

(e) Representative samples of each lot of packaged and labeled dietary ingredients or dietary supplements to determine whether the packaging and labeling of the finished packaged and labeled dietary ingredients or dietary supplements meet specifications established in accordance with §111.70(g), and as applicable, §111.70(a).

§111.83 What are the requirements for reserve samples?

(a) You must collect and hold reserve samples of each lot of packaged and labeled dietary ingredients or dietary supplements that you distribute.

(b) The reserve samples must:

(1) Be held using the same container-closure system in which the packaged and labeled dietary ingredient or dietary supplement is distributed, or if distributing dietary ingredients or dietary supplements to be packaged and labeled, using a container-closure system that provides essentially the same characteristics to protect against contamination or deterioration as the one in which it is distributed for packaging and labeling elsewhere;

(2) Be identified with the batch, lot, or control number;

(3) Be retained for 1 year past the shelf life date (if shelf life dating is used), or for 2 years from the date of distribution of the last batch of dietary ingredients or dietary supplements associated with the reserve sample, for use in appropriate investigations; and

(4) Consist of at least twice the quantity necessary for all tests or examinations to determine whether or not the dietary ingredient or dietary supplement meets product specifications.

§111.87 Who conducts a material review and makes a disposition decision?

Quality control personnel must conduct all required material reviews and make all required disposition decisions.

§111.90 What requirements apply to treatments, in-process adjustments, and reprocessing when there is a deviation or unanticipated occurrence or when a specification established in accordance with §111.70 is not met?

(a) You must not reprocess a rejected dietary ingredient or dietary supplement or treat or provide an in-process adjustment to a component, packaging, or label to make it suitable for use in the manufacture of a dietary ingredient or dietary supplement unless:

(1) Quality control personnel conduct a material review and make a disposition decision to approve the reprocessing, treatment, or in-process adjustment; and

(2) The reprocessing, treatment, or in-process adjustment is permitted by §111.77;

(b) You must not reprocess any dietary ingredient or dietary supplement or treat or provide an in-process adjustment to a component to make it suitable for use in the manufacture of a dietary ingredient or dietary supplement, unless:

(1) Quality control personnel conduct a material review and make a disposition decision that is based on a scientifically valid reason and approves the reprocessing, treatment, or in-process adjustment; and

(2) The reprocessing, treatment or in-process adjustment is permitted by §111.77;

(c) Any batch of dietary ingredient or dietary supplement that is reprocessed, that contains components that you have treated, or to which you have made in-process adjustments to make them suitable for use in the manufacture of the dietary ingredient or dietary supplement must be approved by quality control personnel and comply with §111.123(b) before releasing for distribution.

§111.95 Under this subpart E, what records must you make and keep?

(a) You must make and keep records required under this subpart E in accordance with subpart P of this part.

(b) Under this subpart E, you must make and keep the following records:

(1) The specifications established;

(2) Documentation of your qualification of a supplier for the purpose of relying on the supplier's certificate of analysis;

(3) Documentation for why meeting in-process specifications, in combination with meeting component specifications, helps ensure that the dietary ingredient or dietary supplement meets the specifications for identity, purity, strength, and composition; and for limits on those types of contamination that may adulterate or may lead to adulteration of the finished batch of the dietary ingredient or dietary supplement; and

(4) Documentation for why the results of appropriate tests or examinations for the product specifications selected under §111.75(c)(1) ensure that the dietary ingredient or dietary supplement meets all product specifications;

(5) Documentation for why any component and in-process testing, examination, or monitoring, and any other information, will ensure that a product specification that is exempted under §111.75(d) is met without verification through periodic testing of the finished batch, including documentation that the selected specifications tested or examined under §111.75 (c)(1) are not able to verify that the production and process control system is producing a dietary ingredient or dietary supplement that meets the exempted product specification and there is no scientifically valid method for testing or examining such exempted product specification at the finished batch stage.

(6) Documentation of FDA's response to a petition submitted under §111.75(a)(1)(ii) providing for an exemption from the provisions of §111.75(a)(1)(i).

[72 FR 34942, June 25, 2007, as amended at 72 FR 34968, June 25, 2007]

Subpart F—Production and Process Control System: Requirements for Quality Control

§111.103 What are the requirements under this subpart F for written procedures?

You must establish and follow written procedures for the responsibilities of the quality control operations, including written procedures for conducting a material review and making a disposition decision, and for approving or rejecting any reprocessing.

§111.105 What must quality control personnel do?

Quality control personnel must ensure that your manufacturing, packaging, labeling, and holding operations ensure the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record. To do so, quality control personnel must perform operations that include:

(a) Approving or rejecting all processes, specifications, written procedures, controls, tests, and examinations, and deviations from or modifications to them, that may affect the identity, purity, strength, or composition of a dietary ingredient or dietary supplement;

(b) Reviewing and approving the documentation setting forth the basis for qualification of any supplier;

(c) Reviewing and approving the documentation setting forth the basis for why meeting in-process specifications, in combination with meeting component specifications, will help ensure that the identity, purity, strength, and composition of the dietary ingredient or dietary supplement are met;

(d) Reviewing and approving the documentation setting forth the basis for why the results of appropriate tests or examinations for each product specification selected under §111.75(c)(1) will ensure that the finished batch of the dietary ingredient or dietary supplement meets product specifications;

(e) Reviewing and approving the basis and the documentation for why any product specification is exempted from the verification requirements in §111.75(c)(1), and for why any component and in-process testing, examination, or monitoring, or other methods will ensure that such exempted product specification is met without verification through periodic testing of the finished batch;

(f) Ensuring that required representative samples are collected;

(g) Ensuring that required reserve samples are collected and held;

(h) Determining whether all specifications established under §111.70(a) are met; and

(i) Performing other operations required under this subpart.

§111.110 What quality control operations are required for laboratory operations associated with the production and process control system?

Quality control operations for laboratory operations associated with the production and process control system must include:

(a) Reviewing and approving all laboratory control processes associated with the production and process control system;

(b) Ensuring that all tests and examinations required under §111.75 are conducted; and

(c) Reviewing and approving the results of all tests and examinations required under §111.75.

§111.113 What quality control operations are required for a material review and disposition decision?

(a) Quality control personnel must conduct a material review and make a disposition decision if:

(1) A specification established in accordance with §111.70 is not met;

(2) A batch deviates from the master manufacturing record, including when any step established in the master manufacturing record is not completed and including any deviation from specifications;

(3) There is any unanticipated occurrence during the manufacturing operations that adulterates or may lead to adulteration of the component, dietary supplement, or packaging, or could lead to the use of a label not specified in the master manufacturing record;

(4) Calibration of an instrument or control suggests a problem that may have resulted in a failure to ensure the quality of a batch or batches of a dietary ingredient or dietary supplement; or

(5) A dietary ingredient or dietary supplement is returned.

(b)(1) When there is a deviation or unanticipated occurrence during the production and in-process control system that results in or could lead to adulteration of a component, dietary supplement, or packaging, or could lead to the use of a label not specified in the master manufacturing record, quality control personnel must reject the component, dietary supplement, packaging, or label unless it approves a treatment, an in-process adjustment, or reprocessing to correct the applicable deviation or occurrence.

(2) When a specification established in accordance with §111.70 is not met, quality control personnel must reject the component, dietary supplement, package or label, unless quality control personnel approve a treatment, an in-process adjustment, or reprocessing, as permitted in §111.77.

(c) The person who conducts a material review and makes the disposition decision must, at the time of performance, document that material review and disposition decision.

§111.117 What quality control operations are required for equipment, instruments, and controls?

Quality control operations for equipment, instruments, and controls must include:

(a) Reviewing and approving all processes for calibrating instruments and controls;

(b) Periodically reviewing all records for calibration of instruments and controls;

(c) Periodically reviewing all records for calibrations, inspections, and checks of automated, mechanical, or electronic equipment; and

(d) Reviewing and approving controls to ensure that automated, mechanical, or electronic equipment functions in accordance with its intended use.

§111.120 What quality control operations are required for components, packaging, and labels before use in the manufacture of a dietary ingredient or dietary supplement?

Quality control operations for components, packaging, and labels before use in the manufacture of a dietary ingredient or dietary supplement must include:

(a) Reviewing all receiving records for components, packaging, and labels;

(b) Determining whether all components, packaging, and labels conform to specifications established under §111.70 (b) and (d);

(c) Conducting any required material review and making any required disposition decision;

(d) Approving or rejecting any treatment and in-process adjustments of components, packaging, or labels to make them suitable for use in the manufacture of a dietary ingredient or dietary supplement; and

(e) Approving, and releasing from quarantine, all components, packaging, and labels before they are used.

§111.123 What quality control operations are required for the master manufacturing record, the batch production record, and manufacturing operations?

(a) Quality control operations for the master manufacturing record, the batch production record, and manufacturing operations must include:

(1) Reviewing and approving all master manufacturing records and all modifications to the master manufacturing records;

(2) Reviewing and approving all batch production-related records;

(3) Reviewing all monitoring required under subpart E;

(4) Conducting any required material review and making any required disposition decision;

(5) Approving or rejecting any reprocessing;

(6) Determining whether all in-process specifications established in accordance with §111.70(c) are met;

(7) Determining whether each finished batch conforms to product specifications established in accordance with §111.70(e); and

(8) Approving and releasing, or rejecting, each finished batch for distribution, including any reprocessed finished batch.

(b) Quality control personnel must not approve and release for distribution:

(1) Any batch of dietary ingredient or dietary supplement for which any component in the batch does not meet its identity specification;

(2) Any batch of dietary ingredient or dietary supplement, including any reprocessed batch, that does not meet all product specifications established in accordance with §111.70(e);

(3) Any batch of dietary ingredient or dietary supplement, including any reprocessed batch, that has not been manufactured, packaged, labeled, and held under conditions to prevent adulteration under section 402(a)(1), (a)(2), (a)(3), and (a)(4) of the act; and

(4) Any product received from a supplier for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier) for which sufficient assurance is not provided to adequately identify the product and to determine that the product is consistent with your purchase order.

§111.127 What quality control operations are required for packaging and labeling operations?

Quality control operations for packaging and labeling operations must include:

(a) Reviewing the results of any visual examination and documentation to ensure that specifications established under §111.70(f) are met for all products that you receive for packaging and labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier);

(b) Approving, and releasing from quarantine, all products that you receive for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier) before they are used for packaging or labeling;

(c) Reviewing and approving all records for packaging and label operations;

(d) Determining whether the finished packaged and labeled dietary ingredient or dietary supplement conforms to specifications established in accordance with §111.70(g);

(e) Conducting any required material review and making any required disposition decision;

(f) Approving or rejecting any repackaging of a packaged dietary ingredient or dietary supplement;

(g) Approving or rejecting any relabeling of a packaged and labeled dietary ingredient or dietary supplement; and

(h) Approving for release, or rejecting, any packaged and labeled dietary ingredient or dietary supplement (including a repackaged or relabeled dietary ingredient or dietary supplement) for distribution.

§111.130 What quality control operations are required for returned dietary ingredients or dietary supplements?

Quality control operations for returned dietary ingredients or dietary supplements must include:

(a) Conducting any required material review and making any required disposition decision; including:

(1) Determining whether tests or examination are necessary to determine compliance with product specifications established in accordance with §111.70(e); and

(2) Reviewing the results of any tests or examinations that are conducted to determine compliance with product specifications established in accordance with §111.70(e);

(b) Approving or rejecting any salvage and redistribution of any returned dietary ingredient or dietary supplement;

(c) Approving or rejecting any reprocessing of any returned dietary ingredient or dietary supplement; and

(d) Determining whether the reprocessed dietary ingredient or dietary supplement meets product specifications and either approving for release, or rejecting, any returned dietary ingredient or dietary supplement that is reprocessed.

§111.135 What quality control operations are required for product complaints?

Quality control operations for product complaints must include reviewing and approving decisions about whether to investigate a product complaint and reviewing and approving the findings and followup action of any investigation performed.

§111.140 Under this subpart F, what records must you make and keep?

(a) You must make and keep the records required under this subpart F in accordance with subpart P of this part.

(b) You must make and keep the following records:

(1) Written procedures for the responsibilities of the quality control operations, including written procedures for conducting a material review and making a disposition decision and written procedures for approving or rejecting any reprocessing;

(2) Written documentation, at the time of performance, that quality control personnel performed the review, approval, or rejection requirements by recording the following:

(i) Date that the review, approval, or rejection was performed; and

(ii) Signature of the person performing the review, approval, or rejection; and

(3) Documentation of any material review and disposition decision and followup. Such documentation must be included in the appropriate batch production record and must include:

(i) Identification of the specific deviation or the unanticipated occurrence;

(ii) Description of your investigation into the cause of the deviation from the specification or the unanticipated occurrence;

(iii) Evaluation of whether or not the deviation or unanticipated occurrence has resulted in or could lead to a failure to ensure the quality of the dietary ingredient or dietary supplement or a failure to package and label the dietary ingredient or dietary supplement as specified in the master manufacturing record;

(iv) Identification of the action(s) taken to correct, and prevent a recurrence of, the deviation or the unanticipated occurrence;

(v) Explanation of what you did with the component, dietary supplement, packaging, or label;

(vi) A scientifically valid reason for any reprocessing of a dietary ingredient or dietary supplement that is rejected or any treatment or in-process adjustment of a component that is rejected; and

(vii) The signature of the individual(s) designated to perform the quality control operation, who conducted the material review and made the disposition decision, and of each qualified individual who provides information relevant to that material review and disposition decision.

Subpart G—Production and Process Control System: Requirements for Components, Packaging, and Labels and for Product That You Receive for Packaging or Labeling as a Dietary Ingredient or Dietary Supplement

§111.153 What are the requirements under this subpart G for written procedures?

You must establish and follow written procedures for fulfilling the requirements of this subpart G.

§111.155 What requirements apply to components of dietary ingredients or dietary supplements?

(a) You must visually examine each immediate container or grouping of immediate containers in a shipment that you receive for appropriate content label, container damage, or broken seals to determine whether the container condition may have resulted in contamination or deterioration of the components;

(b) You must visually examine the supplier's invoice, guarantee, or certification in a shipment you receive to ensure the components are consistent with your purchase order;

(c) You must quarantine components before you use them in the manufacture of a dietary ingredient or dietary supplement until:

(1) You collect representative samples of each unique lot of components (and, for components that you receive, of each unique shipment, and of each unique lot within each unique shipment);

(2) Quality control personnel review and approve the results of any tests or examinations conducted on components; and

(3) Quality control personnel approve the components for use in the manufacture of a dietary ingredient or dietary supplement, including approval of any treatment (including in-process adjustments) of components to make them suitable for use in the manufacture of a dietary ingredient or dietary supplement, and releases them from quarantine.

(d)(1) You must identify each unique lot within each unique shipment of components that you receive and any lot of components that you produce in a manner that allows you to trace the lot to the supplier, the date received, the name of the component, the status of the component (e.g., quarantined, approved, or rejected); and to the dietary ingredient or dietary supplement that you manufactured and distributed.

(2) You must use this unique identifier whenever you record the disposition of each unique lot within each unique shipment of components that you receive and any lot of components that you produce.

(e) You must hold components under conditions that will protect against contamination and deterioration, and avoid mixups.

§111.160 What requirements apply to packaging and labels received?

(a) You must visually examine each immediate container or grouping of immediate containers in a shipment for appropriate content label, container damage, or broken seals to determine whether the container condition may have resulted in contamination or deterioration of the packaging and labels.

(b) You must visually examine the supplier's invoice, guarantee, or certification in a shipment to ensure that the packaging or labels are consistent with your purchase order.

(c) You must quarantine packaging and labels before you use them in the manufacture of a dietary ingredient or dietary supplement until:

(1) You collect representative samples of each unique shipment, and of each unique lot within each unique shipment, of packaging and labels and, at a minimum, conduct a visual identification of the immediate containers and closures;

(2) Quality control personnel review and approve the results of any tests or examinations conducted on the packaging and labels; and

(3) Quality control personnel approve the packaging and labels for use in the manufacture of a dietary ingredient or dietary supplement and release them from quarantine.

(d)(1) You must identify each unique lot within each unique shipment of packaging and labels in a manner that allows you to trace the lot to the supplier, the date received, the name of the packaging and label, the status of the packaging and label (e.g., quarantined, approved, or rejected); and to the dietary ingredient or dietary supplement that you distributed; and

(2) You must use this unique identifier whenever you record the disposition of each unique lot within each unique shipment of packaging and labels.

(e) You must hold packaging and labels under conditions that will protect against contamination and deterioration, and avoid mixups.

§111.165 What requirements apply to a product received for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier)?

(a) You must visually examine each immediate container or grouping of immediate containers in a shipment of product that you receive for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier) for appropriate content label, container damage, or broken seals to determine whether the container condition may have resulted in contamination or deterioration of the received product.

(b) You must visually examine the supplier's invoice, guarantee, or certification in a shipment of the received product to ensure that the received product is consistent with your purchase order.

(c) You must quarantine the received product until:

(1) You collect representative samples of each unique shipment, and of each unique lot within each unique shipment, of received product;

(2) Quality control personnel review and approve the documentation to determine whether the received product meets the specifications that you established under §111.70(f); and

(3) Quality control personnel approve the received product for packaging or labeling as a dietary ingredient or dietary supplement and release the received product from quarantine.

(d)(1) You must identify each unique lot within each unique shipment of received product in a manner that allows you to trace the lot to the supplier, the date received, the name of the received product, the status of the received product (e.g., quarantined, approved, or rejected), and to the product that you packaged or labeled and distributed as a dietary ingredient or dietary supplement.

(2) You must use this unique identifier whenever you record the disposition of each unique lot within each unique shipment of the received product.

(e) You must hold the received product under conditions that will protect against contamination and deterioration, and avoid mixups.

§111.170 What requirements apply to rejected components, packaging, and labels, and to rejected products that are received for packaging or labeling as a dietary ingredient or dietary supplement?

You must clearly identify, hold, and control under a quarantine system for appropriate disposition any component, packaging, and label, and any product that you receive for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier), that is rejected and unsuitable for use in manufacturing, packaging, or labeling operations.

§111.180 Under this subpart G, what records must you make and keep?

(a) You must make and keep records required under this subpart G in accordance with subpart P of this part.

(b) You must make and keep the following records:

(1) Written procedures for fulfilling the requirements of this subpart.

(2) Receiving records (including records such as certificates of analysis, suppliers' invoices, and suppliers' guarantees) for components, packaging, and labels and for products that you receive for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier); and

(3) Documentation that the requirements of this subpart were met.

(i) The person who performs the required operation must document, at the time of performance, that the required operation was performed.

(ii) The documentation must include:

(A) The date that the components, packaging, labels, or products that you receive for packaging or labeling as a dietary ingredient or dietary supplement were received;

(B) The initials of the person performing the required operation;

(C) The results of any tests or examinations conducted on components, packaging, or labels, and of any visual examination of product that you receive for packaging or labeling as a dietary ingredient or dietary supplement; and

(D) Any material review and disposition decision conducted on components, packaging, labels, or products that you receive for packaging or labeling as a dietary ingredient or dietary supplement.

Subpart H—Production and Process Control System: Requirements for the Master Manufacturing Record

§111.205 What is the requirement to establish a master manufacturing record?

(a) You must prepare and follow a written master manufacturing record for each unique formulation of dietary ingredient or dietary supplement that you manufacture, and for each batch size, to ensure uniformity in the finished batch from batch to batch.

(b) The master manufacturing record must:

(1) Identify specifications for the points, steps, or stages in the manufacturing process where control is necessary to ensure the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record; and

(2) Establish controls and procedures to ensure that each batch of dietary ingredient or dietary supplement that you manufacture meets the specifications identified in accordance with paragraph (b)(1) of this section.

(c) You must make and keep master manufacturing records in accordance with subpart P of this part.

§111.210 What must the master manufacturing record include?

The master manufacturing record must include:

(a) The name of the dietary ingredient or dietary supplement to be manufactured and the strength, concentration, weight, or measure of each ingredient (in the case of dietary ingredients) or dietary ingredient (in the case of dietary supplements) for each batch size;

(b) A complete list of components to be used;

(c) An accurate statement of the weight or measure of each component to be used;

(d) For dietary supplements, ~~T~~the identity and weight or measure of each dietary ingredient that will be declared on the Supplement Facts label and the identity of each ingredient that will be declared on the ingredients list of the dietary supplement. For dietary ingredients, the identity and weight or measure of each component;

(e) A statement of any intentional overage amount of an ingredient (in the case of dietary ingredients) or dietary ingredient (in the case of dietary supplements);

(f) 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 ensure the quality of the dietary ingredient or dietary supplement, 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 necessary and material review is conducted and disposition decision is made;

(g) A description of packaging and a representative label, or a cross-reference to the physical location of the actual or representative label;

(h) Written instructions, including the following:

(1) Specifications for each point, step, or stage in the manufacturing process where control is necessary to ensure the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record;

(2) Procedures for sampling and a cross-reference to procedures for tests or examinations;

(3) Specific actions necessary to perform and verify points, steps, or stages in the manufacturing process where control is necessary to ensure the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record.

(i) Such specific actions must include verifying the weight or measure of any component and verifying the addition of any component; and

(ii) For manual operations, such specific actions must include:

(A) One person weighing or measuring a component and another person verifying the weight or measure; and

(B) One person adding the component and another person verifying the addition.

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

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

Subpart I—Production and Process Control System: Requirements for the Batch Production Record

§111.255 What is the requirement to establish 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;

(b) Your batch production record must include complete information relating to the production and control of each batch;

(c) Your batch production record must accurately follow the appropriate master manufacturing record and you must perform each step in the production of the batch; and

(d) You must make and keep batch production records in accordance with subpart P of this part.

§111.260 What must the batch record include?

The batch production record must include the following:

(a) The batch, lot, or control number:

(1) Of the finished batch of dietary ingredient or dietary supplement; and

(2) That you assign in accordance with §111.415(f) for the following:

(i) Each lot of packaged and labeled dietary ingredient or dietary supplement from the finished batch of dietary ingredient or dietary supplement;

(ii) Each lot of dietary ingredient or dietary supplement, from the finished batch of dietary ingredient or dietary supplement, that you distribute to another person for packaging or labeling;

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

(c) The date and time of the maintenance, cleaning, and sanitizing of the equipment and processing lines used in producing the batch, or a cross-reference to records, such as individual equipment logs, where this information is retained;

(d) The unique identifier that you assigned to each component (or, when applicable, to a product that you receive from a supplier for packaging or labeling as a dietary ingredient or dietary supplement), packaging, and label used;

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

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

(g) The actual results obtained during any monitoring operation;

(h) The results of any testing or examination performed during the batch production, or a cross-reference to such results;

(i) Documentation that the finished dietary ingredient or dietary supplement meets specifications established in accordance with §111.70(e) and (g);

(j) Documentation, at the time of performance, of the manufacture of the batch, including:

(1) The date on which each step of the master manufacturing record was performed; and

(2) The initials of the persons performing each step, including:

(i) The initials of the person responsible for weighing or measuring each component used in the batch;

(ii) The initials of the person responsible for verifying the weight or measure of each component used in the batch;

(iii) The initials of the person responsible for adding the component to the batch; and

(iv) The initials of the person responsible for verifying the addition of components to the batch;

(k) Documentation, at the time of performance, of packaging and labeling operations, including:

(1) The unique identifier that you assigned to packaging and labels used, the quantity of the packaging and labels used, and, when label reconciliation is required, reconciliation of any discrepancies between issuance and use of labels;

(2) An actual or representative label, or a cross-reference to the physical location of the actual or representative label specified in the master manufacturing record; and

(3) The results of any tests or examinations conducted on packaged and labeled dietary ingredient or dietary supplements (including repackaged or relabeled dietary ingredients or dietary supplements), or a cross-reference to the physical location of such results;

(l) Documentation at the time of performance that quality control personnel:

(1) Reviewed the batch production record, including:

(i) Review of any monitoring operation required under subpart E of this part; and

(ii) Review of the results of any tests and examinations, including tests and examinations conducted on components, in-process materials, finished batches of dietary ingredients or dietary supplements, and packaged and labeled dietary ingredients or dietary supplements;

(2) Approved or rejected any reprocessing or repackaging; and

(3) Approved and released, or rejected, the batch for distribution, including any reprocessed batch; and

(4) Approved and released, or rejected, the packaged and labeled dietary ingredient or dietary supplement, including any repackaged or relabeled dietary ingredient or dietary supplement.

(m) Documentation at the time of performance of any required material review and disposition decision.

(n) Documentation at the time of performance of any reprocessing.

Subpart J—Production and Process Control System: Requirements for Laboratory Operations

§111.303 What are the requirements under this subpart J for written procedures?

You must establish and follow written procedures for laboratory operations, including written procedures for the tests and examinations that you conduct to determine whether specifications are met.

§111.310 What are the requirements for the laboratory facilities that you use?

You must use adequate laboratory facilities to perform whatever testing and examinations are necessary to determine whether:

(a) Components that you use meet specifications;

(b) In-process specifications are met as specified in the master manufacturing record; and

(c) Dietary ingredients or ~~D~~dietary supplements that you manufacture meet specifications.

§111.315 What are the requirements for laboratory control processes?

You must establish and follow laboratory control processes that are reviewed and approved by quality control personnel, including the following:

(a) Use of criteria for establishing appropriate specifications;

(b) Use of sampling plans for obtaining representative samples, in accordance with subpart E of this part, of:

(1) Components, packaging, and labels;

(2) In-process materials;

(3) Finished batches of dietary ingredients or dietary supplements;

(4) Product that you receive for packaging or labeling as a dietary ingredient or dietary supplement (and for distribution rather than for return to the supplier); and

(5) Packaged and labeled dietary ingredients or dietary supplements.

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

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

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

§111.320 What requirements apply to laboratory methods for testing and examination?

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

(b) You must identify and use an appropriate scientifically valid method for each established specification for which testing or examination is required to determine whether the specification is met.

§111.325 Under this subpart J, what records must you make and keep?

(a) You must make and keep records required under this subpart J in accordance with subpart P of this part.

(b) You must make and keep the following records:

(1) Written procedures for laboratory operations, including written procedures for the tests and examinations that you conduct to determine whether specifications are met;

(2) Documentation that laboratory methodology established in accordance with this subpart J is followed.

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

(ii) The documentation for laboratory tests and examinations must include the results of the testing and examination.

Subpart K—Production and Process Control System: Requirements for Manufacturing Operations

§111.353 What are the requirements under this subpart K for written procedures?

You must establish and follow written procedures for manufacturing operations.

§111.355 What are the design requirements for manufacturing operations?

You must design or select manufacturing processes to ensure that product specifications are consistently met.

§111.360 What are the requirements for sanitation?

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

§111.365 What precautions must you take to prevent contamination?

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:

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

(b) Washing or cleaning components that contain soil or other contaminants;

(c) Using water that, at a minimum, complies with the applicable Federal, State, and local requirements and does not contaminate the dietary ingredient or dietary supplement when the water may become a component of the finished batch of dietary ingredient or dietary supplement;

(d) Performing chemical, microbiological, or other testing, as necessary to prevent the use of contaminated components;

(e) 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;

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

(g) Identifying and holding any components or dietary supplements, for which a material review and disposition decision is required, in a manner that protects components or dietary supplements that are not under a material review against contamination and mixups with those that are under a material review;

(h) 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, by, for example:

(1) Cleaning and sanitizing contact surfaces;

(2) Using temperature controls; and

(3) Using time controls.

(i) Using effective measures to protect against the inclusion of metal or other foreign material in components or dietary supplements, by, for example:

(1) Filters or strainers,

(2) Traps,

(3) Magnets, or

(4) Electronic metal detectors.

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

(k) 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.

§111.370 What requirements apply to rejected dietary ingredients or dietary supplements?

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

§111.375 Under this subpart K, what records must you make and keep?

(a) You must make and keep records required under this subpart K in accordance with subpart P of this part.

(b) You must make and keep records of the written procedures for manufacturing operations.

Subpart L—Production and Process Control System: Requirements for Packaging and Labeling Operations

§111.403 What are the requirements under this subpart L for written procedures?

You must establish and follow written procedures for packaging and labeling operations.

§111.410 What requirements apply to packaging and labels?

(a) You must take necessary actions to determine whether packaging for dietary ingredients or dietary supplements meets specifications so that the condition of the packaging will ensure the quality of your dietary ingredients or dietary supplements;

(b) You must control the issuance and use of packaging and labels and reconciliation of any issuance and use discrepancies. Label reconciliation is not required for cut or rolled labels if a 100-percent examination for correct labels is performed by appropriate electronic or electromechanical equipment during or after completion of finishing operations; and

(c) You must examine, before packaging and labeling operations, packaging and labels for each batch of dietary ingredient or dietary supplement to determine whether the packaging and labels conform to the master manufacturing record; and

(d) You must be able to determine the complete manufacturing history and control of the packaged and labeled dietary ingredient or dietary supplement through distribution.

§111.415 What requirements apply to filling, assembling, packaging, labeling, and related operations?

You must fill, assemble, package, label, and perform other related operations in a way that ensures the quality of the dietary ingredient or dietary supplement and that the dietary ingredient or dietary supplement is packaged and labeled as specified in the master manufacturing record. You must do this using any effective means, including the following:

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

(b) Protecting manufactured dietary ingredients or dietary supplements from contamination, particularly airborne contamination;

(c) Using sanitary handling procedures;

(d) Establishing physical or spatial separation of packaging and label operations from operations on other components and dietary supplements to prevent mixups;

(e) 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;

(f) Assigning a batch, lot, or control number to:

(1) Each lot of packaged and labeled dietary ingredient or dietary supplement from a finished batch of dietary ingredient or dietary supplement; and,

(2) Each lot of dietary ingredient or dietary supplement, from a finished batch of dietary ingredient or dietary supplement, that you distribute to another person for packaging or labeling.

(g) Examining a representative sample of each batch of the packaged and labeled dietary ingredient or dietary supplement to determine whether the dietary ingredient or dietary supplement meets specifications established in accordance with §111.70(g); and

(h) Suitably disposing of labels and 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.

§111.420 What requirements apply to repackaging and relabeling?

(a) You may repackage or relabel dietary ingredients or dietary supplements only after quality control personnel have approved such repackaging or relabeling.

(b) You must examine a representative sample of each batch of repackaged or relabeled dietary ingredients or dietary supplements to determine whether the repackaged or relabeled dietary ingredients or dietary supplements meet all specifications established in accordance with §111.70(g).

(c) Quality control personnel must approve or reject each batch of repackaged or relabeled dietary ingredient or dietary supplement prior to its release for distribution.

§111.425 What requirements apply to a packaged and labeled dietary ingredient or dietary supplement that is rejected for distribution?

You must clearly identify, hold, and control under a quarantine system for appropriate disposition any packaged and labeled dietary ingredient or dietary supplement that is rejected for distribution.

§111.430 Under this subpart L, what records must you make and keep?

(a) You must make and keep records required under this subpart L in accordance with subpart P of this part.

(b) You must make and keep records of the written procedures for packaging and labeling operations.

Subpart M—Holding and Distributing

§111.453 What are the requirements under this subpart for M written procedures?

You must establish and follow written procedures for holding and distributing operations.

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

(a) You must hold components and dietary supplements under appropriate conditions of temperature, humidity, and light so that the identity, purity, strength, and composition of the components and dietary supplements are not affected.

(b) You must hold packaging and labels under appropriate conditions so that the packaging and labels are not adversely affected.

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

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

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

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

§111.465 What requirements apply to holding reserve samples of dietary ingredients or dietary supplements?

(a) You must hold reserve samples of dietary ingredients or dietary supplements in a manner that protects against contamination and deterioration. This includes:

(1) Holding the reserve samples under conditions consistent with product labels or, if no storage conditions are recommended on the label, under ordinary storage conditions; and

(2) Using the same container-closure system in which the packaged and labeled dietary ingredient or dietary supplement is distributed, or if distributing dietary ingredients or dietary supplements to be packaged and labeled, using a container-closure system that provides essentially the same characteristics to protect against contamination or deterioration as the one in which you distribute the dietary ingredient or dietary supplement for packaging and labeling elsewhere.

(b) You must retain reserve samples for 1 year past the shelf life date (if shelf life dating is used), or for 2 years from the date of distribution of the last batch of dietary supplements associated with the reserve samples, for use in appropriate investigations.

§111.470 What requirements apply to distributing dietary ingredients and dietary supplements?

You must distribute dietary ingredients or dietary supplements under conditions that will protect the dietary ingredients or dietary supplements against contamination and deterioration.

§111.475 Under this subpart M, what records must you make and keep?

(a) You must make and keep records required under this subpart M in accordance with subpart P of this part.

(b) You must make and keep the following records:

(1) Written procedures for holding and distributing operations; and

(2) Records of product distribution.

Subpart N—Returned Dietary Ingredients or Dietary Supplements

§111.503 What are the requirements under this subpart N for written procedures?

You must establish and follow written procedures to fulfill the requirements of this subpart.

§111.510 What requirements apply when a returned dietary ingredient or dietary supplement is received?

You must identify and quarantine returned dietary ingredients or dietary supplements until quality control personnel conduct a material review and make a disposition decision.

§111.515 When must a returned dietary ingredient or dietary supplement be destroyed, or otherwise suitably disposed of?

You must destroy, or otherwise suitably dispose of, any returned dietary ingredient or dietary supplement unless the outcome of a material review and disposition decision is that quality control personnel do the following:

(a) Approve the salvage of the returned dietary ingredient or dietary supplement for redistribution or

(b) Approve the returned dietary ingredient or dietary supplement for reprocessing.

§111.520 When may a returned dietary ingredient or dietary supplement be salvaged?

You may salvage a returned dietary ingredient or dietary supplement only if quality control personnel conduct a material review and make a disposition decision to allow the salvage.

§111.525 What requirements apply to a returned dietary ingredient or dietary supplement that quality control personnel approve for reprocessing?

(a) You must ensure that any returned dietary ingredient or dietary supplements that are reprocessed meet all product specifications established in accordance with §111.70(e); and

(b) Quality control personnel must approve or reject the release for distribution of any returned dietary ingredient or dietary supplement that is reprocessed.

§111.530 When must an investigation be conducted of your manufacturing processes and other batches?

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

§111.535 Under this subpart N, what records must you make and keep?

(a) You must make and keep records required under this subpart N in accordance with subpart P of this part.

(b) You must make and keep the following records:

(1) Written procedures for fulfilling the requirements of this subpart N.

(2) Any material review and disposition decision on a returned dietary ingredient or dietary supplement;

(3) The results of any testing or examination conducted to determine compliance with product specifications established under §111.70(e); and,

(4) Documentation of the reevaluation by quality control personnel of any dietary ingredient or dietary supplement that is reprocessed and the determination by quality control personnel of whether the reprocessed dietary ingredient or dietary supplement meets product specifications established in accordance with §111.70(e).

Subpart O—Product Complaints

§111.553 What are the requirements under this subpart O for written procedures?

You must establish and follow written procedures to fulfill the requirements of this subpart O.

§111.560 What requirements apply to the review and investigation of a product complaint?

(a) A qualified person must:

(1) Review all product complaints to determine whether the product 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 111, including those specifications and other requirements that, if not met, may result in a risk of illness or injury; and

(2) Investigate any product complaint that 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 risk of illness or injury.

(b) Quality control personnel must review and approve decisions about whether to investigate a product complaint and review and approve the findings and followup action of any investigation performed.

(c) The review and investigation of the product complaint by a qualified person, and the review by quality control personnel about whether to investigate a product complaint, and the findings and followup action of any investigation performed, must extend to all relevant batches and records.

§111.570 Under this subpart O, what records must you make and keep?

(a) You must make and keep the records required under this subpart O in accordance with subpart P of this part.

(b) You must make and keep the following records:

(1) Written procedures for fulfilling the requirements of this subpart,

(2) A written record of every product complaint that is related to good manufacturing practice,

(i) The person who performs the requirements of this subpart must document, at the time of performance, that the requirement was performed.

(ii) The written record of the product complaint must include the following:

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

(B) The batch, lot, or control number of the dietary ingredient or dietary supplement, if available;

(C) The date the complaint was received and the name, address, or telephone number of the complainant, if available;

(D) The nature of the complaint including, if known, how the product was used;

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

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

Subpart P—Records and Recordkeeping

§111.605 What requirements apply to the records that you make and keep?

(a) You must keep written records required by this part for 1 year past the shelf life date, if shelf life dating is used, or 2 years beyond the date of distribution of the last batch of dietary ingredient or dietary supplements associated with those records.

(b) Records 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.

(c) All electronic records must comply with part 11 of this chapter.

§111.610 What records must be made available to FDA?

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

(b) If you use reduction techniques, such as microfilming, you must make suitable reader and photocopying equipment readily available to FDA.