



*Producers of Quality
Nonprescription Medicines and
Dietary Supplements for Self-Care*

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

Formerly Nonprescription Drug Manufacturers Association

August 20, 1999

Docket Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. 99N-1174: Stakeholder Input on CFSAN's
Overall Strategic Plan for Dietary Supplements:

CHPA's Second Set of Comments Re: the June 8th Meeting and
May 13th Federal Register Announcement: **Operational Issues**

Dear Madam or Sir:

The Consumer Healthcare Products Association (CHPA) submits these comments as part of its detailed oral and written comments provided at the June 8, 1999, Stakeholders Meeting in response to FDA's May 13th call for comments in the Federal Register, and in follow-up to the June 30, 1999, meeting between CHPA and CFSAN on a variety of operational issues.

Founded in 1881, CHPA represents producers of quality nonprescription medicines and dietary supplements, including over 200 member companies across the manufacturing, distribution, supply and service sectors of the self-care industry.

Executive Summary

1. In setting its priorities for program activities, CFSAN should place safety first – enforcement, GMPs and AERs. The refinement of the infrastructure of the Office of Special Nutritionals and other components of CFSAN should be part of this safety priority and be accomplished through creation of an overall strategic plan. (See Attachment A and page 3.)

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- a. As part of an overall strategy for dietary supplements, the complementary relationship between FDA and FTC should be reviewed and strengthened. A public workshop for all stakeholders on this matter would be helpful to understand the current relationship between FDA and FTC and provide input on ways to further develop that relationship.
 - b. CHPA recommends that FDA place publication of ANPR for GMPs as a top priority in 1999 and consider the additional specific comments CHPA has developed and appended to these comments in developing the NPR on dietary supplement GMPs (see Attachment B).
 - c. CHPA recommends that CFSAN develop a written plan for and adopt a systems approach to AER management.
 - d. CHPA recommends a re-proposal of the structure/function proposed rule as a focused regulatory statement that closely incorporates the specific intent of DSHEA, appropriately amends FDA's proposed re-definition of disease per CHPA's comments to FDA on August 4, 1999, and omits the proposed confusing and ambiguous proposed criteria. (See Attachment C.)
 - e. CHPA recommends that CFSAN define in its overall strategic plan and its human and fiscal resource needs to accomplish the plan, either directly or through a gap analysis.
2. CHPA also recommends development of specific enhancements to CFSAN's infrastructure that would optimize its operational interaction with external constituencies, including:
- A systems approach to AER management;
 - A public calendar of planned activities and events;
 - A better advance notification policy and procedure;
 - A policy and procedure for meetings with external constituencies (see also Attachment D);
 - Continued partnership in meetings;
 - Continued use of the working group format of the Foods Advisory Committee to address dietary supplement issues.

These recommendations are outlined below in detail.

Detailed Comments

CHPA's detailed comments are organized according to the following outline:

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I. Overview of CHPA's June 8th Comments on CFSAN's Development of an Overall Strategic Plan for Dietary Supplements

A. Introduction

Pursuant to FDA's published call for comments on CFSAN's 1999 Program Priority Activity for developing an overall strategic plan for dietary supplements, CHPA submitted detailed comments to the Docket and made detailed oral comments at the June 8th stakeholders meeting. CHPA also met with CFSAN on June 30th to discuss a variety of operational aspects of CFSAN's interaction with its external constituencies. These comments provide a framing overview of the

industry's June 8th comments and a written summary of recommendations made at the June 30th meeting.

B. Overview

- **Priorities:** In setting its priorities for program activities, CFSAN should place safety first – enforcement, GMPs and AERs. The refinement of the infrastructure of the Office of Special Nutritionals and other components of CFSAN should be part of this safety priority and be accomplished through creation of an overall strategic plan. While activity on issues pertaining to claims might proceed as priority is given to safety issues, its completion should be targeted further in the future than that for resolving the safety and operational issues.

- **Safety First**
 - **Enforcement:** In passing DSHEA, Congress intended that consumers would use dietary supplements for health promotion, health maintenance and disease risk reduction (i.e., health claims). Consumer confidence is essential to product use. Allegations that the dietary supplement industry is “unregulated” or that FDA is not using its statutory authority to act can undermine consumer confidence. Therefore, foundational to CFSAN’s overall strategy for dietary supplements is an effective enforcement policy that removes unsafe products from the marketplace and ensures truthful, not misleading, and substantiated claims on dietary supplements. As part of an overall strategy for dietary supplements, therefore, the complementary relationship between FDA and FTC should be reviewed and strengthened.

A public workshop for all stakeholders on this matter would be helpful to understand the current relationship between FDA and FTC and provide

input on ways to further develop that relationship.

- **Good Manufacturing Practices:** CHPA recommends that FDA place publication of ANPR for GMPs as a top priority in 1999 and consider the additional specific comments that CHPA has developed and appended to these comments in developing the NPR on dietary supplement GMPs (Attachment B).

Special *FDA-adopted* GMPs for dietary supplements are important for the following reasons: a) differing needs of dietary supplements vs. foods, specifically related to manufacturing processes, laboratory controls and QC/QA specifications, and b) there are at least three sets of GMPs now in use for dietary supplements, specifically, the food GMPs, the dietary supplement industry-proposed GMPs and GMPs used under the voluntary program of the National Nutritional Foods Association. *FDA-adopted* dietary supplement GMPs would lead to uniformity in how manufacturing processes are evaluated, and would raise the level of awareness among suppliers, manufacturers and distributors regarding the need for quality operations.

- **Adverse Experience Reporting:** Public discussion on putative safety issues relating to dietary supplements should appropriately focus on the science, not the quality of administrative methods used to document AERs. Therefore, as stated in its May 27, 1999 comments to the House Committee on Government Reform, CHPA recommends that CSFAN:
 - Create a written plan for and adopt a systems approach to AER management;
 - Create written protocols and keep them updated, including detailed decision tree for filtering AERs;
 - Create policy and procedures for timely sharing of serious AERs with affected companies;

- Establish specific CFSAN training manuals and procedures for quality collection, analysis and reporting of AERs;
 - Review the core competency of the personnel who would operate different facets of an adequate AER system on dietary supplements;
 - Re-engineer the public access to AER reports for dietary supplements;
 - Ensure public input in the development of policies and procedures be used in CFSAN's systems approach to AER management.
- **Claims:** CHPA recommends the following as part of CFSAN's development of an overall strategy on dietary supplements:
- Re-proposal of the structure/function proposed rule as a focused regulatory statement that closely incorporates the specific intent of DSHEA, appropriately amends FDA's proposed re-definition of disease per CHPA's comments to FDA on August 4, 1999, and omits the confusing and ambiguous proposed criteria;

Specifically, as outlined in Attachment C (CHPA's comments on August 4, 1999), CHPA pointed out to CFSAN that the definitions of disease in 101.14 (re: NLEA) and in the proposed structure/function rule are overly broad, demonstrating that there is likely no "bright line" as FDA hopes to find. Therefore, CHPA recommends a definition of disease that encompasses both the adverse nature of disease, on one hand, and the concept of "natural state or process," on the other, in order to better focus the issue of defining structure/function claims within the disease definition itself.

CHPA's Proposed Definition of Disease: "... a disease is any adverse deviation from, or impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms, ~~including laboratory or clinical measurements~~ that are not characteristic of a ~~disease~~ natural state or

process.”

(Note: underlined portions are additions and strikeouts are deletions from FDA’s proposed definition of disease.)

“Any deviation” is too broad; “any **adverse** deviation” appropriately defines the nature of the deviation; “laboratory or clinical measurements” are redundant and included under the concept of “signs”, and “not characteristic of a natural state or process” appropriately encompasses Congress’ intent to allow health promotion/maintenance claims. CHPA also recommends natural state or process be defined by regulation, as follows:

“A natural state or process is a life change or physiologic manifestation expected in the normal course of life progression.”

- Development of an overall guidance on statements of nutritional support (structure/function) claims for dietary supplements, consistent with DSHEA and including and modeled after the FTC advertising guidance to industry.

- **CFSAN’s 3-to-5 Year Strategic Plan and Resources:** CFSAN’s development of an overall strategy for dietary supplements should be undertaken as a 3-to-5 year plan and/or gaps analysis, which is typically viewed as a “living” document that appropriately evolves dependent on the changing climate. As part of such a strategic plan, CFSAN should define its human and fiscal resource needs, including expanded use of outside contractors (e.g., for AER management). As stated under priorities, CFSAN should concentrate on its overall strategic plan with safety first, followed by claims and other activities.

II. Detailed Comments on Operational Aspects of CFSAN's Interaction with Its External Constituents

A. Overview

On June 30, 1999, members of CHPA and CFSAN met to discuss a variety of issues pertaining to the operational aspects of CFSAN's interaction with its external constituents. These issues include the following:

- Calendar
- Notification
- Meetings with External Constituents
- Partnership in Meetings
- AER Management
- Use of Outside Experts

B. Calendar

CHPA recommends that CFSAN publish a 6-to-9 month public calendar of its planned activities and events. Clearly, development of a useful strategic plan would help define this calendar. Undoubtedly and understandably, imminent issues relating to safety, for example, would necessarily take priority over on-going issues. The reshaping of a calendar by unexpected priority events is not unexpected and is a part of any well-organized operational function.

Importantly, the use of a public calendar is a matter of good review management and has precedence in the Center for Drug Evaluation and Research Office of OTC Drug Products, where there is a unified regulatory agenda (i.e., calendar) for the OTC Review publications and an agreement by CDER to notify industry concerning the 6-month calendar for the Nonprescription Drugs Advisory Committee.

The advantages for the use of a public calendar are:

- Better internal planning management;

- Facilitation of input from external constituencies, as outside groups, such as Association's with many members, are better able to plan and develop input from diverse sources;
- Improved quality of the decision-making process due to enhanced preparedness of participants.

Use of the public calendar would obviously be complimented by use of a constantly updated internal calendar and tied to the strategic plan and performance review.

C. Notification

CFSAN has often planned important meetings with limited notice to industry. For example, the June meeting of the Foods Advisory Committee was preceded by about 2 weeks notice. According to the Administrative Procedures Act, a government agency must give 15 days notice for major meetings with external constituencies. However, as a practical matter 2 weeks notice is an extremely short period to develop meaningful detailed comments on the highly complex issues found on the typical agendas of FDA advisory committees.

On the OTC drug side of the regulation of self-care, we are typically given 6-8 weeks or more to prepare for FDA advisory committees. CHPA's discussions with the Office of OTC Drug Products on this aspect of review management were tied to the use of a public and internal calendar. CHPA has maintained that in order to ensure comprehensive input from industry, a trade association needs more than 2 weeks to:

- Bring members together;
- Prepare draft detailed comments;
- Achieve consensus within and among member companies;
- Incorporate member comments into the final submission by association staff;
- Development of specific meeting materials;

- Sharing meeting materials with FDA and its advisors sufficiently in advance of the meeting (i.e., 10-14 days).

We ask CFSAN to take these considerations into account. Longer notification times of major meetings are essential for informed decision-making. Use of a public calendar can help the notification process. Both the public calendar and longer notification times should be top priorities for an effective CFSAN operational policy on dietary supplements.

D. Meetings with External Constituents

At the April 28, 1999, stakeholders meeting convened by FDA Commissioner Jane Henney, CHPA recommended that FDA consider a sharing of best operational practices among the various FDA Centers. Specifically, we suggested that CFSAN adopt a manual of policies and procedures format similar to CDER in relation to the scheduling, organization, management, documenting and follow-up of meetings between CFSAN and external constituencies.

Through meetings with CHPA, the CDER Office of Review Management created MaPP 4512.1 (Attachment D) which has been extremely successful in further improving the efficiency of the meetings between CDER and pharmaceutical companies and related Associations. Many features of MaPP 4512.1 were subsequently adopted and somewhat expanded as a legal requirement through the 1998 FDA Modernization Act. At our June 30th meeting with CFSAN representatives, it was suggested that we renew our recommendation in the context of our other interests in CFSAN's operational infrastructure for CFSAN.

A formal public document defining the management specifications for meetings MaPP:

- Provides specifications for sharing materials prior to a meeting to help ensure the agency has sufficient time to evaluate industry's agenda and issues,

thereby helping to optimize the potential for achieving resolution of issues at the meeting;

- Provides consistency among FDA's external constituents in terms of how meetings are handled;
- Provides specifics for how minutes are written, ensuring a timely and accurate record of issues, agreements and commitments;
- Provides specifics for agreed upon follow-up action items, including agreed upon timeframes and next steps;
- Make meetings more efficient, thereby saving time.

Effective and efficient meetings management is part of an overall operational perspective, and – in conjunction with a public and internal calendar process and a more reasonable notification process – will help in time and resource management with CFSAN.

E. Nonprescription Electronic Library – Dietary Supplements (NEL-DS)

Since the early 1970's CHPA has maintained a constantly updated hard copy compilation of OTC-related and selected nutraceutical-related laws and regulations. In the early 1990's, we added an electronic version of the CHPA Compilation of Laws and Regulations, and both the paper and electronic versions are widely used by industry.

In January 1999, in conjunction with CHPA's broadened role in representing dietary supplements, CHPA expanded the electronic library, renaming it with the addition of "DS" (dietary supplements) – The CHPA Nonprescription Electronic Library -- Dietary Supplements (NEL-DS). The library – or database – uses special consumer-friendly software that allows the very rapid searching of tens of thousands of pages of Federal Register documents by key words and phrases.

As a result of the June 30th meeting between CHPA and CFSAN, and follow-up to that meeting, we understand that CFSAN will now help facilitate the transfer of

key information to NEL-DS, consistent with FOIA and FDA policy. We very much appreciate this development.

NEL-DS is a unique database of tremendous value to both FDA and industry. Consequently, we seek to continually tailor and expand its usefulness to subscribers. We ask that CFSAN understand the priority that industry places on NEL-DS and plan to continue to help facilitate the transfer of FOIA-related materials to the database.

F. Partnerships in Meetings

CFSAN participation in external meetings is an important aspect of ensuring communication between the regulated and the regulators. CFSAN has contributed in this regard, and we are very appreciative of this form of outreach by FDA.

We encourage CFSAN to continue this policy.

G. Adverse Experience Reporting (AER) Management

CHPA provided detailed comments on CFSAN's AER management at the time of the June 8th stakeholders meeting. A summary listing of CHPA's initial recommendations in this regard are found in Section I.B. above.

CHPA is still in the process of looking into the details of how CDER will adopt – for *medical* products -- the May 1999 report requested by FDA Commissioner Jane Henney “Managing the Risks from Medical Product Use: Creating a Risk Management Framework.” As CHPA learns more of CDER's activities on this subject, and as those activities might be applied to CFSAN's management of AERs, we plan to share this information with CFSAN. In light of the emergent nature of this issue at CDER, given the relatively recent date of the May 1999 report, we request that CFSAN be open to receipt of additional comments in this area.

H. Use of Outside Experts

At the June 8th Stakeholders Meeting, CHPA provided oral and written remarks about CFSAN's priority needs in developing an infrastructure to manage the evolving dietary supplement environment. CHPA provided support for CFSAN's use of outside experts through the Foods Advisory Committee and its various ad hoc working groups that have been dealing with infrastructure issues pertaining to dietary supplements (e.g., identity and AERs).

At this time, CHPA urges FDA to continue to use this approach of special working groups to the Foods Advisory Committee for the following reasons:

- Dietary supplements are foods;
- The issues handled by CFSAN's various stakeholders meeting are of sufficient complexity from a legal and regulatory perspective and of sufficient breadth in terms of scope and extent of stakeholder commentary, that CFSAN has likely chosen the correct format of FDA-mediated panels of external constituents to address such issues as CFSAN's overall strategic plan, structure/function claims, etc.
- The types of technical issues that have been important to resolve (e.g., identity, AERs) are best handled in a working group structure where the needed industry input – and the level of that input – is not constrained by policies and procedures that would be inherent in the development of a formal advisory committee on dietary supplements;
- The agenda items for dietary supplements outside the stakeholders meetings (see above) are likely not of sufficient on-going quantity to warrant a formal advisory committee on dietary supplements;
- There are sufficient cross-sectional issues with claims for conventional and functional foods and dietary supplements that were a health claims issue to arise to a level requiring advisory committee review, the Foods Advisory Committee (perhaps augmented by additional experts) is in place to be able to appropriately handle such issues (e.g., an FDA approved health claim, which

would likely be requested for foods and dietary supplements, although there have been relatively few requests for FDA approved health claims).

III. Conclusion

In conclusion, these comments represent the second set of CHPA submissions to CFSAN on its overall strategic plan for dietary supplements. In these comments we focus on a number of specific operational (i.e., infrastructure) issues, which if addressed, will help efficient interactions between industry and CFSAN, particularly the Office of Special Nutritionals. They include: a systems approach to AER management; a public calendar of planned activities and events; a better advance notification policy and procedure; a policy and procedure for meetings between CFSAN and external constituencies, continued contribution to the CHPA/INCAD electronic library of pertinent laws and regulations affecting dietary supplements and OTC medicines; continued partnership in meetings; and continued use of the working group format of the Foods Advisory Committee to address dietary supplement issues.

Sincerely yours,



R. William Soller, Ph.D.
Senior Vice President and
Director of Science & Technology



Leila Saldanha, Ph.D., R.D.
Vice President – Nutritional Sciences

- Attachments: A CHPA's Comments at the June 8, 1999, Stakeholders Meeting.
B CHPA's Amended Comments on GMPs for Dietary Supplements
C CHPA's Comments of August 4, 1999 on FDA's Proposed Rule on Structure/Function Claims
D CDER Manual of Policy and Procedures: Meetings with External Constituencies, MaPP 4512.1



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CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

Formerly Manufacturer of Drug Manufacturers Assoc of

June 8, 1999

Docket Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20857

Re: Docket No. 99N-1174

Dear Madam or Sir:

These comments are submitted in response to the May 13, 1999 Federal Register announcement of a pair of meetings scheduled to obtain stakeholder input on the development of an overall strategy for dietary supplements with respect to their regulation of dietary supplements under the Dietary Supplement and Health Education Act (DSHEA). The Consumer Healthcare Products Association (CHPA) supports this effort, as stated in its comments to Congress at the March 25, 1999 hearing of the House Committee on Government Reform and to FDA in relation to the agency's April 28, 1999 Stakeholder Meetings.

Founded in 1881, CHPA represents producers of quality nonprescription medicines and dietary supplements, including over 200 member companies across the manufacturing, distribution, supply and service sectors of the self-care industry.

Our comments are organized according to the following outline:

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I. Summary of CHPA's Recommendations

1. **Priorities:** In setting its priorities for program activities, CFSAN should place safety first – enforcement, GMPs and AERs. Refining the infrastructure of the Office of Special Nutritionals and other components of CFSAN should be part of this "safety priority."

From the standpoint of operations, CFSAN should place as another top priority the development and publication of its 3-to-5-year strategic plan, which is a logical outcome of this current set of Stakeholders Meetings on June 8th and July 20th.

The definition of "boundaries" among claims for different types of products (e.g., the boundary between a dietary supplement and a drug, or a food, or a cosmetic) has been complicated by a proposed rule on structure/function claims and requires a fresh perspective that embraces the intent of DSHEA. While activity in this area may proceed as priority is given to safety issues, its completion should be targeted farther in the future than that for resolving the safety issues and publishing a 3-5 year strategic plan for dietary supplements.

2. **Enforcement:** In passing DSHEA, Congress intended that consumers would use dietary supplements for health promotion, health maintenance and disease risk reduction (i.e., health claims). Consumer confidence is essential to product use. Allegations that the dietary supplement industry is "unregulated" or that FDA is not using its statutory authority to act can undermine consumer confidence.

Therefore, foundational to CFSAN's overall strategy for dietary supplements is an effective enforcement policy that removes unsafe products from the marketplace and that ensures truthful, not misleading, and substantiated claims on dietary supplements. The Food, Drug and Cosmetic Act gives FDA substantial authority, including, for example, the authority to stop the sale of dietary supplements that are toxic or unsanitary, pose significant unreasonable risk of illness or injury or bear false or unsubstantiated claims or claims that a product cures or treats a disease.

Because of the complementary jurisdictions of FDA and the Federal Trade Commission (FTC) to address the marketing of dietary supplements, wherein FTC has primary responsibility for advertising and FDA has primary responsibility for labeling, the two agencies must coordinate closely to ensure that their actions are consistent to the fullest extent feasible given the statutory authority of each. A public workshop on this matter would be helpful for all stakeholders to understand the current relationship between FDA and FTC.

3. **Good Manufacturing Practices (GMPs):** While section 402(g) of the act does not require that the Secretary (and by delegation, FDA) adopt regulations that prescribe GMPs, the dietary supplement industry has maintained that such regulations would be helpful for ensuring that dietary supplements are: safe and not adulterated or misbranded; have the identity and provide the quantity of dietary ingredients declared in labeling; and meet the quality specifications that the supplement is represented to meet.

As a result of its recent broadened mission, CHPA convened a special Dietary Supplement GMP Section within its Manufacturing Controls Committee, which has undertaken a comparison of food GMPs and the industry proposed GMPs in the light of botanical products. As a result of this new review, we have identified certain aspects of the original industry proposal that CHPA believes should be considered as FDA prepares the Notice of Proposed Rulemaking. A side-by-side comparison of current Food GMPs and CHPA's amended industry-recommended GMPs are appended.

CHPA recommends that FDA make the dietary supplement GMPs a top priority in 1999 and consider the additional specific comments that CHPA has developed and appended to these comments in developing the NPR on dietary supplement GMPs.

4. **Adverse Experience Reporting:** In controversial safety-related situations, a refined integrated system with documented policies and procedures is vital to help ensure that the details of such situations are as accurately documented and professionally handled as

possible. Public discussion on putative safety issues relating to dietary supplements should more appropriately focus on the science, not the quality of administrative methods used to document AERs.

Therefore, as stated in its May 27, 1999 comments to the House Committee on Government Reform, CHPA recommends:

- a. CFSAN prepare a written plan for and adopt a systems approach, similar to that recommended in FDA's May 1999 document "Managing the Risks from Medical Product Use: Creating a Risk Management Framework" to the management of AERs on dietary supplements, grounding this approach in the agency's current safety policy (i.e., "warnings, or discussions on product availability: should be scientifically documented, clinically significant and important to the safe and effective use of the product by the consumer");
- b. CFSAN should keep current written protocols for CFSAN personnel handling AERs to expedite accurate data collection, including a detailed decision tree for use by those whose responsibility it is to filter serious and non-serious reports and route these reports for expeditious follow-up;
- c. CFSAN should have a policy and procedures for timely sharing of serious AERs with affected companies, in order to help facilitate adequate follow-up and so address incompleteness and inaccuracies in AE reports;
- d. Specific CFSAN training manuals and procedures should be established to ensure quality collection, analysis and reporting of AERs.
- e. CFSAN should undertake a review of the core competency of the personnel who would operate different facets of an adequate AER system on dietary supplements.
- f. A re-engineering of the public access to AERs for dietary supplements is needed. AERs should be available to the public in a timely fashion when FDA (a.) has communicated with the affected company identified in the AER and (b.) is prepared to provide publicly a complete file of the report omitting confidential information.

A specific "causality assessment" should not be applied to each AER received by FDA, since causality cannot be established for most AERs by virtue of their retrospective nature and the fact that the overall strength of the reported association, which seeks to define likelihood of a reported association, encompasses much more information and data than just one or a few AERs.

- g. Public input is needed in the development of policies and procedures to be used in CFSAN's systems approach to AER management.

5. **Claims:** "Boundaries" between different types of products (e.g., drugs, conventional foods, dietary supplements, cosmetics) should be based on a product's claim(s), which define(s) the intended use(s) of the product. In this way, a product may have more than one intended use, which should not be considered as overlapping but rather as properly co-existent.

Importantly, because of the two major confounding issues in FDA's structure/function proposal related to the overly broad re-definition of disease, which was proposed to exclude products from disease-related claims, and to the intricate inter-relationship between health promotion/maintenance and disease prevention, FDA should: (a.) amend its proposed definition of disease¹ to properly limit its reach; and (b.) address implied claims by the statutorily required disclaimer on structure/function claims. When combined with the use of disclaimers for certain claims, the regulatory "line" is drawn more clearly by focusing on the truthfulness of the claim and the dissemination of accurate information and not the categorical nature of the product (i.e., "drug" vs "dietary supplement"). As a result, implied disease claims on dietary supplements are not confused as drug claims.

CHPA therefore recommends the following as part of CFSAN's development of an overall strategy on dietary supplements:

- a. Re-proposal of the structure/function proposed rule as a focused regulatory statement that closely incorporates the specific intent of DSHEA, appropriately amends FDA's proposed re-definition of disease per CHPA's comments to FDA, omits the confusing and ambiguous proposed criteria, and relies on the DSHEA disclaimer to address implied disease claims.
- b. Development of an overall guidance on structure/function claims for dietary supplements, consistent with DSHEA and modeled after the FTC advertising guidance to industry.

6. **Dietary Supplement Advisory Committee**

CHPA does not recommend that CFSAN move forward at this time with the appointment of a Dietary Supplement Advisory Committee. CHPA considers the priorities of safety, an overall strategic plan and claims policy of sufficient potential resource intensity that the appointment of a another special advisory committee would detract at this time with the needed refinements in CFSAN's operations and activities.

It is our understanding that other trade associations share CHPA's view, including the American herbal Products Association, the National Nutritional Foods Association, and the Utah Natural Products Alliance.

¹ See CHPA's comments on structure/function claims submitted to Docket No. 98N-0044 on 9/24/98.

7. **CFSAN's 3-to-5-Year Strategic Plan and Resources:** Industry has an interest in helping to ensure that FDA is appropriately staffed and funded to meet its statutory obligations of promoting and protecting the public health.

CFSAN's development of an overall strategy for dietary supplements should be undertaken as a 3-to-5-year plan, which is would be viewed as a "living" document that appropriately evolves dependent on the changing climate. As part of such a strategic plan, CFSAN should define its human and fiscal resource needs, including expanded use of outside contractors (e.g., for AER management). As stated under priorities, CFSAN should concentrate on its overall strategic plan and safety first, followed by claims and other activities.

II. Safety Priorities First: Enforcement, GMPs and AERs

A. Enforcement

1. Introduction: Maintaining Consumer Confidence in Dietary Supplements

During the passage of DSHEA, Congress found that dietary supplements are safe across a broad spectrum of use and intake and provide important benefits relating to health promotion, health maintenance, and disease prevention (i.e., health claims). To promote usage of dietary supplements by consumers, Congress established a statutory framework for the dissemination of useful and accurate information about the benefits of dietary supplements, so that consumer are able to make personal, health-related, informed choices about these products.

In passing DSHEA, Congress intended that consumers would use dietary supplements for health promotion, health maintenance and disease risk reduction (i.e., health claims). Consumer confidence in products is essential to the usage of any product and therefore the realization of that intent of Congress. Negative media coverage portrays the dietary supplement industry as "unregulated" erodes this confidence and thereby undermines the intent of Congress. Both FDA and FTC have stated that they have enforcement powers for dietary supplements. At the March 25 and May 27, 1999 hearings of the House Committee on Government Reform, both FDA Commissioner Jane Henney and CFSAN Director Joseph Levitt stated that FDA has authority for enforcement activities pertaining to dietary supplements; neither called for more authority. On March 16, 1999, FTC issued a comprehensive guidance to the dietary supplement industry concerning FTC's substantiation standard. FTC issued this guide to clarify how long-standing FTC policies and enforcement practices relate to dietary supplement advertising. This guide appears to be a useful reference for advertising-related enforcement activities.

Furthermore, FDA has had cooperation from the members of the major trade associations in various actions that it has taken to remove unsafe products, such as those containing

GBL. from the market. When FDA does not take enforcement action in accordance with the authorities given to it by Congress, both industry and consumers suffer.

2. Powers of FDA and FTC

Indeed, Congress' action in passing DSHEA did not leave FDA or FTC without specific enforcement powers over dietary supplements. The Food and Drug Administration (FDA) and the Federal Trade Commission (FTC) work together under a long-standing agreement governing the division of responsibilities between the two agencies. As applied to dietary supplements:²

- FDA has the primary responsibility for claims on the product labeling, including packaging, inserts, and other promotional materials distributed at the point of sale;
- FTC has primary responsibility for claims in advertising, including print and broadcast ads, infomercials, catalogs, and similar direct-marketing materials. Because of their shared jurisdiction, the two agencies work closely to ensure their enforcement efforts are consistent to the fullest extent feasible.

FDA's and FTC's statutory powers are sufficient for both agencies to cooperatively regulate the field of dietary supplements.

FDA has the power to:

- Stop any company from selling a dietary supplement that is toxic or unsanitary [see Food Drug and Cosmetic (FDC) Act, Section 402(a)];
- Stop the sale of a dietary supplement that has false or unsubstantiated claims [see FDC Act, Section 403(r)(6)];
- Take action against dietary supplements that pose "a significant unreasonable risk of illness or injury" [see FDC Act, Section 402(f)];
- Stop any company making a claim that a product cures or treats a disease [see FDC Act, Section 201(g)];
- Stop a new dietary ingredient from being marketed if FDA does not receive enough safety data in advance (see FDC Act, Section 413);
- Require dietary supplements to meet strict manufacturing requirements (Good Manufacturing Practices), including potency, cleanliness and stability [see FDC Act, Section 402(g)].

FTC has the power to:

- Enforce laws outlawing "unfair or deceptive acts or practices" to ensure consumers get accurate information about dietary supplements, so they can make informed decisions about these products [see Federal Trade Commission (FTC) Act, Section 5];

² Federal Trade Commission, Bureau of Consumer Protection: Dietary Supplements: An Advertising Guide for Industry. 1998.

- An unfair trade practice is one that: causes or is likely to cause substantial injury to consumers; is not reasonably avoidable by consumers themselves; and not outweighed by countervailing benefits to consumers or competition (see FTC's Deception Policy Statement and Advertising Substantiation Policy Statement):
- Challenge and stop advertising that is not adequately substantiated (see FTC's Deception Policy Statement and Advertising Substantiation Policy Statement):
- Investigate complaints or questionable trade practices:
 - FTC can investigate either informally or formally, where it has strong compulsory investigative authority, including the power to require a respondent to produce documents, give testimony, or answer written questions [see FTC Act, Sections 6(a and b) and 9];
- Following its own investigation, negotiate a consent order or proceed through an FTC adjudication resulting in a cease and desist order, which can be quite broad in its scope (see FTC Act, Section 5);
- Seek preliminary and permanent injunctions to stop false advertisements or other violations of the FTC Act [see FTC Act, Section 12 and 13];
- Seek civil penalties for violations of trade regulation rules [FTC Act, Section 5] or of cease and desist orders (see FTC Act Section 5).

3. Recommendations

Therefore, foundational to CFSAN's overall strategy for dietary supplements is an effective enforcement policy that removes unsafe products from the marketplace and that ensures truthful, not misleading, and substantiated claims on dietary supplements. The Food, Drug and Cosmetic Act gives FDA substantial authority, including, for example, the authority to stop the sale of dietary supplements that are toxic or unsanitary, pose significant unreasonable risk of illness or injury, bear false or unsubstantiated claims or claims that a product cures or treats a disease.

Because of the complementary jurisdictions of FDA and the Federal Trade Commission (FTC) to address the marketing of dietary supplements, wherein FTC has primary responsibility for advertising and FDA has primary responsibility for labeling, the two agencies must coordinate closely to ensure that their actions are consistent to the fullest extent feasible given the statutory authority of each. A public workshop on this matter would be helpful for all stakeholders to understand the current relationship between FDA and FTC.

B. Good Manufacturing Practices

1. Introduction

Dietary supplements are considered foods and are subject to requirements of "Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Human Food." These regulations provide guidelines with regard to maintenance of buildings and facilities, requirements for food handlers, and cleanliness of equipment, as well as

procedural requirements for maintaining safety during the production and processing of foods.

DSHEA authorizes FDA to establish GMP regulations governing the preparation, packing, and holding of dietary supplements under conditions that ensure their safety. DSHEA amended the FDC Act with section 402(g) (21 U.S.C. 342(g)), which provides, in part, that: The Secretary may by regulation prescribe good manufacturing practices for dietary supplements. Such regulations shall be modeled after current good manufacturing practice regulations for food and may not impose standards for which there is no current and generally available analytical methodology.

While section 402(g) of the act does not require that the Secretary (and by delegation, FDA) adopt regulations that prescribe GMPs, the dietary supplement industry has maintained that such regulations would be helpful for ensuring that dietary supplements are: safe and not adulterated or misbranded; have the identity and provide the quantity of dietary ingredients declared in labeling; and meet the quality specifications that the supplement is represented to meet. The industry created proposed GMPs for dietary supplements, which were submitted to FDA and subsequently published in February 1997 as an ANPR in the Federal Register.

In its Report, the Commission on Dietary Supplement Labeling supported these efforts of FDA and the industry to develop appropriate GMPs for dietary supplements. In the ANPR, the agency said it would establish dietary supplement GMPs if, after public comment, it determined that GMPs for conventional foods are not adequate to cover dietary supplements as well.

The industry submission was patterned after the food GMP regulation contained in part 110, but also contained requirements beyond those in part 110. When dietary supplement constituents are prepared for incorporation in liquid, tablet, capsule, or bulk powder form, requirements beyond food GMPs are needed to optimize controls for preparation, packing, and holding, including, for example, the omission of conventional food-specific provisions, and the addition of provisions on records, quality control, and laboratory operations.

2. Recommendations

At the time of the submission to FDA of industry-recommended GMPs for dietary supplements on November 30, 1995, CHPA represented manufacturers and distributors of nonprescription medicines as well as vitamins and minerals. Members of CHPA (then called the Nonprescription Drug Manufacturers Association) supported the industry-recommended GMPs. Since that time, the Association undertook a broader self-care mission to represent all dietary supplements as well as nonprescription medicines.

As a result of its recent broadened mission, CHPA convened a special Dietary Supplement GMP Section within its Manufacturing Controls Committee, which has

undertaken a comparison of food GMPs and the industry proposed GMPs in the light of botanical products. As a result of this new review, we have identified certain aspects of the original industry proposal which CHPA believes should be considered as FDA prepares the Notice of Proposed Rulemaking. A side-by-side comparison of current Food GMPs and the CHPA amended industry- recommended GMPs are appended.

CHPA recommends that FDA place the publication of proposed GMPs as a top priority in 1999 and in developing the dietary supplement GMPs, consider the additional specific comments developed by CHPA (appended).

C. Adverse Experience Reporting

1. Overview

By way of background, the vast majority of dietary supplements have a very wide margin of safety. Garlic, ginseng, ginger, St. John's wort, saw palmetto, calcium, all the fat- and water-soluble vitamins, bioflavonoids, and many, many others have use profiles often spanning hundreds and hundreds of years. As a result, the total number of spontaneous adverse events that are reported annually to FDA as associated with dietary supplement use is relatively low compared to drugs, thereby suggesting fewer resource needs in this regard for CFSAN than, for example, CDER.

In addition, FDA has at least three systems in place for capturing AERs reportedly associated with dietary supplements: MedWatch, SN/AEMS, and Consumer Hotlines. These AER sources -- in addition to those maintained by the Consumer Product Safety Commission, the United States Pharmacopeia, the American Association of Poison Control Centers, the National Institute of Drug Abuse, and the Centers for Disease Control -- are similar for drugs and dietary supplements. There is general agreement that these current sourcing mechanisms are adequate as signal generators of potential problems with consumer products, though systems integration is needed. Hence, we do not recommend an attempt to develop new sources of DS AERs.

In addition, we are aware of certain concerns expressed about CFSAN's handling of AERs on, for example, ephedra, and this issue was the subject of the May 27th hearing of the House Committee on Government Reform. We take a direct interest in ensuring that, in the future, the right infrastructure and policies are in place at CFSAN to enable it to handle efficiently, expeditiously, and fairly any and all AERs on dietary supplements.

2. Recommendations

Based on the foregoing discussion (Section B.1.), CHPA has three general recommendations and a series of specific recommendations in relation to CFSAN's management of AERs reportedly associated with dietary supplements. We urged the House Committee on Government Reform on May 27, 1999 to take an interest in these recommendations which we have set forth for CFSAN's management of AERs on dietary

supplements, and we have recommended that the House Committee consider a specific inquiry to FDA, asking for a detailed allocation plan for any resources needed to adopt our recommendations.

First, as part of Dr. Jane Henney's initial directives as FDA Commissioner, FDA studied drug approvals pre and post PDUFA, issuing a report in May entitled "Managing the Risks from Medical Product Use: Creating a Risk Management Framework." Focusing on medical products, the report calls for adoption of a systems approach to FDA's management of AERs' including:

- establishing "separate quality assurance/quality control units."
- ensuring and documenting "ongoing professional education and core competency training for all reviewers,"
- maintaining current "good review practice documents,"
- ensuring rapid completion of AERs, and
- integrating "existing post-marketing systems so analytical tools, data entry, and editing can be uniformly applied, and information is readily available to all reviewers."

We support this "total quality management" approach for the Center for Food Safety and Applied Nutrition as well.

Second, we support renewed emphasis within CFSAN of FDA's long-standing overarching safety policy for foods and drugs. The policy states:

"Warnings shall be scientifically documented, clinically significant and important to the safe and effective use of the product by the consumer."

The value of this policy is that it focuses us on the most critical step -- scientific documentation. Without rigorous, critical evaluation of how AER data are collected, analyzed and reported, it is literally impossible to determine their significance.

In sum, then, as stated in our May 27, 1999 comments to the House Committee on Government Reform, we recommend attention be given to the following seven areas to further refine CFSAN's AER program for dietary supplements:

- CFSAN should prepare a written plan for and adopt a systems approach to managing AERs on dietary supplements, grounded in its current safety policy (i.e., "warnings, or discussions on product availability, should be scientifically documented, clinically significant and important to the safe and effective use of the product by the consumer;" see above).

- CFSAN should keep current written protocols for CFSAN personnel handling AERs to expedite accurate data collection, including a detailed decision tree for use by those whose responsibility it is to filter serious and non-serious reports and route these reports for expeditious follow-up;
- CFSAN needs a policy and procedures for timely sharing of serious AERs with affected companies and timely follow-up in order to help facilitate adequate follow up to facilitate completeness and accuracy of AE reports;
- Specific CFSAN training manuals and procedures should be established to ensure quality collection, analysis and reporting of AERs.
- CFSAN should undertake a review of the core competency of the personnel who would operate different facets of an adequate AER system on dietary supplements.
- A re-engineering of the public access to AER reports for dietary supplements is needed. AERs should be available to the public in a timely fashion when FDA (a.) has communicated with the affected company identified in the AER and (b.) is prepared to provide publicly a complete file of the report omitting confidential information.

A specific "causality assessment" should not be applied to each AER received by FDA, since causality cannot be established for most AERs by virtue of their retrospective nature and because the overall strength of the reported association, which seeks to define likelihood of a reported association, encompasses much more information and data than just one or a few AERs.

- Public input is needed in the development of policies and procedures to be used in CFSAN's systems approach to AER management.

III. Claims

A. "Boundaries"

As part of CFSAN's 1999 Program Priority A activities to develop an overall strategic plan for dietary supplements, FDA has asked for comments on what are the "boundaries" between dietary supplements and drugs, dietary supplements and foods, and dietary supplements and cosmetics. By use of the word "boundaries" in conjunction with product categories, FDA seems to imply that there are "bright lines" between these categories of products, which might therefore be used to regulate dietary supplement labeling claims.

CHPA maintains that "boundaries" between different types of products (e.g., drugs, conventional foods, dietary supplements, cosmetics) should be based on a product's claim(s), which define(s) the intended use(s) of the product. In this way, a product may have more than one intended use,

which should not be considered as overlapping but rather as properly co-existent.

Importantly, because the two major confounding issues in FDA's structure/function proposal related to the overly broad re-definition of disease, which as proposed inappropriately excludes claims for dietary supplements, and the intricate inter-relationship between health promotion/maintenance and disease prevention, FDA should: (a.) amend its proposed definition of disease (see below); and (b.) address implied claims by the statutorily required disclaimer on structure/function claims. When combined with the use of disclaimers, for example, for structure/function claims, the regulatory "line" is drawn clearly by focusing on the truthfulness of the claim and the dissemination of accurate information. As a result, implied disease claims on dietary supplements are not confused as drug claims.

B. Redefinition of Disease

CHPA's September 24, 1998 comments to FDA³ address needed changes to the proposed redefinition of disease and the specific problematic aspects of the proposed criteria for defining drug claims.

Specifically, CHPA's comments included the following recommended changes to FDA's proposed rule on structure/function claims:

1. CHPA strongly recommends that FDA take a more measured approach to its implementation of DSHEA and not issue the proposed rule as a final regulation without significant amendment of its scope and specifics.
2. CHPA supports adoption by regulation of a definition of disease for the purposes of DSHEA, provided that the suggested changes that immediately follow are made.
 - a. FDA's proposed definition for "disease" should be amended to correctly denote the negative aspect of any deviation from normal structure or function as being characteristic of a disease, as follows:

"a disease is any adverse deviation from, impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a ~~characteristic~~ set of one or more signs or symptoms ~~including laboratory or clinical measurements~~ that are characteristic of a disease but not of natural states or processes." (Emphasis and strikeout show CHPA's recommended changes.)

CHPA's proposed changes are consistent with FDA's rationale for its proposed definition of disease found in the preamble to the proposed rule.

³ Docket No. 98N-0044: Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body. *Federal Register* 63: 23624-32, April 29, 1998.

- b. FDA should define "natural state or process" (see above. CHPA's proposed definition) as follows: "A natural state or process is a life change or physiologic manifestation expected in the normal course of life progression that is not defined as a disease."
 - c. We recommend our proposed amendments to FDA's proposed redefinition of disease be incorporated into proposed §101.93(g)(1) and 101.14(a)(6).
 - d. In the event that FDA does not agree with CHPA's proposed amendments to the FDA's proposed redefinition of disease, then, for the purposes of structure/function claims under DSHEA, FDA should amend the definition of "disease" found in NLEA regulations, by deleting the phrase "or health related condition," as follows: "a disease ~~or health related condition~~ means damage to an organ, part, or structure, or system of the body such that it does not function properly . . . or a state of health leading to such dysfunctioning . . . except that disease resulting from essential nutritional deficiencies (e.g., scurvy, pellegra) are not included in this definition."
 - e. In any case, however, FDA's proposed definition of disease may not be constructed or construed to restrict or otherwise alter the provisions of DSHEA relating to permissible structure/function claims for dietary supplements.
3. CHPA supports a regulatory interpretation of DSHEA that would include and be limited to the following three-part claim standard (in addition to the above-mentioned changes to FDA's definition of disease), in order to set forth an explicit set of clear rules that cut through the potential ambiguities created by FDA's proposal. The following three-part standard should be the regulatory basis of determining whether a reference to a sign and/or symptom (or set thereof) constitutes a claim about a specific disease or class of diseases:
- a. The words, "diagnose," "prevent," "treat," "cure," "mitigate" (or other grammatical forms of these verbs) should not be used in a statement of nutritional support (i.e., a structure/function claim), since statements permitted under 403(r)(6) of DSHEA "may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases;"
 - b. The words, "stimulate," "maintain," "support," "regulate," and "promote" -- or other words of this nature or other grammatical forms of these verbs -- may be used in a structure/function claim to distinguish the claim from a specific disease claim;
 - c. The potential for clinical endpoints to be recognizable to health professionals or consumers as being related to a disease or implied to be related to a disease is addressed through the claim construction per points a. and b., above, and per the

DSHEA-required disclaimer.

4. CHPA recommends that FDA extend the compliance date of the new regulation to 6 months after the publication of the regulation for any product that is marketed for the first time after publication of the final rule, and any new claims made for an existing product for the first time after publication of the final rule. Further, NDMA recommends that there be no distinction between small and large companies in the compliance date for products currently on the market at the time of issuance of the final rule and that the compliance date for all such products be 15 months.

C. Use of Disclaimers

As stated, CHPA recommends that in defining boundaries between dietary supplements and other product categories FDA should focus on claims, which in turn allows a focus on the intended use of the product. Further, as in the case of structure/function claims, a DSHEA-mandated disclaimer allows consumers to exercise judgement when buying a product regardless of FDA's evaluation of the claim.

Emphasizing this point in *Pearson v Shalala*, the D.C. Circuit Court rejected FDA's argument that claims made without "significant scientific agreement" regarding their basis would *inherently* mislead consumers. The Court concluded a lack of "significant scientific agreement," alone, would not render claims *inherently* misleading. Rather, the Court conceded that the four health claims in question could be *potentially* misleading because consumers would have difficulty independently verifying the claims and because consumers might also believe the FDA approved the claims. Despite these possibilities, the Court believed FDA should have considered disclaimers, rather than an outright ban, to cure potentially misleading claims.

Hence, disclaimers have been supported as useful vehicles to help ensure the dissemination of truthful and not misleading information through product claims. In particular, they are important for overcoming the intricate interrelationship between health promotion/maintenance and disease prevention (i.e., a drug claim). The DSHEA disclaimer for structure/function claims clarifies any implication that the product affects a specific disease (i.e., "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.").

D. FTC's Guidance to the Dietary Supplement Industry

CHPA members have found the FTC Guidance to industry on dietary supplements to be a helpful expression of case examples of FTC's interpretation of its statutory mandate to ensure that advertising of dietary supplements is truthful and not misleading. We suggest that FDA may wish to model a guidance on structure/function claims along the lines of the FTC guidance, noting the need to ensure that the intent of DSHEA is followed in any

such document.

E. Recommendations

CHPA therefore recommends the following as part of CFSAN's development of an overall strategy on dietary supplements:

- a. Re-proposal of the structure/function proposed rule as a focused regulatory statement that closely incorporates the specific intent of DSHEA, appropriately amends FDA's proposed re-definition of disease and creates a three-part standard per CHPA's comments to FDA, omits the confusing and ambiguous proposed criteria, and relies on the DSHEA disclaimer to addimplied disease claims.
- b. Development of an overall guidance on structure/function claims for dietary supplements, consistent with DSHEA and modeled after the FTC advertising guidance to industry.

In sum, it is the label claim that defines the intended use of the product, not the product type that defines the type of claim which may be used on the product. A product with more than one labeled claim may have more than one intended use. Adoption of this perspective by FDA would help the development of a "regulatory line" between categories of claims and overcome the problems created, for example, in the proposed structure/function rule of implied claims.

IV. CFSAN's 3-to-5-Year Strategic Plan and Resources

A. An Adequately Staffed and Funded FDA

FDA should be appropriately staffed and funded to meet its statutory obligations of promoting and protecting the public health.

B. Dietary Supplement Advisory Committee, Not At This Time

CHPA does not recommend that CFSAN move forward at this time with the appointment of a Dietary Supplement Advisory Committee. CHPA considers the priorities of safety, an overall strategic plan and claims policy of sufficient potential resource intensity that the appointment of another special advisory committee would detract at this time from the needed refinements in CFSAN's operations and activities.

It is our understanding that other trade associations share CHPA's view, including the American Herbal Products Association, the National Nutritional Foods Association, and the Utah Natural Products Alliance.

CFSAN and other Centers in FDA have an operational model to address advisory committee review of special topics. For example, in the case of plaque and gingivitis, CDER convened a subcommittee of the Nonprescription Drugs Advisory Committee (NDAC) to address this OTC

category, since NDAC members were not experts in this area. We understand that CFSAN uses this type of model for deliberations on microbial limits on foods. Indeed, the Foods Advisory Committee uses special working groups to address such issues as GMPs and AERs related to dietary supplements. Thus, the operational mechanism appears to be working given the nature and extent of the agenda for dietary supplements at this time.

C. Recommendations: 3-to-5-Year Strategic Plan and Priorities

CFSAN's development of an overall strategy for dietary supplements should be undertaken as a 3-to-5-year plan, which is typically viewed as a "living" document that appropriately evolves dependent on the changing climate. As part of such a strategic plan, CFSAN should define its human and fiscal resource needs, including expanded use of outside contractors (e.g., for AER management). As stated under priorities, CFSAN should concentrate on its overall strategic plan and safety first, followed by claims and other activities.

At the May 27, 1999 hearing of the House Committee on Government Reform, CHPA asked the Committee to make a specific inquiry to CFSAN for a detailed allocation plan to implement CHPA's recommendations for CFSAN management of AERs reportedly associated with dietary supplements. CHPA made this request because of the lack of specificity in FDA's budget for the \$2.5 million requested by CFSAN for post-marketing surveillance activities. With a 3-to-5-year publicly available strategic plan, specificity can be given not only to CFSAN's priorities and the timing of accomplishing these priorities, but also to the resources needed to accomplish the defined program activities.

In setting its priorities for program activities, CFSAN should place safety first – enforcement, GMPs and AERs. Refining the infrastructure of the Office of Special Nutritionals and other components of CFSAN should be part of this "safety priority."

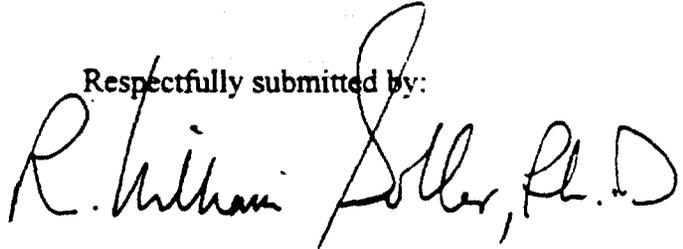
From the standpoint of operations, CFSAN should make as another top priority the development of its 3-to-5-year strategic plan, which is an outcome of this current set of stakeholder meetings on June 8th and July 20th.

The definition of "boundaries" among claims for different types of products (e.g., the "boundary a dietary supplement and a drug, or a food, or a cosmetic) has been complicated by a proposed rule on structure/function claims and requires a fresh perspective that embraces the intent of DSHEA. While activity in this area may proceed as priority is given to safety issues, its completion should be targeted farther in the future than that for resolving the safety issues and publishing a 3-to-5-year strategic plan for dietary supplements.

V. Conclusion

In conclusion, CHPA supports the efforts of CFSAN to develop an overall strategy on dietary supplements and offers these comments as a means to help that activity. Further, CHPA supports the stakeholder process whereby CFSAN is developing its strategic plan.

Respectfully submitted by:

A handwritten signature in black ink that reads "R. William Soller, Ph.D." The signature is written in a cursive style with a large, looped initial "R".

R. William Soller, Ph.D.
Senior Vice President and
Director of Science & Technology

Attachment: CHPA Proposed Dietary Supplements GMPs and Comparison with Food GMPs

WS/jqDIETSUPP/CFSAN/STRATPLAN/June99final6/8



International Quality
Nonprescription Medicines Standards
Dietary Supplement Standards

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

Formerly Manufacturers Drug Manufacturers Association

Consumer Healthcare Products Association Proposed Dietary Supplement GMPs and Comparison With Food GMPs

This is a side-by-side comparison of the current food GMPs and the proposed GMPs for dietary supplement products.

The first column consists of the **Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Human Food**, 21 CFR 110.

The second column consists of the proposed Dietary Supplement Good Manufacturing Practices, published as an Advance Notice of Proposed Rulemaking on February 6, 1997, with comments by CHPA. CHPA comments are designated by ~~strikeouts~~ indicating recommended deletions, and underlines indicating recommended additions.

Shaded areas indicate where there are no sections comparable to the section opposite in the other column.

WB/b
6/7/99

Consumer Healthcare Products Association
Proposed Dietary Supplement GMPs
 and Comparison With Food GMPs

Current Food GMPs	Proposed Dietary Supplement GMPs, Including CHPA Comments*
<p>§ 110.3 Definitions. The definitions and interpretations of terms in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) are applicable to such terms when used in this part. The following definitions shall also apply:</p>	<p>Definitions The definitions and interpretations of terms in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) are applicable to such terms when used in this part. The following definitions shall also apply:</p>
(a) Acid foods or acidified foods means foods that have an equilibrium pH of 4.6 or below.	
(b) Adequate means that which is needed to accomplish the intended purpose in keeping with good public health practice.	(a) "Adequate" means that which is needed to accomplish the intended purpose in keeping with good public health practice
(c) Batter means a semifluid substance, usually composed of flour and other ingredients, into which principal components of food are dipped or with which they are coated, or which may be used directly to form bakery foods.	
	(b) "Batch or Lot" means a specific quantity of a finished product or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.
(d) Blanching, except for tree nuts and peanuts, means a prepackaging heat treatment of foodstuffs for a sufficient time and at a sufficient temperature to partially or completely inactivate the naturally occurring enzymes and to effect other physical or biochemical changes in the food.	(c) "Blanching" means a prepackaging heat treatment of a dietary product for a sufficient time and at a sufficient temperature to partially or completely inactivate the naturally occurring enzymes and to effect other physical or biochemical changes in the product.
	(d) "Composition" means, as appropriate: (1) the identity of a dietary ingredient or dietary supplement, and (2) the concentration of a dietary ingredient (e.g., weight or other unit of use/weight or volume), or the potency or activity of one or more dietary ingredients, as indicated by appropriate procedures.
(e) Critical control point means a point in a food process where there is a high probability that improper control may cause, allow, or contribute to a hazard or to filth in the final food or decomposition of the final food.	
	(e) "Dietary ingredient" means an ingredient intended for use or used in a dietary supplement that is: (1) a vitamin, (2) a mineral, (3) an herb or other botanical, (4) an amino acid, (5) a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or (6) a concentrate, metabolite, constituent, extract, or combination of any of the foregoing ingredients.
	(f) "Dietary product" means either a dietary ingredient or dietary supplement as defined in this Part.
	(g) "Dietary supplement" means dietary supplement as defined in section 201(ff) of the act.
(f) Food means food as defined in section 201(f) of the act and includes raw materials and ingredients.	
(g) Food-contact surfaces are those surfaces that contact human food and those surfaces from which drainage onto the food or onto surfaces that contact the food ordinarily occurs during the normal course of operations. "Food-contact surfaces" includes utensils and food-contact	

Current Food GMPs	Proposed Dietary Supplement GMPs, Including CHPA Comments
surfaces of equipment:	
	(h) "In-process material" means any material fabricated, compounded, blended, ground, extracted, sifted, sterilized, derived by chemical reaction or processed in any other way that is produced for and used in the preparation of a dietary product.
(h) Lot means the food produced during a period of time indicated by a specific code.	(i) "Lot" means "batch" as defined in this part.
	(j) "Lot number" means any distinctive combination of letters, numbers, or symbols, or any combination of them from which the complete history of the manufacture, processing, packing, holding, and distribution of a batch or lot of a finished dietary ingredient, dietary supplement or other material can be determined.
	(k) "Manufacture" or "manufacturing" includes all operations associated with the production of dietary products, including packaging and labeling operations, testing, and quality control of a dietary ingredient or dietary supplement.
(i) Microorganisms means yeasts, molds, bacteria, and viruses and includes, but is not limited to, species having public health significance. The term "undesirable microorganisms" includes those microorganisms that are of public health significance, that subject food to decomposition, that indicate that food is contaminated with filth, or that otherwise may cause food to be adulterated within the meaning of the act. Occasionally in these regulations, FDA used the adjective "microbial" instead of using an adjectival phrase containing the word microorganism.	(l) "Microorganisms" means yeasts, molds, bacteria, and viruses and includes, but is not limited to, species having public health significance. The term "undesirable microorganisms" includes those microorganisms that are of public health significance, that subject food to decomposition, that indicate that a dietary ingredient or dietary supplement is contaminated with filth, or that otherwise may cause a dietary product to be adulterated within the meaning of the act. Occasionally in these regulations, the adjective "microbial" is used instead of using an adjectival phrase containing the word microorganism.
(j) Pest refers to any objectionable animals or insects including, but not limited to, birds, rodents, flies, and larvae.	(m) "Pest" refers to any objectionable animals or insects including, but not limited to, bird, rodents, flies, and larvae.
(k) Plant means the building or facility or parts thereof, used for or in connection with the manufacturing, packaging, labeling, or holding of human food.	(n) "Plant" means the building or facility or parts thereof, used for or connection with the manufacturing, packaging, labeling, or holding of dietary product.
(l) Quality control operation means a planned and systematic procedure for taking all actions necessary to prevent food from being adulterated within the meaning of the act.	(o) "Quality control operation" means a planned and systematic procedure for taking all actions necessary to prevent a dietary product from being adulterated within the meaning of the act.
	(p) "Quality control unit" means any person or organizational element designated by the firm to be responsible for the duties relating to quality control operations.
	(q) "Raw material" means any ingredient intended for use in the manufacture of a dietary ingredient or dietary supplement, including those that may not appear in such finished product.
	(r) "Representable sample" means a sample that consists of a number of units that are drawn based on rational criteria, such as random sampling, and is intended to assure that the sample accurately port the material being sampled.
(m) Rework means clean, unadulterated food that has been removed from processing for reasons other than insanitary conditions or that has been successfully reconditioned by reprocessing and that is suitable for use as food.	(s) "Rework" means clean, unadulterated material that has been removed from processing for reasons other than insanitary conditions or material that has been successfully reconditioned by reprocessing and that is suitable for use in the manufacture of a dietary product.
(n) Safe-moisture level is a level of moisture low enough to prevent the growth of undesirable microorganisms in the finished product under the intended conditions of manufacturing, storage, and distribution. The maximum safe moisture level for a food is based on its water activity (a_w). An a_w will be considered safe for a food if adequate data are available that demonstrate that the food at or below the given a_w will not support the growth of undesirable microorganisms.	

Current Food GMPs	Proposed Dietary Supplement GMPs, Including CHPA Comments
(o) Sanitize means to adequately treat food-contact surfaces by a process that is effective in destroying vegetative cells of microorganisms of public health significance, and in substantially reducing numbers of other undesirable microorganisms, but without adversely affecting the product or its safety for the consumer.	(t) "Sanitize" means to adequately treat equipment, containers, or utensils by a process that is effective in destroying vegetative cells of microorganisms of public health significance, and in substantially reducing numbers of other undesirable microorganisms but without adversely affecting the product or its safety for the consumer.
(p) Shall is used to state mandatory requirements.	(u) "Shall" is used to state mandatory requirements.
(q) Should is used to state recommended or advisory procedures or identify recommended equipment.	(v) "Should" is used to state recommended or advisory procedures or identify recommended equipment.
(r) Water activity (a_w) is a measure of the free moisture in a food and is the quotient of the water vapor pressure of the substance divided by the vapor pressure of pure water at the same temperature.	(w) "Water activity (a_w)" is a measure of the free moisture in a dietary ingredient 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.
<p>§ 110.10 Personnel. The plant management shall take all reasonable measures and precautions to ensure the following:</p> <p>(a) Disease control. Any person who, by medical examination or supervisory observation, is shown to have, or appears to have, an illness, open lesion, including boils, sores, or infected wounds, or any other abnormal source of microbial contamination by which there is a reasonable possibility of food, food-contact surfaces, or food-packaging materials becoming contaminated, shall be excluded from any operations which may be expected to result in such contamination until the condition is corrected. Personnel shall be instructed to report such health conditions to their supervisors.</p>	<p>Personnel The plant management shall take all reasonable measures and precautions to assure the following:</p> <p>(a) Disease control. Any person who, by medical examination or supervisory observation, is shown to have, or appears to have, an illness, open lesion, including boils, sores, or infected wounds, or any other abnormal source of microbial contamination by which there is a reasonable possibility of an in-process or finished dietary product becoming adulterated, or processing equipment, utensils or packaging materials becoming contaminated, shall be excluded from any operations which may be expected to result in such adulteration or contamination until the condition is corrected. Personnel shall be instructed to report such health conditions to their supervisors.</p>
(b) Cleanliness. All persons working in direct contact with food, food-contact surfaces, and food-packaging materials shall conform to hygienic practices while on duty to the extent necessary to protect against contamination of food. The methods for maintaining cleanliness include, but are not limited to:	(b) Cleanliness. All persons working in direct contact with raw material, in-process or finished dietary products, processing equipment, utensils or packaging materials shall conform to hygienic practices while on duty to the extent necessary to protect against adulteration or contamination of such materials. The methods for maintaining cleanliness include, but are not limited to:
(1) Wearing outer garments suitable to the operation in a manner that protects against the contamination of food, food-contact surfaces, or food-packaging materials.	(1) Wearing outer garments suitable to the operation in a manner that protects against the adulteration of in-process or finished dietary products, or contamination of processing
(2) Maintaining adequate personal cleanliness.	(2) Maintaining adequate personal cleanliness.
(3) Washing hands thoroughly (and sanitizing if necessary to protect against contamination with undesirable microorganisms) in an adequate hand-washing facility before starting work, after each absence from the work station, and at any other time when the hands may have become soiled or contaminated.	(3) Washing hands thoroughly (and sanitizing if necessary to protect against contamination with undesirable microorganisms) in an adequate hand-washing facility before starting work, after each absence from the work station, and at any other time when the hands may have become soiled or contaminated.
(4) Removing all unsecured jewelry and other objects that might fall into food, equipment, or containers, and removing hand jewelry that cannot be adequately sanitized during periods in which food is manipulated by hand. If such hand jewelry cannot be removed, it may be covered by material which can be maintained in an intact, clean, and sanitary condition and which effectively protects against the contamination by these objects of the food, food-contact surfaces, or food-packaging materials.	(4) Removing all unsecured jewelry and other objects that might fall in raw materials, in-process or finished dietary product, equipment, or containers, and removing hand jewelry that cannot be adequately sanitized during periods in which in-process or finished product is manipulated by hand. If such hand jewelry cannot be removed, it may be covered by material which can be maintained in an intact, clean, and sanitary condition and which effectively protects against the adulteration of dietary products or contamination of processing equipment, utensils or packaging materials.
(5) Maintaining gloves, if they are used in food handling, in an intact, clean, and sanitary condition. The gloves should be of an impermeable material.	(5) Maintaining gloves, if they are used in-process or finished product handling, in an intact, clean, and sanitary condition. The gloves should be of a material that adequately protects the product from contamination.
(6) Wearing, where appropriate, in an effective manner, hair nets, headbands, caps, beard covers, or other effective hair restraints.	(6) Wearing, where appropriate, in an effective manner, hair nets, caps, beard covers, or other effective hair restraints.
(7) Storing clothing or other personal belongings in areas other than	(7) Storing clothing or other personal belongings in areas other than

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where food is exposed or where equipment or utensils are washed	where in-process or finished product is exposed or where processing equipment or utensils are washed
(8) Confining the following to areas other than where food may be exposed or where equipment or utensils are washed: eating food, chewing gum, drinking beverages, or using tobacco.	(8) Confining the following to areas other than where in-process or finished product may be stored or exposed, or where processing equipment or utensils are washed: eating food, chewing gum, drinking beverages, or using tobacco, <u>or using drugs (Rx or OTC) or other dietary supplement products</u>
(9) Taking any other necessary precautions to protect against contamination of food, food-contact surfaces, or food-packaging materials with microorganisms or foreign substances including, but not limited to, perspiration, hair, cosmetics, tobacco, chemicals, and medicines applied to the skin.	(9) Taking any other necessary precautions to protect against: adulteration of raw materials, in-process or finished product, or contamination of processing equipment, utensils or packaging materials with micro-organisms or foreign substances including, but not limited to perspiration, hair, cosmetics, tobacco, chemicals, and medicines applied to the skin.
(c) Education and training. Personnel responsible for identifying sanitation failures or food contamination should have a background of education or experience, or a combination thereof, to provide a level of competency necessary for production of clean and safe food. Food handlers and supervisors should receive appropriate training in proper food handling techniques and food-protection principles and should be informed of the danger of poor personal hygiene and insanitary practices.	(c) Education and training. Each person engaged in the manufacture of a dietary product should have the proper education, training and experience (or any combination thereof) needed to perform the assigned functions. Training should be in the particular operation(s) that the employee performs as they relate to the employee's functions. <u>Employees should also receive training relating to GMPs and sanitary health procedures.</u> Appropriate documentation of training shall be retained by the manufacturer.
(d) Supervision. Responsibility for assuring compliance by all personnel with all requirements of this part shall be clearly assigned to competent supervisory personnel.	(d) Supervision. Responsibility for assuring compliance by all personnel with all requirements of this part shall be clearly assigned to qualified personnel with proper education, training and experience (or any combination thereof).
<p>§ 110.19 Exclusions.</p> <p>(a) The following operations are not subject to this part: Establishments engaged solely in the harvesting, storage, or distribution of one or more "raw agricultural commodities," as defined in section 201(r) of the act, which are ordinarily cleaned, prepared, treated, or otherwise processed before being marketed to the consuming public.</p> <p>(b) FDA, however, will issue special regulations if it is necessary to cover these excluded operations.</p>	<p>Exclusions</p> <p>The following operations are not subject to this part: Establishments engaged solely in the harvesting, storage, or distribution of one or more "raw agricultural commodities," as defined in section 201(r) of the act which are ordinarily cleaned, prepared, treated, or otherwise processed before being marketed to the consuming public.</p>
<p>Subpart B_Buildings and Facilities</p> <p>§ 110.20 Plant and grounds.</p> <p>(a) Grounds. The grounds about a food plant under the control of the operator shall be kept in a condition that will protect against the contamination of food. The methods for adequate maintenance of grounds include, but are not limited to:</p>	<p>Plant and Grounds</p> <p>(a) Grounds. The grounds about a dietary product manufacturing plant under the control of the operator shall be kept in a condition that will protect against the adulteration of dietary products. The methods adequate maintenance of grounds include, but are not limited to:</p>
(1) Properly storing equipment, removing litter and waste, and cutting weeds or grass within the immediate vicinity of the plant buildings or structures that may constitute an attractant, breeding place, or harborage for pests.	(1) Properly storing equipment, removing litter and waste, and cutting weeds or grass within the immediate vicinity of the plant buildings or structures that may constitute an attractant, breeding place or harborage for pests.
(2) Maintaining roads, yards, and parking lots so that they do not constitute a source of contamination in areas where food is exposed.	(2) Maintaining roads, yards, and parking lots so that they do not constitute a source of adulteration in areas where product is exposed.
(3) Adequately draining areas that may contribute contamination to food by seepage, foot-borne filth, or providing a breeding place for pests.	(3) Adequately draining areas that may contribute to product adulteration by seepage, foot-borne filth, or providing a breeding place for pests.
(4) Operating systems for waste treatment and disposal in an adequate manner so that they do not constitute a source of contamination in areas where food is exposed. If the plant grounds are bordered by grounds not under the operator's control and not maintained in the manner described in paragraph (a) (1) through (3) of this section, care shall be exercised in the plant by inspection, extermination, or other means to exclude pests, dirt, and filth that may be a source of food contamination.	(4) Operating systems for waste treatment and disposal in an adequate manner so that they do not constitute a source of adulteration in areas where product is exposed. If the plant grounds are bordered by grounds not under the operator's control and not maintained in the manner described in paragraph (a)(1) through (3) of this section, care shall be exercised in the plant by inspection, extermination, or other means to exclude pests, dirt, and filth that may be a source of product adulteration.
(b) Plant construction and design. Plant buildings and structures shall be	(b) Plant construction and design. Plant buildings and structures shall be

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suitable in size, construction, and design to facilitate maintenance and sanitary operations for food-manufacturing purposes. The plant and facilities shall.	be suitable in size, construction, and design to facilitate maintenance, cleaning and sanitary operations for dietary product manufacturing purposes and to prevent mixups between different raw materials and products. The plant and facilities shall.
(1) Provide sufficient space for such placement of equipment and storage of materials as is necessary for the maintenance of sanitary operations and the production of safe food.	(1) Provide sufficient space for such placement of equipment and storage of materials as is necessary for the prevention of mixups, maintenance of sanitary operations and the production of safe dietary products.
(2) Permit the taking of proper precautions to reduce the potential for contamination of food, food-contact surfaces, or food-packaging materials with microorganisms, chemicals, filth, or other extraneous material. The potential for contamination may be reduced by adequate food safety controls and operating practices or effective design, including the separation of operations in which contamination is likely to occur, by one or more of the following means: location, time, partition, air flow, enclosed systems, or other effective means.	(2) Permit the taking of proper precautions to reduce the potential for mixups or adulteration of in-process or finished dietary product, or contamination of processing equipment, utensils or packaging materials with microorganisms, chemicals, filth, or other extraneous material. The potential for mixups and product adulteration may be reduced by adequate product safety controls and operating practices or effective design, including the separation of operations in which contamination is likely to occur, by one or more of the following means: Location, time, partition, air flow, enclosed systems, or other effective means.
(3) Permit the taking of proper precautions to protect food in outdoor bulk fermentation vessels by any effective means, including: (i) Using protective coverings. (ii) Controlling areas over and around the vessels to eliminate harborage for pests. (iii) Checking on a regular basis for pests and pest infestation. (iv) Skimming the fermentation vessels, as necessary.	(3) Permit the taking of proper precautions to protect dietary ingredients or dietary supplements in outdoor bulk fermentation vessels by any effective means, including: (i) Using protective coverings (ii) Controlling areas over and around the vessels to eliminate harborage for pests. (iii) Checking on a regular basis for pests and pest infestation (iv) Skimming the fermentation vessels, as necessary.
(4) Be constructed in such a manner that floors, walls, and ceilings may be adequately cleaned and kept clean and kept in good repair; that drip or condensate from fixtures, ducts and pipes does not contaminate food, food-contact surfaces, or food-packaging materials; and that aisles or working spaces are provided between equipment and walls and are adequately unobstructed and of adequate width to permit employees to perform their duties and to protect against contaminating food or food-contact surfaces with clothing or personal contact.	(4) Be constructed in such a manner that floors, walls, and ceilings may be adequately cleaned and kept clean and kept in good repair; that drip or condensate from fixtures, ducts and pipes does not adulterate raw materials, in-process or finished dietary products, or contaminate product containers, utensils or packaging materials; and that aisles or working spaces are provided between equipment and walls and are adequately unobstructed and of adequate width to permit employees to perform their duties and to protect against adulterating in-process or finished product, or contaminating processing equipment with clothing or personal contact.
(5) Provide adequate lighting in hand-washing areas, dressing and locker rooms, and toilet rooms and in all areas where food is examined, processed, or stored and where equipment or utensils are cleaned; and provide safety-type light bulbs, fixtures, skylights, or other glass suspended over exposed food in any step of preparation or otherwise protect against food contamination in case of glass breakage.	(5) Provide adequate lighting in hand-washing areas, dressing and locker rooms, and toilet rooms and in all areas where product is examined, processed, or stored and where equipment or utensils are cleaned; and provide safety-type light bulbs, fixtures, sky-lights, or other glass suspended over exposed product in any step of preparation or otherwise protect against product adulteration in case of glass breakage.
(6) Provide adequate ventilation or control equipment to minimize odors and vapors (including steam and noxious fumes) in areas where they may contaminate food; and locate and operate fans and other air-blowing equipment in a manner that minimizes the potential for contaminating food, food-packaging materials, and food-contact surfaces.	(6) Provide adequate ventilation or control equipment to maintain adequate control over microorganisms, dust, humidity, and temperature, when appropriate, for the manufacture of dietary product to minimize odors and vapors (including steam and noxious fumes) in areas where they may adulterate dietary products; and locate and operate fans and other air-blowing equipment in a manner that minimizes the potential for adulterating raw materials, in-process or finished dietary products, or contaminating processing equipment, utensils or packaging materials.
(7) Provide, where necessary, adequate screening or other protection against pests.	(7) Provide, where necessary, adequate screening or other protect against pests.
<p>§ 110.35 Sanitary operations.</p> <p>(a) General maintenance. Buildings, fixtures, and other physical facilities of the plant shall be maintained in a sanitary condition and shall be kept in repair sufficient to prevent food from becoming adulterated within the meaning of the act.</p>	<p>Sanitation of Buildings and Facilities</p> <p>(a) General maintenance. Buildings, fixtures, and other physical facilities of the plant shall be maintained in a sanitary condition and shall be kept in repair sufficient to prevent raw materials, in-process finished dietary products from becoming adulterated within the mean of the act.</p>
(b) Substances used in cleaning and sanitizing; storage of toxic	(b) Cleaning and sanitizing materials.

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materials	
<p>(1) Cleaning compounds and sanitizing agents used in cleaning and sanitizing procedures shall be free from undesirable microorganisms and shall be safe and adequate under the conditions of use. Compliance with this requirement may be verified by any effective means including purchase of these substances under a supplier's guarantee or certification, or examination of these substances for contamination. Only the following toxic materials may be used or stored in a plant where food is processed or exposed:</p> <p>(i) Those required to maintain clean and sanitary conditions;</p> <p>(ii) Those necessary for use in laboratory testing procedures;</p> <p>(iii) Those necessary for plant and equipment maintenance and operation; and</p> <p>(iv) Those necessary for use in the plant's operations.</p>	<p>(1) Cleaning compounds and sanitizing agents used in cleaning and sanitizing procedures shall be free from undesirable microorganisms and shall be safe and adequate under the conditions of use. Compliance with this requirement may be verified by any effective means including purchase of these substances under a supplier's guarantee or certification, or examination of these substances for contamination. Only the following toxic materials may be used or stored in a plant where product is processed or exposed:</p> <p>(i) Those required to maintain clean and sanitary conditions;</p> <p>(ii) Those necessary for use in laboratory testing procedures;</p> <p>(iii) Those necessary for plant and equipment maintenance and operation; and</p> <p>(iv) Those necessary for use in the plant's operations.</p>
<p>(2) Toxic cleaning compounds, sanitizing agents, and pesticide chemicals shall be identified, held, and stored in a manner that protects against contamination of food, food-contact surfaces, or food-packaging materials. All relevant regulations promulgated by other Federal, State, and local government agencies for the application, use, or holding of these products should be followed.</p>	<p>(2) Toxic cleaning compounds, sanitizing agents, and pesticide chemicals shall be identified, used, held, and stored in a manner that protects against adulteration of raw materials, in-process or finished product, or contamination of processing equipment or packaging materials. All relevant regulations promulgated by other Federal, State, and local government agencies for the application, use or holding of these products should be followed. Rodenticides, insecticides, and fungicides should be registered and used in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act.</p>
<p>(c) Pest control. No pests shall be allowed in any area of a food plant. Guard or guide dogs may be allowed in some areas of a plant if the presence of the dogs is unlikely to result in contamination of food, food-contact surfaces, or food-packaging materials. Effective measures shall be taken to exclude pests from the processing areas and to protect against the contamination of food on the premises by pests. The use of insecticides or rodenticides is permitted only under precautions and restrictions that will protect against the contamination of food, food-contact surfaces, and food-packaging materials.</p>	<p>(c) Pest control. No pests shall be allowed in any area of a dietary product manufacturing plant. Effective measures shall be taken to exclude pests from the processing areas and to protect against the adulteration of product on the premises by pests. The use of insecticides or rodenticides is permitted only under precautions and restrictions that will protect against the adulteration of raw materials, in-process or finished product, or contamination of processing equipment, utensils or packaging materials.</p>
<p>§ 110.37 Sanitary facilities and controls. Each plant shall be equipped with adequate sanitary facilities and accommodations including, but not limited to:</p>	
<p>(a) Water supply. The water supply shall be sufficient for the operations intended and shall be derived from an adequate source. Any water that contacts food or food-contact surfaces shall be safe and of adequate sanitary quality. Running water at a suitable temperature, and under pressure as needed, shall be provided in all areas where required for the processing of food, for the cleaning of equipment, utensils, and food-packaging materials, or for employee sanitary facilities.</p>	<p>(d) Water supply. Potable water, <u>as a minimum quality standard</u>, at a suitable temperature, and under pressure as needed, shall be provided in all areas where required for the processing of dietary products, for cleaning of processing equipment, utensils, and packaging material for employee sanitary facilities. Any water that contacts in-process or finished dietary products, utensils or processing equipment shall meet the standards prescribed in the Environmental Protection Agency's Primary Drinking Water Regulations (40 CFR part 141).</p>
<p>(b) Plumbing. Plumbing shall be of adequate size and design and adequately installed and maintained to:</p>	<p>(e) Plumbing. Plumbing shall be of adequate size and design and adequately installed and maintained to:</p>
<p>(1) Carry sufficient quantities of water to required locations throughout the plant.</p>	<p>(1) Carry sufficient quantities of water to required locations throughout the plant.</p>
<p>(2) Properly convey sewage and liquid disposable waste from the plant.</p>	<p>(2) Properly convey sewage and liquid disposable waste from the plant.</p>
<p>(3) Avoid constituting a source of contamination to food, water supplies, equipment, or utensils or creating an unsanitary condition.</p>	<p>(3) Avoid constituting a source of adulteration to product, or contamination of water supplies, processing equipment, or utensils creating an unsanitary condition.</p>
<p>(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.</p>	<p>(4) Provide adequate floor drainage or other appropriate means water removal 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.</p>
<p>(5) Provide that there is not backflow from, or cross-connection between,</p>	<p>(5) Provide that there is not backflow from, or crossconnection</p>

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piping systems that discharge waste water or sewage and piping systems that carry water for food or food manufacturing	between piping systems that discharge waste water or sewage and piping systems that carry water used for the manufacture of dietary products.
(c) Sewage disposal. Sewage disposal shall be made into an adequate sewerage system or disposed of through other adequate means.	(f) Sewage disposal. Sewage disposal shall be made into an adequate sewerage system or disposed of through other adequate means.
(d) Toilet facilities. Each plant shall provide its employees with adequate, readily accessible toilet facilities. Compliance with this requirement may be accomplished by:	(g) Toilet facilities. Each plant shall provide its employees with adequate, readily accessible toilet facilities. Compliance with this requirement may be accomplished by
(1) Maintaining the facilities in a sanitary condition.	(1) Maintaining the facilities in a sanitary condition
(2) Keeping the facilities in good repair at all times.	(2) Keeping the facilities in good repair at all times
(3) Providing self-closing doors.	(3) Providing self-closing doors
(4) Providing doors that do not open into areas where food is exposed to airborne contamination, except where alternate means have been taken to protect against such contamination (such as double doors or positive air-flow systems).	(4) Providing doors that do not open into areas where dietary product is exposed to airborne contamination, except where alternate means have been taken to protect against such contamination (such as double doors or positive air-flow systems).
(e) Hand-washing facilities. Hand-washing facilities shall be adequate and convenient and be furnished with running water at a suitable temperature. Compliance with this requirement may be accomplished by providing:	(h) Hand-washing facilities. Hand-washing facilities shall be adequate and convenient and be furnished with running water at a suitable temperature. Compliance with this requirement may be accomplished by providing:
(1) Hand-washing and, where appropriate, hand-sanitizing facilities at each location in the plant where good sanitary practices require employees to wash and/or sanitize their hands.	(1) Hand-washing and, where appropriate, hand-sanitizing facilities each location in the plant where good sanitary practices require employees to wash and/or sanitize their hands.
(2) Effective hand-cleaning and sanitizing preparations.	(2) Effective hand-cleaning and sanitizing preparations.
(3) Sanitary towel service or suitable drying devices.	(3) Air driers, sanitary towel service or suitable drying devices.
(4) Devices or fixtures, such as water control valves, so designed and constructed to protect against recontamination of clean, sanitized hands.	(4) Devices or fixtures, such as water control valves, so designed constructed to protect against recontamination of clean, sanitized hands.
(5) Readily understandable signs directing employees handling unprotected food, unprotected food-packaging materials, or food-contact surfaces to wash and, where appropriate, sanitize their hands before they start work, after each absence from post of duty, and when their hands may have become soiled or contaminated. These signs may be posted in the processing room(s) and in all other areas where employees may handle such food, materials, or surfaces.	(5) Readily understandable signs directing employees handling unprotected product, packaging materials, utensils or processing equipment to wash and, where appropriate, sanitize their hands before they start work, after each absence from post of duty, and when the hands may have become soiled or contaminated. These signs may be posted in the processing room(s) and in all other areas where employees may handle such products, materials, utensils or equipment.
(6) Refuse receptacles that are constructed and maintained in a manner that protects against contamination of food.	(6) Refuse receptacles that are constructed and maintained in a manner that protects against adulteration of dietary products.
(f) Rubbish and offal disposal. Rubbish and any offal shall be so conveyed, stored, and disposed of as to minimize the development of odor, minimize the potential for the waste becoming an attractant and harborage or breeding place for pests, and protect against contamination of food, food-contact surfaces, water supplies, and ground surfaces.	(i) Rubbish disposal. Rubbish shall be so conveyed, stored, and disposed of as to minimize the development of odor, minimize the potential for the waste becoming an attractant and harborage or breeding place for pests, and protect against adulteration of raw materials, in-process or finished dietary products, or contamination utensils, processing equipment, water supplies, and ground surface.
	(j) Supervision. Overall sanitation of the plant shall be under the supervision of one or more individuals qualified by education, experience and training (or any combination thereof) assigned responsibility for assuring that sanitation procedures are accomplished.
Subpart C_Equipment § 110.40 Equipment and utensils.	Equipment and Utensils (a) Design and construction.
(a) All plant equipment and utensils shall be so designed and of such material and workmanship as to be adequately cleanable, and shall be properly maintained.	(1) All plant equipment and utensils shall be so designed and of material and workmanship as to be adequately cleanable, and shall be properly maintained.

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The design, construction, and use of equipment and utensils shall preclude the adulteration of food with lubricants, fuel, metal fragments, contaminated water, or any other contaminants.	(2) The design, construction and use of equipment and utensils shall preclude the adulteration of raw materials, packaging materials, in-process materials or finished product with lubricants, fuel, metal fragments, contaminated water, or any other contaminants.
All equipment should be so installed and maintained as to facilitate the cleaning of the equipment and of all adjacent spaces. Food-contact surfaces shall be corrosion-resistant when in contact with food. They shall be made of nontoxic materials and designed to withstand the environment of their intended use and the action of food, and, if applicable, cleaning compounds and sanitizing agents. Food-contact surfaces shall be maintained to protect food from being contaminated by any source, including unlawful indirect food additives.	(3) All equipment should be so installed and maintained as to facilitate the cleaning of the equipment and of all adjacent spaces. Processing equipment and utensils shall be corrosion-resistant when in contact with raw materials, in-process or finished dietary product. They shall be made of nontoxic materials and designed to withstand the environment of their intended use and the action of dietary products and, if applicable, cleaning compounds and sanitizing agents. Processing equipment and utensils shall be maintained to protect dietary products from being adulterated by any source.
(b) Seams on food-contact surfaces shall be smoothly bonded or maintained so as to minimize accumulation of food particles, dirt, and organic matter and thus minimize the opportunity for growth of microorganisms.	(4) Seams on utensils and processing equipment shall be smoothly bonded or maintained so as to minimize accumulation of product, dirt and organic matter and thus minimize the opportunity for growth of microorganisms.
(c) Equipment that is in the manufacturing or food-handling area and that does not come into contact with food shall be so constructed that it can be kept in a clean condition.	(5) Equipment that is <u>used</u> in the manufacturing or product handling area and that does not come into contact with a dietary product shall be so constructed that it can be kept in a clean condition.
(d) Holding, conveying, and manufacturing systems, including gravimetric, pneumatic, closed, and automated systems, shall be of a design and construction that enables them to be maintained in an appropriate sanitary condition.	(6) Holding, conveying, and manufacturing systems, including gravimetric, pneumatic, closed, and automated systems, shall be of a design and construction that enables them to be maintained in an appropriate clean condition.
(e) Each freezer and cold storage compartment used to store and hold food capable of supporting growth of microorganisms shall be fitted with an indicating thermometer, temperature-measuring device, or temperature-recording device so installed as to show the temperature accurately within the compartment, and should be fitted with an automatic control for regulating temperature or with an automatic alarm system to indicate a significant temperature change in a manual operation.	(7) Each freezer and cold storage compartment used to store and hold a dietary product capable of supporting growth of microorganisms shall be fitted with an indicating thermometer, temperature-measuring device, or temperature-recording device so installed as to show the temperature accurately within the compartment, and should be fitted with an automatic control for regulating temperature or with an automatic alarm system to indicate a significant temperature change in a manual operation.
(f) Instruments and controls used for measuring, regulating, or recording temperatures, pH, acidity, water activity, or other conditions that control or prevent the growth of undesirable microorganisms in food shall be accurate and adequately maintained, and adequate in number for their designated uses.	(8) Instruments and controls used in the manufacture, processing, packing or holding dietary products, including instruments and control used for measuring, regulating, or recording temperatures, pH, acidity, water activity, or other conditions that control or prevent the growth of undesirable microorganisms in such products shall be accurate and adequately maintained, and adequate in number for their designated uses.
(g) Compressed air or other gases mechanically introduced into food or used to clean food-contact surfaces or equipment shall be treated in such a way that food is not contaminated with unlawful indirect food additives.	(9) Compressed air or other gases mechanically introduced into a dietary product or used to clean equipment or utensils shall be treated in such a way that dietary ingredients or dietary supplements are not adulterated.
§ 110.35 Sanitary operations	(b) Sanitation of equipment and utensils.
... Cleaning and sanitizing of utensils and equipment shall be conducted in a manner that protects against contamination of food, food-contact surfaces, or food-packaging materials.	(1) Cleaning and sanitizing of utensils and equipment shall be conducted in a manner that protects against adulteration of raw materials, in-process or finished dietary product, processing equipment, utensils or packaging materials.
(d) Sanitation of food-contact surfaces. All food-contact surfaces, including utensils and food-contact surfaces of equipment, shall be cleaned as frequently as necessary to protect against contamination of food.	(2) All utensils and processing equipment shall be cleaned as frequently as necessary to protect against product adulteration.
(1) Food-contact surfaces used for manufacturing or holding low-moisture food shall be in a dry, sanitary condition at the time of use. When the surfaces are wet-cleaned, they shall, when necessary, be sanitized and thoroughly dried before subsequent use.	(3) Utensils and processing equipment used for manufacturing or holding of dry dietary products shall be in a dry, sanitary condition at time of use. When the surfaces are wet-cleaned, they shall, when necessary, be sanitized and thoroughly dried before subsequent use.

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(2) In wet processing when cleaning is necessary to protect against the introduction of microorganisms into food, all food-contact surfaces shall be cleaned and sanitized before use and after any interruption during which the food-contact surfaces may have become contaminated. Where equipment and utensils are used in a continuous production operation, the utensils and food-contact surfaces of the equipment shall be cleaned and sanitized as necessary.	(4) In wet processing when cleaning is necessary to protect against the introduction of microorganisms into a dietary product, all utensils and processing equipment shall be cleaned and sanitized as appropriate before use and after any interruption during which the utensils or processing equipment may have become contaminated. Where equipment and utensils are used in a continuous production operation or in back-to-back operations involving different batches of the same products, the utensils and product-contact surfaces of the equipment shall be cleaned and sanitized as appropriate.
(3) Non-food-contact surfaces of equipment used in the operation of food plants should be cleaned as frequently as necessary to protect against contamination of food.	(5) Nonproduct-contact surfaces of equipment should be cleaned as frequently as necessary to protect against product adulteration.
(4) Single-service articles (such as utensils intended for one-time use, paper cups, and paper towels) should be stored in appropriate containers and shall be handled, dispensed, used, and disposed of in a manner that protects against contamination of food or food-contact surfaces.	(6) Single-service articles (such as utensils intended for one-time use, paper cups, and paper towels) should be stored in appropriate containers and shall be handled, dispensed, used, and disposed of in a manner that protects against adulteration of dietary products, and contamination of utensils and processing equipment.
(5) Sanitizing agents shall be adequate and safe under conditions of use. Any facility, procedure, or machine is acceptable for cleaning and sanitizing equipment and utensils if it is established that the facility, procedure, or machine will routinely render equipment and utensils clean and provide adequate cleaning and sanitizing treatment.	(7) Sanitizing agents shall be adequate and safe under conditions of use. Any facility, procedure, or machine is acceptable for cleaning and sanitizing equipment and utensils if it is established that the facility, procedure, or machine will routinely render equipment and utensils clean and provide adequate cleaning and sanitizing treatment.
(e) Storage and handling of cleaned portable equipment and utensils. Cleaned and sanitized portable equipment with food-contact surfaces and utensils should be stored in a location and manner that protects food-contact surfaces from contamination.	(8) Cleaned and sanitized portable equipment with product-contact surfaces and utensils should be stored in a location and manner that protects product-contact surfaces from contamination.
<p>§ 110.80 (b) Manufacturing operations.</p> <p>(1) Equipment and utensils and finished food containers shall be maintained in an acceptable condition through appropriate cleaning and sanitizing, as necessary. Insofar as necessary, equipment shall be taken apart for thorough cleaning.</p>	(9) Equipment and utensils and finished product containers shall be maintained in an acceptable condition through appropriate cleaning and sanitizing, as necessary. Insofar as necessary, equipment shall be taken apart for thorough cleaning.
	(10) Written procedures shall be established and followed for cleaning and maintaining equipment and utensils used in the manufacture of dietary products.
	(11) A written record of major equipment cleaning and use shall be maintained in individual equipment logs that show the date, product lot number of each batch processed. The persons performing the cleaning shall record in the log that the work was performed. Entries in the log should be in chronological order.
(7) Equipment, containers, and utensils used to convey, hold, or store raw materials, work-in-process, rework, or food shall be constructed, handled, and maintained during manufacturing or storage in a manner that protects against contamination.	(12) Equipment, containers, and utensils used to convey, hold, or store raw materials, in-process material, rework, or finished product shall be constructed, handled, and maintained during manufacturing storage in a manner that protects against contamination.
<p>§ 110.80 Processes and controls.</p> <p>... Appropriate quality control operations shall be employed to ensure that food is suitable for human consumption and that food-packaging materials are safe and suitable.</p>	<p>Quality Control and Laboratory Operations</p> <p>Appropriate quality control operations shall be employed to assure that dietary products conform to appropriate standards of purity, quality and composition, and that packaging materials are safe and suitable for their intended purpose.</p>
	(a) Quality control unit. (1) There shall be a quality control unit that has the responsibility authority to:
	(i) Approve or reject all procedures, specifications, controls, tests and examinations, or deviations from them, that impact the purity, quality and composition of a dietary ingredient or dietary supplement.
	(ii) Approve or reject all raw materials, packaging materials, label and finished dietary products, including products manufactured.

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	<p>processed, packed, or held under contract by another company, based on adequate determination of conformance to established specifications; and</p> <p>(iii) Assure that completed production records are reviewed as appropriate. Quality control shall be responsible for evaluation of errors committed in the manufacture of a product and shall have the final authority to determine if the error may be corrected in such manner that the product can be approved for distribution or must be destroyed. Such evaluations and their resolution must be documented and maintained with and/or cross referenced in the batch production record.</p>
	<p>(2) Adequate laboratory facilities should be available, as needed, to the quality control unit.</p>
	<p>(3) The responsibilities and procedures applicable to the quality control unit shall be established in writing and followed.</p>
	<p>(b) Laboratory records. Laboratory records shall be maintained and shall include complete data derived from all specified tests.</p>
	<p>(c) Expiration dating.</p>
	<p>(1) Whenever a shelf life or an expiration date for a dietary ingredient or dietary supplement, whichever is appropriate, bears an expiration date, such date shall be supported by data and rationale to reasonably assure that the product meets established specifications at the expiration specified date. Testing or inspection of the product shall be appropriate to the particular dietary ingredient or dietary supplement product.</p>
	<p>(2) Appropriate accelerated stability studies or data from similar product formulations may be used for an initial determination of shelf life. Product shelf life shall be confirmed and may be extended on the basis of real time studies on product stored under labeled storage conditions.</p>
	<p>Production and Process Controls (a) Master production and control records.</p>
	<p>(1) To assure uniformity from batch to batch, a master production and control record shall be prepared for the manufacture of each dietary ingredient and dietary supplement, and shall be reviewed and approved by the quality control unit.</p>
	<p>(2) Master production and control records shall include, as appropriate.</p> <p>(i) A complete list of raw materials used in the manufacture of a dietary product, designated by names or codes sufficiently specific to indicate any special quality characteristic(s).</p> <p>(ii) An accurate statement of the weight or measure of each raw material used in the manufacture of a dietary product. Each batch shall be formulated with the intent to provide not less than 100 percent of each claimed dietary ingredient.</p> <p>(iii) For dietary supplements, the name and weight or measure of each dietary ingredient per unit or portion or per unit of weight or measure of the supplement.</p> <p>(iv) A statement concerning any calculated excess of dietary ingredient contained in a dietary supplement finished product intended for consumption by a consumer.</p> <p>(v) A statement of the total weight or measure of any dietary supplement unit.</p> <p>(vi) A statement of theoretical weight or measure of a dietary ingredient or dietary supplement expected at the conclusion of manufacture, including the maximum and minimum percentages of theoretical yield beyond which investigation is required.</p> <p>(vii) A description of the product container(s), closure(s), and other packaging materials, including positive identification of all finished product packaging labeling used.</p>

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	(viii) Manufacturing and control instructions designed to assure that the dietary product has the purity, composition, and quality as represented to possess
	(b) Batch production and control records
	(1) Individual batch production and control records shall be prepared and followed for each batch of dietary product produced and shall include complete information relating to the production and control of each batch.
	(2) These records shall be an accurate reproduction of the appropriate master production and control record and shall include documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished, including: <ul style="list-style-type: none"> (i) Dates; (ii) Identity of individual major equipment and lines used; (iii) Specific identification, including lot number, of each raw material or in-process material used; (iv) Weight or measure of each raw material used in the course of processing; (v) Quality control results; (vi) Inspection of the packaging and labeling area; (vii) A statement of the actual yield at the conclusion of manufacture and a statement of the percentage of theoretical yield, as appropriate possible; (viii) Label control records, including specimens, copies, or record of all labels used; (ix) Description of product containers and closures used; and (x) Any special notes of investigations or deviations from the described process.
	(3) Any deviation from written, approved specifications, standards, test procedures, or other laboratory control mechanisms shall be recorded and justified.
§ 110.80 (a) Raw materials and other ingredients.	(c) Handling and storage of raw materials, in-process materials and rework
(1) Raw materials and other ingredients shall be inspected and segregated or otherwise handled as necessary to ascertain that they are clean and suitable for processing into food and shall be stored under conditions that will protect against contamination and minimize deterioration. ... Containers and carriers of raw materials should be inspected on receipt to ensure that their condition has not contributed to the contamination or deterioration of food. (7) Liquid or dry raw materials and other ingredients received and stored in bulk form shall be held in a manner that protects against contamination.	(1) Raw materials, in-process materials and rework shall be inspected and segregated or otherwise handled as necessary to ascertain that they are clean and suitable for processing into dietary products and shall be stored under conditions that will protect against adulteration and minimize deterioration. Containers of raw materials should be inspected on receipt to assure that their condition has not contributed to the adulteration or deterioration of the contents. Liquid or dry raw materials and other ingredients received and stored in bulk form shall be held in a manner that protects against contamination.
Raw materials shall be washed or cleaned as necessary to remove soil or other contamination. Water used for washing, rinsing, or conveying food shall be safe and of adequate sanitary quality. Water may be reused for washing, rinsing, or conveying food if it does not increase the level of contamination of the food.	(2) Raw agricultural materials that contain soil or other contaminants shall be washed or cleaned as necessary. Water used for washing, rinsing, or conveying raw agricultural materials shall be safe and of adequate sanitary quality. Notwithstanding the general requirement for potable water, water may be reused for washing, rinsing, or conveying raw agricultural materials, if it does not increase the level of contamination of the such materials.
(5) Raw materials, other ingredients, and rework shall be held in bulk, or in containers designed and constructed so as to protect against contamination and shall be held at such temperature and relative humidity and in such a manner as to prevent the food from becoming adulterated within the meaning of the act. Material scheduled for rework shall be identified as such.	(3) Raw materials, in-process materials, and rework shall be held in bulk, or in containers designed and constructed so as to protect against adulteration and shall be held at such temperature and relative humidity and in such a manner as to prevent a dietary ingredient or dietary supplement from becoming adulterated within the meaning of the act. Material scheduled for rework shall be identified as such.
(6) Frozen raw materials and other ingredients shall be kept frozen. If	(4) Frozen raw materials and other ingredients shall be kept frozen

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thawing is required prior to use. It shall be done in a manner that prevents the raw materials and other ingredients from becoming adulterated within the meaning of the act.	thawing is required prior to use. It shall be done in a manner that prevents the raw materials and other ingredients from becoming adulterated within the meaning of the act.
	(5) Written procedures shall be established and followed describing the receipt, identification, examination, handling, sampling, testing and approval or rejection of raw materials.
	(6) Each lot of raw material shall be identified with a distinctive lot number and shall be appropriately controlled according to its status (e.g., quarantined, approved, rejected).
<p>(4) Raw materials, other ingredients, and rework susceptible to contamination with pests, undesirable microorganisms, or extraneous material shall comply with applicable Food and Drug Administration regulations, guidelines, and defect action levels for natural or unavoidable defects if a manufacturer wishes to use the materials in manufacturing food. Compliance with this requirement may be verified by any effective means, including purchasing the materials under a supplier's guarantee or certification, or examination of these materials for contamination.</p> <p>(2) Raw materials and other ingredients shall either not contain levels of microorganisms that may produce food poisoning or other disease in humans, or they shall be pasteurized or otherwise treated during manufacturing operations so that they no longer contain levels that would cause the product to be adulterated within the meaning of the act. Compliance with this requirement may be verified by any effective means, including purchasing raw materials and other ingredients under a supplier's guarantee or certification.</p>	<p>(7) Raw material samples shall be examined and tested as follows:</p> <p>(i) Each lot of raw material, in-process material, and rework that is liable to adulteration with filth, insect infestation, or other visually evident extraneous material shall be examined against established specifications for such adulteration, and shall comply with any applicable Food and Drug Administration regulations and guidelines. In lieu of such examination by the manufacturer, a guarantee or certification of examination may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's examination.</p> <p>(ii) Each lot of a raw material that is liable to microbiological contamination that is objectionable in view of its intended use shall be subjected to microbiological tests before use. Raw materials shall either not contain levels of microorganisms that may produce food poisoning or other disease in humans, or they shall be otherwise treated during manufacturing operations so that they no longer contain levels that would cause the product to be adulterated within the meaning of the act. In lieu of such testing by the manufacturer, a guarantee or certification of analysis may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's analyses.</p>
<p>(3) Raw materials and other ingredients susceptible to contamination with aflatoxin or other natural toxins shall comply with current Food and Drug Administration regulations, guidelines, and action levels for poisonous or deleterious substances before these materials or ingredients are incorporated into finished food. Compliance with this requirement may be accomplished by purchasing raw materials and other ingredients under a supplier's guarantee or certification, or may be verified by analyzing these materials and ingredients for aflatoxins and other natural toxins.</p>	<p>(iii) Raw materials and other ingredients susceptible to adulteration with aflatoxin or other natural toxins shall comply with current Food and Drug Administration regulations, guidelines, and action levels for poisonous or deleterious substances before these materials or ingredients are incorporated into a finished dietary ingredient or dietary supplement. Compliance with this requirement may be accomplished by analyzing these materials and ingredients for aflatoxins and other natural toxins or, in lieu of such testing by the manufacturer, a guarantee or certification of analysis may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's analyses.</p> <p>(iv) Each lot of raw material shall undergo at least one test by the manufacturer to verify its identity. Such tests may include any appropriate test with sufficient specificity to determine identity, including chemical and laboratory tests, gross organoleptic analysis, microscopic identification, or analysis of constituent markers.</p> <p>(v) Each lot of raw material shall be tested for conformity with all other established specifications. In lieu of such testing by the manufacturer, a guarantee or certification of analysis may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's analyses.</p>
	(8) Approved raw materials shall be rotated so that the oldest approved stock is used first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.
	(9) Raw materials subject to degradation shall be retested or reexamined and approved or rejected by the quality control unit at specified time in storage or after exposure to air, heat, or other conditions that are likely to adversely affect the purity, quality, or composition of the raw material.
	(10) Rejected raw materials, shall be identified and controlled u

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	system that prevents their use in manufacturing or processing operations for which they are unsuitable
§ 110.80(b) Manufacturing operations.	(d) Manufacturing operations.
	(1) All operations in the receiving, inspecting, transporting, segregating, preparing, manufacturing, packaging, and storing of dietary products shall be conducted in accordance with adequate sanitation principles.
	(2) All reasonable precautions shall be taken to assure that production procedures do not contribute adulteration from any source. Chemical, microbial, or extraneous-material testing procedures shall be used where necessary to identify sanitation failures or possible product adulteration.
	(3) All product that has become contaminated to the extent that it is adulterated within the meaning of the act shall be rejected, or if permissible, treated or processed to eliminate the contamination.
<p>(2) All food manufacturing, including packaging and storage, shall be conducted under such conditions and controls as are necessary to minimize the potential for the growth of microorganisms, or for the contamination of food.</p> <p>One way to comply with this requirement is careful monitoring of physical factors such as time, temperature, humidity, aw, pH, pressure, flow rate, and manufacturing operations such as freezing, dehydration, heat processing, acidification, and refrigeration to ensure that mechanical breakdowns, time delays, temperature fluctuations, and other factors do not contribute to the decomposition or contamination of food.</p>	<p>(4) All product manufacturing, including packaging and storage, shall be conducted under such conditions and controls as are necessary to minimize the potential for the growth of microorganisms, or for the adulteration of raw materials, in-process materials and finished product</p>
<p>(3) Food that can support the rapid growth of undesirable microorganisms, particularly those of public health significance, shall be held in a manner that prevents the food from becoming adulterated within the meaning of the act. Compliance with this requirement may be accomplished by any effective means, including:</p> <p>(i) Maintaining refrigerated foods at 45 °F (7.2 °C) or below as appropriate for the particular food involved.</p> <p>(ii) Maintaining frozen foods in a frozen state.</p> <p>(iii) Maintaining hot foods at 140 °F (60 °C) or above.</p> <p>(iv) Heat treating acid or acidified foods to destroy mesophilic microorganisms when those foods are to be held in hermetically sealed containers at ambient temperatures.</p>	
<p>(4) Measures such as sterilizing, irradiating, pasteurizing, freezing, refrigerating, controlling pH or controlling a_w that are taken to destroy or prevent the growth of undesirable microorganisms, particularly those of public health significance, shall be adequate under the conditions of manufacture, handling, and distribution to prevent food from being adulterated within the meaning of the act.</p>	<p>(5) Measures such as sterilizing, irradiating, pasteurizing, freezing, refrigerating, controlling pH or controlling water activity (a_w) that are taken to destroy or prevent the growth of undesirable microorganisms, particularly those of public health significance, shall be adequate under the conditions of manufacture, handling, and distribution to prevent dietary products from being adulterated within the meaning of the act.</p>
<p>(5) Work-in-process shall be handled in a manner that protects against contamination.</p>	<p>(6) Work-in-process shall be handled in a manner that protects against adulteration.</p>
<p>(6) Effective measures shall be taken to protect finished food from contamination by raw materials, other ingredients, or refuse. When raw materials, other ingredients, or refuse are unprotected, they shall not be handled simultaneously in a receiving, loading, or shipping area if that handling could result in contaminated food. Food transported by conveyor shall be protected against contamination as necessary.</p>	<p>(7) Effective measures shall be taken to protect finished dietary ingredients and dietary supplements from adulteration by raw materials, in-process materials or refuse. When raw materials, in-process materials or refuse are unprotected, they shall not be handled simultaneously in a receiving, loading, or shipping area if that handling could result in adulterated dietary products. Dietary ingredients and dietary supplements transported by conveyor shall be protected against adulteration as necessary.</p>
	<p>(8) All raw material containers, compounding and storage containers, processing lines and major equipment used during the production of</p>

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	batch shall be properly identified at all times to indicate the contents and when necessary, the phase of processing of the batch.
(8) Effective measures shall be taken to protect against the inclusion of metal or other extraneous material in food. Compliance with this requirement may be accomplished by using sieves, traps, magnets, electronic metal detectors, or other suitable effective means.	(9) Effective measures shall be taken as necessary to protect against the inclusion of metal or other extraneous material in product. Compliance with this requirement may be accomplished by using sieves, traps, magnets, electronic metal detectors, or other suitable effective means.
(9) Food, raw materials, and other ingredients that are adulterated within the meaning of the act shall be disposed of in a manner that protects against the contamination of other food. . .	(10) Dietary products, raw materials, and in-process materials that are rejected or adulterated within the meaning of the act shall be identified, stored and disposed of in a manner that protects against the adulteration of other products.
	(11) Written procedures shall be established and followed that describe appropriate tests, and/or examinations to be conducted that may be necessary to assure the purity, composition, and quality of the finished product.
(9) . . . If the adulterated food is capable of being reconditioned, it shall be reconditioned using a method that has been proven to be effective or it shall be reexamined and found not to be adulterated within the meaning of the act before being incorporated into other food.	(12) Written procedures shall be established and followed prescribing the method for reprocessing batches or operational start-up materials that do not conform to finished goods standards or specifications. Finished goods manufactured using such materials shall meet all established purity, composition, and quality standards.
(10) Mechanical manufacturing steps such as washing, peeling, trimming, cutting, sorting and inspecting, mashing, dewatering, cooling, shredding, extruding, drying, whipping, defatting, and forming shall be performed so as to protect food against contamination. Compliance with this requirement may be accomplished by providing adequate physical protection of food from contaminants that may drip, drain, or be drawn into the food. Protection may be provided by adequate cleaning and sanitizing of all food-contact surfaces, and by using time and temperature controls at and between each manufacturing step.	(13) Mechanical manufacturing steps such as cutting, sorting, inspecting, shredding, drying, grinding, blending, and sifting shall be performed so as to protect dietary ingredients and dietary supplements against adulteration. Compliance with this requirement may be accomplished by providing adequate physical protection of dietary products from contact with adulterants. Protection may be provided by adequate cleaning and sanitizing of all processing equipment between each manufacturing step, <u>as necessary</u> .
(11) Heat blanching, when required in the preparation of food, should be effected by heating the food to the required temperature, holding it at this temperature for the required time, and then either rapidly cooling the food or passing it to subsequent manufacturing without delay. Thermophilic growth and contamination in blanchers should be minimized by the use of adequate operating temperatures and by periodic cleaning. Where the blanched food is washed prior to filling, water used shall be safe and of adequate sanitary quality.	(14) Heat blanching, when required in the preparation of a dietary product, should be effected by heating the product to the required temperature, holding it at this temperature for the required time, and then either rapidly cooling the material or passing it to subsequent manufacturing without delay. Thermophilic growth and contamination in blanchers should be minimized by the use of adequate operating temperatures and by periodic cleaning. Where the blanched product is washed prior to filling, potable water shall be used.
(12) Batters, breadings, sauces, gravies, dressings, and other similar preparations shall be treated or maintained in such a manner that they are protected against contamination. Compliance with this requirement may be accomplished by any effective means, including one or more of the following: (i) Using ingredients free of contamination. (ii) Employing adequate heat processes where applicable. (iii) Using adequate time and temperature controls. (iv) Providing adequate physical protection of components from contaminants that may drip, drain, or be drawn into them. (v) Cooling to an adequate temperature during manufacturing. (vi) Disposing of batters at appropriate intervals to protect against the growth of microorganisms.	
(14) Food such as, but not limited to, dry mixes, nuts, intermediate moisture food, and dehydrated food, that relies on the control of a_w for preventing the growth of undesirable microorganisms shall be processed to and maintained at a safe moisture level. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices: (i) Monitoring the a_w of food. (ii) Controlling the soluble solids-water ratio in finished food. (iii) Protecting finished food from moisture pickup, by use of a moisture barrier or by other means, so that the a_w of the food does not increase to	(15) Intermediate or dehydrated dietary products that rely on the control of water activity (a_w) for preventing the growth of undesirable microorganisms shall be processed to and maintained at a safe moisture level. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices: (i) Monitoring the water activity (a_w) of the material. (ii) Controlling the soluble solids-water ratio in finished product. (iii) Protecting finished product from moisture pickup, by use of a moisture barrier or by other means, so that the water activity (a_w) of

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an unsafe level.	product does not increase to an unsafe level.
<p>(15) Food such as, but not limited to, acid and acidified food, that relies principally on the control of pH for preventing the growth of undesirable microorganisms shall be monitored and maintained at a pH of 4.6 or below. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices:</p> <p>(i) Monitoring the pH of raw materials, food in process, and finished food.</p> <p>(ii) Controlling the amount of acid or acidified food added to low-acid food.</p>	<p>(16) Dietary ingredients and dietary supplements that rely principally on the control of pH for preventing the growth of undesirable microorganisms shall be monitored and maintained at an appropriate pH. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices:</p> <p>(i) Monitoring the pH of raw materials, in process material, and finished product.</p> <p>(ii) Controlling the amount of acid added to the product.</p>
<p>(16) When ice is used in contact with food, it shall be made from water that is safe and of adequate sanitary quality, and shall be used only if it has been manufactured in accordance with current good manufacturing practice as outlined in this part.</p>	<p>(17) When ice is used in contact with dietary products, it shall be made from potable water, and shall be used only if it has been manufactured in accordance with current good manufacturing practice as outlined in 21 CFR part 110.</p>
<p>(17) Food-manufacturing areas and equipment used for manufacturing human food should not be used to manufacture nonhuman food-grade animal feed or inedible products, unless there is no reasonable possibility for the contamination of the human food.</p>	
	(e) Packaging and labeling operations.
<p>(13) Filling, assembling, packaging, and other operations shall be performed in such a way that the food is protected against contamination. Compliance with this requirement may be accomplished by any effective means, including:</p> <p>(i) Use of a quality control operation in which the critical control points are identified and controlled during manufacturing.</p> <p>(ii) Adequate cleaning and sanitizing of all food-contact surfaces and food containers.</p> <p>(iii) Using materials for food containers and food-packaging materials that are safe and suitable, as defined in § 130.3(d) of this chapter.</p> <p>(iv) Providing physical protection from contamination, particularly airborne contamination.</p> <p>(v) Using sanitary handling procedures.</p>	<p>(1) Filling, assembling, packaging, and other operations shall be performed in such a way that dietary products are protected against adulteration. Compliance with this requirement may be accomplished by any effective means, including:</p> <p>(i) Adequate cleaning and sanitizing of all filling and packaging equipment, utensils, and product containers, as appropriate.</p> <p>(ii) Using materials for product containers and packaging materials that are safe and suitable.</p> <p>(iii) Providing physical protection from adulteration, particularly airborne contamination.</p> <p>(iv) Using sanitary handling procedures.</p>
	<p>(2) Written procedures shall be established and followed describing sufficient detail the control procedures employed for the receipt, storage, handling, sampling, examination, and/or testing that may be necessary to assure the identity of labeling and the appropriate identity cleanliness and quality characteristics of packaging materials for dietary products.</p>
	<p>(3) For dietary supplements, labels and other labeling materials for each different product type, strength, or quantity of contents shall be stored separately with suitable identification.</p>
	<p>(4) Obsolete labels, labeling, and other packaging materials for dietary products shall be destroyed.</p>
	<p>(5) Written procedures shall be established and followed to assure that correct labels, labeling, and packaging materials are issued and used for dietary products.</p>
	<p>(6) Dietary ingredient and dietary supplement packages shall be identified with a lot number that permits determination of the history of the manufacture and control of the batch.</p>
	<p>(7) Packaged and labeled dietary supplements shall be examined provide assurance that containers and packages in the lot have the correct label and lot number. Products not meeting specifications shall be rejected by the quality control unit.</p>
<p>§ 110.93 Warehousing and distribution</p>	<p>Warehousing, Distribution and Post-Distribution Procedures (a) Storage and distribution.</p>

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Storage and transportation of finished food shall be under conditions that will protect food against physical, chemical, and microbial contamination as well as against deterioration of the food and the container.	(1) Storage and transportation of finished product shall be under conditions that will protect product against physical, chemical, and microbial adulteration as well as against deterioration of the product and the container.
	(2) Adequate distribution records shall will be maintained and retained by the manufacturer at least 1 year beyond expected product's shelf life or expiration date, whereby an effective product recall can be achieved should one become necessary.
	(b) Reserve samples. An appropriately identified reserve sample that is representative of each batch of a dietary product should be retained and stored under conditions consistent with the product labeling until at least 1 year after the product's shelf life or expiration date, or if no expiration date is identified on the product, for at least 3 years after the date of manufacture. The reserve sample should be stored in the same immediate container-closure system in which the finished product is marketed or in one that provides similar protection. The reserve sample shall consist of at least twice the quantity necessary to perform all the required tests.
	(c) Records retention.
	(1) Any laboratory, production, control or distribution record specifically associated with a batch of product shall be retained for at least 1 year after the product's shelf life or expiration date of the batch, or if no expiration date is identified on the product, for at least 3 years after the date of manufacture.
	(2) Raw material records shall be maintained for at least 1 year after the product's shelf life or expiration date of the last batch of product incorporating the raw material, or if no expiration date is identified on the product, for at least 3 years after the date of manufacture of the finished product.
	(d) Complaint files.
	(1) Written procedures describing the handling of all written and oral complaints regarding a dietary product shall be established and followed. Such procedures shall include provisions for review by the quality control unit of any complaint involving the possible failure of a product to meet any of its specifications and, for such products, a determination as to the need for an investigation.
	(2) A written record of each complaint shall be maintained, until at least 1 year after the expiration date of the product, or 1 year after the date that the complaint was received, whichever is longer.
	(3) The written record shall include, where known: The name and description of the product, lot number, name of complainant, nature of complaint, and reply to complainant, if any.
	(4) Where an investigation is conducted, the written record shall include the findings of the investigation and followup action taken.
	(e) Returned products. Returned dietary products shall be identified as such and held. If the conditions under which returned dietary products have been held, stored, or shipped before or during their return, or if the condition of the product, its container, carton, or label as a result of storage or shipping, casts doubt on the purity, composition or quality of the product, the returned product shall be destroyed unless examination, testing, or other investigations prove the product meets appropriate standards of purity, composition, and quality. A product may be reprocessed provided the subsequent product meets appropriate specifications. Records pertaining to returned products that are subsequently reprocessed and/or redistributed shall be maintained and shall include the name and description of the product, lot number, reason for the return, quantity returned, date of disposition, and ultimate disposition.

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	disposition of the returned product:
	(f) Product salvaging. Dietary products that have been subjected to improper storage conditions including extremes in temperature humidity smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace. Whenever there is a question whether products have been subjected to such conditions, salvaging operations may be conducted only if there is: (1) Evidence from laboratory tests that the products meet all applicable standards of purity, quality, and composition; and (2) evidence from inspection of the premises that the products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident. Records including name, lot number, and disposition shall be maintained for products subject to this section.
Subpart G Defect Action Levels § 110.110 Natural or unavoidable defects in food for human use that present no health hazard.	(g) Defect action levels.
(a) Some foods, even when produced under current good manufacturing practice, contain natural or unavoidable defects that at low levels are not hazardous to health. The Food and Drug Administration establishes maximum levels for these defects in foods produced under current good manufacturing practice and uses these levels in deciding whether to recommend regulatory action.	(1) Some dietary ingredients and dietary supplements, even when produced under current good manufacturing practice, contain natural or unavoidable defects that at low levels are not hazardous to health. The Food and Drug Administration establishes maximum levels for these defects in dietary products produced under current good manufacturing practice and uses these levels in deciding whether to recommend regulatory action.
(b) Defect action levels are established for foods whenever it is necessary and feasible to do so. These levels are subject to change upon the development of new technology or the availability of new information.	(2) Defect action levels are established for dietary products whenever it is necessary and feasible to do so. These levels are subject to change upon the development of new technology or the availability of new information.
(c) Compliance with defect action levels does not excuse violation of the requirement in section 402(a)(4) of the act that food not be prepared, packed, or held under unsanitary conditions or the requirements in this part that food manufacturers, distributors, and holders shall observe current good manufacturing practice. Evidence indicating that such a violation exists causes the food to be adulterated within the meaning of the act, even though the amounts of natural or unavoidable defects are lower than the currently established defect action levels. The manufacturer, distributor, and holder of food shall at all times utilize quality control operations that reduce natural or unavoidable defects to the lowest level currently feasible.	(3) Compliance with defect action levels does not excuse violation of the requirement in section 402(a)(4) of the act that dietary products not be prepared, packed, or held under unsanitary conditions or the requirements in this part that dietary product manufacturers, distributors, and holders shall observe current good manufacturing practice. Evidence indicating that such a violation exists causes a dietary product to be adulterated within the meaning of the act, even though the amounts of natural or unavoidable defects are lower than the currently established defect action levels. The manufacturer, distributor, and holder of a dietary product shall at all times utilize quality control operations that reduce natural or unavoidable defects to the lowest level currently feasible.
(d) The mixing of a food containing defects above the current defect action level with another lot of food is not permitted and renders the final food adulterated within the meaning of the act, regardless of the defect level of the final food.	(4) The mixing of a dietary ingredient or dietary supplement containing defects above the current defect action level with another lot of dietary ingredient or dietary supplement is not permitted and renders the final product adulterated within the meaning of the act, regardless of the defect level of the final product.
(e) A compilation of the current defect action levels for natural or unavoidable defects in food for human use that present no health hazard may be obtained upon request from the Center for Food Safety and Applied Nutrition (HFS-565), Food and Drug Administration, 200 C St. SW., Washington, DC 20204.	(5) A compilation of the current defect action levels for natural or unavoidable defects in dietary products that present no health hazard may be obtained upon request from the Industry Programs Branch (HFF-326), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 C St. SW., Washington, DC 20204.

* Recommended changes to the proposal published by FDA 2/6/97 are noted as follows:
~~Deletions are marked by strikethrough~~
Additions are marked by underline

Consumer Healthcare Products Association
Proposed Dietary Supplement GMPs
 and Comparison With Food GMPs

Current Food GMPs	Proposed Dietary Supplement GMPs, Including CHPA Comments*
<p>§ 110.3 Definitions. The definitions and interpretations of terms in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) are applicable to such terms when used in this part. The following definitions shall also apply:</p>	<p>Definitions The definitions and interpretations of terms in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) are applicable to such terms when used in this part. The following definitions shall also apply:</p>
<p>(a) Acid foods or acidified foods means foods that have an equilibrium pH of 4.6 or below.</p>	
<p>(b) Adequate means that which is needed to accomplish the intended purpose in keeping with good public health practice.</p>	<p>(a) "Adequate" means that which is needed to accomplish the intended purpose in keeping with good public health practice.</p>
<p>(c) Batter means a semifluid substance, usually composed of flour and other ingredients, into which principal components of food are dipped or with which they are coated, or which may be used directly to form bakery foods.</p>	
	<p>(b) "Batch or Lot" means a specific quantity of a finished product or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.</p>
<p>(d) Blanching, except for tree nuts and peanuts, means a prepackaging heat treatment of foodstuffs for a sufficient time and at a sufficient temperature to partially or completely inactivate the naturally occurring enzymes and to effect other physical or biochemical changes in the food.</p>	<p>(c) "Blanching" means a prepackaging heat treatment of a dietary product for a sufficient time and at a sufficient temperature to partially or completely inactivate the naturally occurring enzymes and to effect other physical or biochemical changes in the product.</p>
	<p>(d) "Composition" means, as appropriate: (1) the identity of a dietary ingredient or dietary supplement, and (2) the concentration of a dietary ingredient (e.g., weight or other unit of use/weight or volume), or the potency or activity of one or more dietary ingredients, as indicated by appropriate procedures.</p>
<p>(e) Critical control point means a point in a food process where there is a high probability that improper control may cause, allow, or contribute to a hazard or to filth in the final food or decomposition of the final food.</p>	
	<p>(e) "Dietary ingredient" means an ingredient intended for use or used in a dietary supplement that is: (1) a vitamin, (2) a mineral, (3) an herb or other botanical, (4) an amino acid, (5) a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or (6) a concentrate, metabolite, constituent, extract, or combination of any of the foregoing ingredients.</p>
	<p>(f) "Dietary product" means either a dietary ingredient or dietary supplement as defined in this Part.</p>
	<p>(g) "Dietary supplement" means dietary supplement as defined in section 201(ff) of the act.</p>
<p>(f) Food means food as defined in section 201(f) of the act and includes raw materials and ingredients.</p>	
<p>(g) Food-contact surfaces are those surfaces that contact human food and those surfaces from which drainage onto the food or onto surfaces that contact the food ordinarily occurs during the normal course of operations. "Food-contact surfaces" includes utensils and food-contact</p>	

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surfaces of equipment.	
	(h) "In-process material" means any material fabricated, compounded, blended, ground, extracted, sifted, sterilized, derived by chemical reaction or processed in any other way that is produced for, and used in, the preparation of a dietary product.
(h) Lot means the food produced during a period of time indicated by a specific code.	(i) "Lot" means "batch" as defined in this part.
	(j) "Lot number" means any distinctive combination of letters, numbers, or symbols, or any combination of them from which the complete history of the manufacture, processing, packing, holding, and distribution of a batch or lot of a finished dietary ingredient, dietary supplement or other material can be determined.
	(k) "Manufacture" or "manufacturing" includes all operations associated with the production of dietary products, including packaging and labeling operations, testing, and quality control of a dietary ingredient or dietary supplement.
(i) Microorganisms means yeasts, molds, bacteria, and viruses and includes, but is not limited to, species having public health significance. The term "undesirable microorganisms" includes those microorganisms that are of public health significance, that subject food to decomposition, that indicate that food is contaminated with filth, or that otherwise may cause food to be adulterated within the meaning of the act. Occasionally in these regulations, FDA used the adjective "microbial" instead of using an adjectival phrase containing the word microorganism.	(l) "Microorganisms" means yeasts, molds, bacteria, and viruses and includes, but is not limited to, species having public health significance. The term "undesirable microorganisms" includes those microorganisms that are of public health significance, that subject food to decomposition, that indicate that a dietary ingredient or dietary supplement is contaminated with filth, or that otherwise may cause a dietary product to be adulterated within the meaning of the act. Occasionally in these regulations, the adjective "microbial" is used instead of using an adjectival phrase containing the word microorganism.
(j) Pest refers to any objectionable animals or insects including, but not limited to, birds, rodents, flies, and larvae.	(m) "Pest" refers to any objectionable animals or insects including, but not limited to, bird, rodents, flies, and larvae.
(k) Plant means the building or facility or parts thereof, used for or in connection with the manufacturing, packaging, labeling, or holding of human food.	(n) "Plant" means the building or facility or parts thereof, used for or in connection with the manufacturing, packaging, labeling, or holding of a dietary product.
(l) Quality control operation means a planned and systematic procedure for taking all actions necessary to prevent food from being adulterated within the meaning of the act.	(o) "Quality control operation" means a planned and systematic procedure for taking all actions necessary to prevent a dietary product from being adulterated within the meaning of the act.
	(p) "Quality control unit" means any person or organizational element designated by the firm to be responsible for the duties relating to quality control operations.
	(q) "Raw material" means any ingredient intended for use in the manufacture of a dietary ingredient or dietary supplement, including those that may not appear in such finished product.
	(r) "Representable sample" means a sample that consists of a number of units that are drawn based on rational criteria, such as random sampling, and is intended to assure that the sample accurately portrays the material being sampled.
(m) Rework means clean, unadulterated food that has been removed from processing for reasons other than insanitary conditions or that has been successfully reconditioned by reprocessing and that is suitable for use as food.	(s) "Rework" means clean, unadulterated material that has been removed from processing for reasons other than insanitary conditions or material that has been successfully reconditioned by reprocessing and that is suitable for use in the manufacture of a dietary product.
(n) Safe-moisture level is a level of moisture low enough to prevent the growth of undesirable microorganisms in the finished product under the intended conditions of manufacturing, storage, and distribution. The maximum safe moisture level for a food is based on its water activity (a_w). An a_w will be considered safe for a food if adequate data are available that demonstrate that the food at or below the given a_w will not support the growth of undesirable microorganisms.	

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(o) Sanitize means to adequately treat food-contact surfaces by a process that is effective in destroying vegetative cells of microorganisms of public health significance, and in substantially reducing numbers of other undesirable microorganisms, but without adversely affecting the product or its safety for the consumer.	(t) "Sanitize" means to adequately treat equipment, containers, or utensils by a process that is effective in destroying vegetative cells of microorganisms of public health significance, and in substantially reducing numbers of other undesirable microorganisms, but without adversely affecting the product or its safety for the consumer.
(p) Shall is used to state mandatory requirements.	(u) "Shall" is used to state mandatory requirements.
(q) Should is used to state recommended or advisory procedures or identify recommended equipment.	(v) "Should" is used to state recommended or advisory procedures or identify recommended equipment.
(r) Water activity (a_w) is a measure of the free moisture in a food and is the quotient of the water vapor pressure of the substance divided by the vapor pressure of pure water at the same temperature.	(w) "Water activity (a_w)" is a measure of the free moisture in a dietary ingredient 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.
<p>§ 110.10 Personnel. The plant management shall take all reasonable measures and precautions to ensure the following:</p> <p>(a) Disease control. Any person who, by medical examination or supervisory observation, is shown to have, or appears to have, an illness, open lesion, including boils, sores, or infected wounds, or any other abnormal source of microbial contamination by which there is a reasonable possibility of food, food-contact surfaces, or food-packaging materials becoming contaminated, shall be excluded from any operations which may be expected to result in such contamination until the condition is corrected. Personnel shall be instructed to report such health conditions to their supervisors.</p>	<p>Personnel The plant management shall take all reasonable measures and precautions to assure the following:</p> <p>(a) Disease control. Any person who, by medical examination or supervisory observation, is shown to have, or appears to have, an illness, open lesion, including boils, sores, or infected wounds, or any other abnormal source of microbial contamination by which there is a reasonable possibility of an in-process or finished dietary product becoming adulterated, or processing equipment, utensils or packaging materials becoming contaminated, shall be excluded from any operations which may be expected to result in such adulteration or contamination until the condition is corrected. Personnel shall be instructed to report such health conditions to their supervisors.</p>
(b) Cleanliness. All persons working in direct contact with food, food-contact surfaces, and food-packaging materials shall conform to hygienic practices while on duty to the extent necessary to protect against contamination of food. The methods for maintaining cleanliness include, but are not limited to:	(b) Cleanliness. All persons working in direct contact with raw materials, in-process or finished dietary products, processing equipment, utensils or packaging materials shall conform to hygienic practices while on duty to the extent necessary to protect against adulteration or contamination of such materials. The methods for maintaining cleanliness include, but are not limited to:
(1) Wearing outer garments suitable to the operation in a manner that protects against the contamination of food, food-contact surfaces, or food-packaging materials.	(1) Wearing outer garments suitable to the operation in a manner that protects against the adulteration of in-process or finished dietary products, or contamination of processing
(2) Maintaining adequate personal cleanliness.	(2) Maintaining adequate personal cleanliness.
(3) Washing hands thoroughly (and sanitizing if necessary to protect against contamination with undesirable microorganisms) in an adequate hand-washing facility before starting work, after each absence from the work station, and at any other time when the hands may have become soiled or contaminated.	(3) Washing hands thoroughly (and sanitizing if necessary to protect against contamination with undesirable microorganisms) in an adequate hand-washing facility before starting work, after each absence from the work station, and at any other time when the hands may have become soiled or contaminated.
(4) Removing all unsecured jewelry and other objects that might fall into food, equipment, or containers, and removing hand jewelry that cannot be adequately sanitized during periods in which food is manipulated by hand. If such hand jewelry cannot be removed, it may be covered by material which can be maintained in an intact, clean, and sanitary condition and which effectively protects against the contamination by these objects of the food, food-contact surfaces, or food-packaging materials.	(4) Removing all unsecured jewelry and other objects that might fall into raw materials, in-process or finished dietary product, equipment, or containers, and removing hand jewelry that cannot be adequately sanitized during periods in which in-process or finished product is manipulated by hand. If such hand jewelry cannot be removed, it may be covered by material which can be maintained in an intact, clean, and sanitary condition and which effectively protects against the adulteration of dietary products or contamination of processing equipment, utensils or packaging materials.
(5) Maintaining gloves, if they are used in food handling, in an intact, clean, and sanitary condition. The gloves should be of an impermeable material.	(5) Maintaining gloves, if they are used in-process or finished product handling, in an intact, clean, and sanitary condition. The gloves should be of a material that adequately protects the product from contamination.
(6) Wearing, where appropriate, in an effective manner, hair nets, headbands, caps, beard covers, or other effective hair restraints.	(6) Wearing, where appropriate, in an effective manner, hair nets, caps, beard covers, or other effective hair restraints.
(7) Storing clothing or other personal belongings in areas other than	(7) Storing clothing or other personal belongings in areas other than

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where food is exposed or where equipment or utensils are washed.	where in-process or finished product is exposed or where processing equipment or utensils are washed.
(8) Confining the following to areas other than where food may be exposed or where equipment or utensils are washed: eating food, chewing gum, drinking beverages, or using tobacco.	(8) Confining the following to areas other than where in-process or finished product may be stored or exposed, or where processing equipment or utensils are washed: eating food, chewing gum, drinking beverages, or using tobacco, or using drugs (Rx or OTC) or other dietary supplement products.
(9) Taking any other necessary precautions to protect against contamination of food, food-contact surfaces, or food-packaging materials with microorganisms or foreign substances including, but not limited to, perspiration, hair, cosmetics, tobacco, chemicals, and medicines applied to the skin.	(9) Taking any other necessary precautions to protect against adulteration of raw materials, in-process or finished product, or contamination of processing equipment, utensils or packaging materials with micro-organisms or foreign substances including, but not limited to, perspiration, hair, cosmetics, tobacco, chemicals, and medicines applied to the skin.
(c) Education and training. Personnel responsible for identifying sanitation failures or food contamination should have a background of education or experience, or a combination thereof, to provide a level of competency necessary for production of clean and safe food. Food handlers and supervisors should receive appropriate training in proper food handling techniques and food-protection principles and should be informed of the danger of poor personal hygiene and insanitary practices.	(c) Education and training. Each person engaged in the manufacture of a dietary product should have the proper education, training, and experience (or any combination thereof) needed to perform the assigned functions. Training should be in the particular operation(s) that the employee performs as they relate to the employee's functions. <u>Employees should also receive training relating to GMPs and sanitary health procedures.</u> Appropriate documentation of training shall be retained by the manufacturer.
(d) Supervision. Responsibility for assuring compliance by all personnel with all requirements of this part shall be clearly assigned to competent supervisory personnel.	(d) Supervision. Responsibility for assuring compliance by all personnel with all requirements of this part shall be clearly assigned to qualified personnel with proper education, training and experience (or any combination thereof).
<p>§ 110.19 Exclusions.</p> <p>(a) The following operations are not subject to this part: Establishments engaged solely in the harvesting, storage, or distribution of one or more "raw agricultural commodities," as defined in section 201(r) of the act, which are ordinarily cleaned, prepared, treated, or otherwise processed before being marketed to the consuming public.</p> <p>(b) FDA, however, will issue special regulations if it is necessary to cover these excluded operations.</p>	<p>Exclusions</p> <p>The following operations are not subject to this part: Establishments engaged solely in the harvesting, storage, or distribution of one or more "raw agricultural commodities," as defined in section 201(r) of the act, which are ordinarily cleaned, prepared, treated, or otherwise processed before being marketed to the consuming public.</p>
<p>Subpart B Buildings and Facilities</p> <p>§ 110.20 Plant and grounds.</p> <p>(a) Grounds. The grounds about a food plant under the control of the operator shall be kept in a condition that will protect against the contamination of food. The methods for adequate maintenance of grounds include, but are not limited to:</p>	<p>Plant and Grounds</p> <p>(a) Grounds. The grounds about a dietary product manufacturing plant under the control of the operator shall be kept in a condition that will protect against the adulteration of dietary products. The methods for adequate maintenance of grounds include, but are not limited to:</p>
(1) Properly storing equipment, removing litter and waste, and cutting weeds or grass within the immediate vicinity of the plant buildings or structures that may constitute an attractant, breeding place, or harborage for pests.	(1) Properly storing equipment, removing litter and waste, and cutting weeds or grass within the immediate vicinity of the plant buildings or structures that may constitute an attractant, breeding place, or harborage for pests.
(2) Maintaining roads, yards, and parking lots so that they do not constitute a source of contamination in areas where food is exposed.	(2) Maintaining roads, yards, and parking lots so that they do not constitute a source of adulteration in areas where product is exposed.
(3) Adequately draining areas that may contribute contamination to food by seepage, foot-borne filth, or providing a breeding place for pests.	(3) Adequately draining areas that may contribute to product adulteration by seepage, foot-borne filth, or providing a breeding place for pests.
(4) Operating systems for waste treatment and disposal in an adequate manner so that they do not constitute a source of contamination in areas where food is exposed. If the plant grounds are bordered by grounds not under the operator's control and not maintained in the manner described in paragraph (a) (1) through (3) of this section, care shall be exercised in the plant by inspection, extermination, or other means to exclude pests, dirt, and filth that may be a source of food contamination.	(4) Operating systems for waste treatment and disposal in an adequate manner so that they do not constitute a source of adulteration in areas where product is exposed. If the plant grounds are bordered by grounds not under the operator's control and not maintained in the manner described in paragraph (a)(1) through (3) of this section, care shall be exercised in the plant by inspection, extermination, or other means to exclude pests, dirt, and filth that may be a source of product adulteration.
(b) Plant construction and design. Plant buildings and structures shall be	(b) Plant construction and design. Plant buildings and structures shall

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suitable in size, construction, and design to facilitate maintenance and sanitary operations for food-manufacturing purposes. The plant and facilities shall:	be suitable in size, construction, and design to facilitate maintenance, cleaning and sanitary operations for dietary product manufacturing purposes and to prevent mixups between different raw materials and products. The plant and facilities shall:
(1) Provide sufficient space for such placement of equipment and storage of materials as is necessary for the maintenance of sanitary operations and the production of safe food.	(1) Provide sufficient space for such placement of equipment and storage of materials as is necessary for the prevention of mixups, maintenance of sanitary operations and the production of safe dietary products.
(2) Permit the taking of proper precautions to reduce the potential for contamination of food, food-contact surfaces, or food-packaging materials with microorganisms, chemicals, filth, or other extraneous material. The potential for contamination may be reduced by adequate food safety controls and operating practices or effective design, including the separation of operations in which contamination is likely to occur, by one or more of the following means: location, time, partition, air flow, enclosed systems, or other effective means.	(2) Permit the taking of proper precautions to reduce the potential for mixups or adulteration of in-process or finished dietary product, or contamination of processing equipment, utensils or packaging materials with microorganisms, chemicals, filth, or other extraneous material. The potential for mixups and product adulteration may be reduced by adequate product safety controls and operating practices or effective design, including the separation of operations in which contamination is likely to occur, by one or more of the following means: Location, time, partition, air flow, enclosed systems, or other effective means.
(3) Permit the taking of proper precautions to protect food in outdoor bulk fermentation vessels by any effective means, including: (i) Using protective coverings. (ii) Controlling areas over and around the vessels to eliminate harborage for pests. (iii) Checking on a regular basis for pests and pest infestation. (iv) Skimming the fermentation vessels, as necessary.	(3) Permit the taking of proper precautions to protect dietary ingredients or dietary supplements in outdoor bulk fermentation vessels by any effective means, including: (i) Using protective coverings. (ii) Controlling areas over and around the vessels to eliminate harborage for pests. (iii) Checking on a regular basis for pests and pest infestation. (iv) Skimming the fermentation vessels, as necessary.
(4) Be constructed in such a manner that floors, walls, and ceilings may be adequately cleaned and kept clean and kept in good repair; that drip or condensate from fixtures, ducts and pipes does not contaminate food, food-contact surfaces, or food-packaging materials; and that aisles or working spaces are provided between equipment and walls and are adequately unobstructed and of adequate width to permit employees to perform their duties and to protect against contaminating food or food-contact surfaces with clothing or personal contact.	(4) Be constructed in such a manner that floors, walls, and ceilings may be adequately cleaned and kept clean and kept in good repair; that drip or condensate from fixtures, ducts and pipes does not adulterate raw materials, in-process or finished dietary products, or contaminate product containers, utensils or packaging materials; and that aisles or working spaces are provided between equipment and walls and are adequately unobstructed and of adequate width to permit employees to perform their duties and to protect against adulterating in-process or finished product, or contaminating processing equipment with clothing or personal contact.
(5) Provide adequate lighting in hand-washing areas, dressing and locker rooms, and toilet rooms and in all areas where food is examined, processed, or stored and where equipment or utensils are cleaned; and provide safety-type light bulbs, fixtures, skylights, or other glass suspended over exposed food in any step of preparation or otherwise protect against food contamination in case of glass breakage.	(5) Provide adequate lighting in hand-washing areas, dressing and locker rooms, and toilet rooms and in all areas where product is examined, processed, or stored and where equipment or utensils are cleaned; and provide safety-type light bulbs, fixtures, sky-lights, or other glass suspended over exposed product in any step of preparation or otherwise protect against product adulteration in case of glass breakage.
(6) Provide adequate ventilation or control equipment to minimize odors and vapors (including steam and noxious fumes) in areas where they may contaminate food; and locate and operate fans and other air-blowing equipment in a manner that minimizes the potential for contaminating food, food-packaging materials, and food-contact surfaces.	(6) Provide adequate ventilation or control equipment to maintain adequate control over microorganisms, dust, humidity, and temperature, when appropriate, for the manufacture of dietary products; to minimize odors and vapors (including steam and noxious fumes) in areas where they may adulterate dietary products; and locate and operate fans and other air-blowing equipment in a manner that minimizes the potential for adulterating raw materials, in-process or finished dietary products, or contaminating processing equipment, utensils or packaging materials.
(7) Provide, where necessary, adequate screening or other protection against pests.	(7) Provide, where necessary, adequate screening or other protection against pests.
§ 110.35 Sanitary operations. (a) General maintenance. Buildings, fixtures, and other physical facilities of the plant shall be maintained in a sanitary condition and shall be kept in repair sufficient to prevent food from becoming adulterated within the meaning of the act.	Sanitation of Buildings and Facilities (a) General maintenance. Buildings, fixtures, and other physical facilities of the plant shall be maintained in a sanitary condition and shall be kept in repair sufficient to prevent raw materials, in-process or finished dietary products from becoming adulterated within the meaning of the act.
(b) Substances used in cleaning and sanitizing; storage of toxic	(b) Cleaning and sanitizing materials.

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materials.	
<p>(1) Cleaning compounds and sanitizing agents used in cleaning and sanitizing procedures shall be free from undesirable microorganisms and shall be safe and adequate under the conditions of use. Compliance with this requirement may be verified by any effective means including purchase of these substances under a supplier's guarantee or certification, or examination of these substances for contamination. Only the following toxic materials may be used or stored in a plant where food is processed or exposed:</p> <p>(i) Those required to maintain clean and sanitary conditions;</p> <p>(ii) Those necessary for use in laboratory testing procedures;</p> <p>(iii) Those necessary for plant and equipment maintenance and operation; and</p> <p>(iv) Those necessary for use in the plant's operations.</p>	<p>(1) Cleaning compounds and sanitizing agents used in cleaning and sanitizing procedures shall be free from undesirable microorganisms and shall be safe and adequate under the conditions of use. Compliance with this requirement may be verified by any effective means including purchase of these substances under a supplier's guarantee or certification, or examination of these substances for contamination. Only the following toxic materials may be used or stored in a plant where product is processed or exposed:</p> <p>(i) Those required to maintain clean and sanitary conditions;</p> <p>(ii) Those necessary for use in laboratory testing procedures;</p> <p>(iii) Those necessary for plant and equipment maintenance and operation; and</p> <p>(iv) Those necessary for use in the plant's operations.</p>
<p>(2) Toxic cleaning compounds, sanitizing agents, and pesticide chemicals shall be identified, held, and stored in a manner that protects against contamination of food, food-contact surfaces, or food-packaging materials. All relevant regulations promulgated by other Federal, State, and local government agencies for the application, use, or holding of these products should be followed.</p>	<p>(2) Toxic cleaning compounds, sanitizing agents, and pesticide chemicals shall be identified, used, held, and stored in a manner that protects against adulteration of raw materials, in-process or finished product, or contamination of processing equipment or packaging materials. All relevant regulations promulgated by other Federal, State, and local government agencies for the application, use or holding of these products should be followed. Rodenticides, insecticides, and fungicides should be registered and used in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act.</p>
<p>(c) Pest control. No pests shall be allowed in any area of a food plant. Guard or guide dogs may be allowed in some areas of a plant if the presence of the dogs is unlikely to result in contamination of food, food-contact surfaces, or food-packaging materials. Effective measures shall be taken to exclude pests from the processing areas and to protect against the contamination of food on the premises by pests. The use of insecticides or rodenticides is permitted only under precautions and restrictions that will protect against the contamination of food, food-contact surfaces, and food-packaging materials.</p>	<p>(c) Pest control. No pests shall be allowed in any area of a dietary product manufacturing plant. Effective measures shall be taken to exclude pests from the processing areas and to protect against the adulteration of product on the premises by pests. The use of insecticides or rodenticides is permitted only under precautions and restrictions that will protect against the adulteration of raw materials, in-process or finished product, or contamination of processing equipment, utensils or packaging materials.</p>
<p>§ 110.37 Sanitary facilities and controls. Each plant shall be equipped with adequate sanitary facilities and accommodations including, but not limited to:</p>	
<p>(a) Water supply. The water supply shall be sufficient for the operations intended and shall be derived from an adequate source. Any water that contacts food or food-contact surfaces shall be safe and of adequate sanitary quality. Running water at a suitable temperature, and under pressure as needed, shall be provided in all areas where required for the processing of food, for the cleaning of equipment, utensils, and food-packaging materials, or for employee sanitary facilities.</p>	<p>(d) Water supply. Potable water, as a minimum quality standard, at a suitable temperature, and under pressure as needed, shall be provided in all areas where required for the processing of dietary products, for the cleaning of processing equipment, utensils, and packaging materials, or for employee sanitary facilities. Any water that contacts in-process or finished dietary products, utensils or processing equipment shall meet the standards prescribed in the Environmental Protection Agency's Primary Drinking Water Regulations (40 CFR part 141).</p>
<p>(b) Plumbing. Plumbing shall be of adequate size and design and adequately installed and maintained to:</p>	<p>(e) Plumbing. Plumbing shall be of adequate size and design and adequately installed and maintained to:</p>
<p>(1) Carry sufficient quantities of water to required locations throughout the plant.</p>	<p>(1) Carry sufficient quantities of water to required locations throughout the plant.</p>
<p>(2) Properly convey sewage and liquid disposable waste from the plant.</p>	<p>(2) Properly convey sewage and liquid disposable waste from the plant.</p>
<p>(3) Avoid constituting a source of contamination to food, water supplies, equipment, or utensils or creating an unsanitary condition.</p>	<p>(3) Avoid constituting a source of adulteration to product, or contamination of water supplies, processing equipment, or utensils or creating an unsanitary condition.</p>
<p>(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.</p>	<p>(4) Provide adequate floor drainage or other appropriate means of water removal 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.</p>
<p>(5) Provide that there is not backflow from, or cross-connection between,</p>	<p>(5) Provide that there is not backflow from, or crossconnection</p>

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piping systems that discharge waste water or sewage and piping systems that carry water for food or food manufacturing.	between, piping systems that discharge waste water or sewage and piping systems that carry water used for the manufacture of dietary products.
(c) Sewage disposal. Sewage disposal shall be made into an adequate sewerage system or disposed of through other adequate means.	(f) Sewage disposal. Sewage disposal shall be made into an adequate sewerage system or disposed of through other adequate means.
(d) Toilet facilities. Each plant shall provide its employees with adequate, readily accessible toilet facilities. Compliance with this requirement may be accomplished by:	(g) Toilet facilities. Each plant shall provide its employees with adequate, readily accessible toilet facilities. Compliance with this requirement may be accomplished by:
(1) Maintaining the facilities in a sanitary condition.	(1) Maintaining the facilities in a sanitary condition.
(2) Keeping the facilities in good repair at all times.	(2) Keeping the facilities in good repair at all times.
(3) Providing self-closing doors.	(3) Providing self-closing doors.
(4) Providing doors that do not open into areas where food is exposed to airborne contamination, except where alternate means have been taken to protect against such contamination (such as double doors or positive air-flow systems).	(4) Providing doors that do not open into areas where dietary product is exposed to airborne contamination, except where alternate means have been taken to protect against such contamination (such as double doors or positive air-flow systems).
(e) Hand-washing facilities. Hand-washing facilities shall be adequate and convenient and be furnished with running water at a suitable temperature. Compliance with this requirement may be accomplished by providing:	(h) Hand-washing facilities. Hand-washing facilities shall be adequate and convenient and be furnished with running water at a suitable temperature. Compliance with this requirement may be accomplished by providing:
(1) Hand-washing and, where appropriate, hand-sanitizing facilities at each location in the plant where good sanitary practices require employees to wash and/or sanitize their hands.	(1) Hand-washing and, where appropriate, hand-sanitizing facilities at each location in the plant where good sanitary practices require employees to wash and/or sanitize their hands.
(2) Effective hand-cleaning and sanitizing preparations.	(2) Effective hand-cleaning and sanitizing preparations.
(3) Sanitary towel service or suitable drying devices.	(3) Air driers, sanitary towel service or suitable drying devices.
(4) Devices or fixtures, such as water control valves, so designed and constructed to protect against recontamination of clean, sanitized hands.	(4) Devices or fixtures, such as water control valves, so designed and constructed to protect against recontamination of clean, sanitized hands.
(5) Readily understandable signs directing employees handling unprotected food, unprotected food-packaging materials, of food-contact surfaces to wash and, where appropriate, sanitize their hands before they start work, after each absence from post of duty, and when their hands may have become soiled or contaminated. These signs may be posted in the processing room(s) and in all other areas where employees may handle such food, materials, or surfaces.	(5) Readily understandable signs directing employees handling unprotected product, packaging materials, utensils or processing equipment to wash and, where appropriate, sanitize their hands before they start work, after each absence from post of duty, and when their hands may have become soiled or contaminated. These signs may be posted in the processing room(s) and in all other areas where employees may handle such products, materials, utensils or equipment.
(6) Refuse receptacles that are constructed and maintained in a manner that protects against contamination of food.	(6) Refuse receptacles that are constructed and maintained in a manner that protects against adulteration of dietary products.
(f) Rubbish and offal disposal. Rubbish and any offal shall be so conveyed, stored, and disposed of as to minimize the development of odor, minimize the potential for the waste becoming an attractant and harborage or breeding place for pests, and protect against contamination of food, food-contact surfaces, water supplies, and ground surfaces.	(i) Rubbish disposal. Rubbish shall be so conveyed, stored, and disposed of as to minimize the development of odor, minimize the potential for the waste becoming an attractant and harborage or breeding place for pests, and protect against adulteration of raw materials, in-process or finished dietary products, or contamination of utensils, processing equipment, water supplies, and ground surfaces.
	(j) Supervision. Overall sanitation of the plant shall be under the supervision of one or more individuals qualified by education, experience and training (or any combination thereof) assigned responsibility for assuring that sanitation procedures are accomplished.
Subpart C_Equipment § 110.40 Equipment and utensils.	Equipment and Utensils (a) Design and construction.
(a) All plant equipment and utensils shall be so designed and of such material and workmanship as to be adequately cleanable, and shall be properly maintained.	(1) All plant equipment and utensils shall be so designed and of such material and workmanship as to be adequately cleanable, and shall be properly maintained.

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The design, construction, and use of equipment and utensils shall preclude the adulteration of food with lubricants, fuel, metal fragments, contaminated water, or any other contaminants.	(2) The design, construction and use of equipment and utensils shall preclude the adulteration of raw materials, packaging materials, in-process materials or finished product with lubricants, fuel, metal fragments, contaminated water, or any other contaminants.
All equipment should be so installed and maintained as to facilitate the cleaning of the equipment and of all adjacent spaces. Food-contact surfaces shall be corrosion-resistant when in contact with food. They shall be made of nontoxic materials and designed to withstand the environment of their intended use and the action of food, and, if applicable, cleaning compounds and sanitizing agents. Food-contact surfaces shall be maintained to protect food from being contaminated by any source, including unlawful indirect food additives.	(3) All equipment should be so installed and maintained as to facilitate the cleaning of the equipment and of all adjacent spaces. Processing equipment and utensils shall be corrosion-resistant when in contact with raw materials, in-process or finished dietary product. They shall be made of nontoxic materials and designed to withstand the environment of their intended use and the action of dietary products, and, if applicable, cleaning compounds and sanitizing agents. Processing equipment and utensils shall be maintained to protect dietary products from being adulterated by any source.
(b) Seams on food-contact surfaces shall be smoothly bonded or maintained so as to minimize accumulation of food particles, dirt, and organic matter and thus minimize the opportunity for growth of microorganisms.	(4) Seams on utensils and processing equipment shall be smoothly bonded or maintained so as to minimize accumulation of product, dirt, and organic matter and thus minimize the opportunity for growth of microorganisms.
(c) Equipment that is in the manufacturing or food-handling area and that does not come into contact with food shall be so constructed that it can be kept in a clean condition.	(5) Equipment that is used in the manufacturing or product handling area and that does not come into contact with a dietary product shall be so constructed that it can be kept in a clean condition.
(d) Holding, conveying, and manufacturing systems, including gravimetric, pneumatic, closed, and automated systems, shall be of a design and construction that enables them to be maintained in an appropriate sanitary condition.	(6) Holding, conveying, and manufacturing systems, including gravimetric, pneumatic, closed, and automated systems, shall be of a design and construction that enables them to be maintained in an appropriate clean condition.
(e) Each freezer and cold storage compartment used to store and hold food capable of supporting growth of microorganisms shall be fitted with an indicating thermometer, temperature-measuring device, or temperature-recording device so installed as to show the temperature accurately within the compartment, and should be fitted with an automatic control for regulating temperature or with an automatic alarm system to indicate a significant temperature change in a manual operation.	(7) Each freezer and cold storage compartment used to store and hold a dietary product capable of supporting growth of microorganisms shall be fitted with an indicating thermometer, temperature-measuring device, or temperature-recording device so installed as to show the temperature accurately within the compartment, and should be fitted with an automatic control for regulating temperature or with an automatic alarm system to indicate a significant temperature change in a manual operation.
(f) Instruments and controls used for measuring, regulating, or recording temperatures, pH, acidity, water activity, or other conditions that control or prevent the growth of undesirable microorganisms in food shall be accurate and adequately maintained, and adequate in number for their designated uses.	(8) Instruments and controls used in the manufacture, processing, packing or holding dietary products, including instruments and controls used for measuring, regulating, or recording temperatures, pH, acidity, water activity, or other conditions that control or prevent the growth of undesirable microorganisms in such products shall be accurate and adequately maintained, and adequate in number for their designated uses.
(g) Compressed air or other gases mechanically introduced into food or used to clean food-contact surfaces or equipment shall be treated in such a way that food is not contaminated with unlawful indirect food additives.	(9) Compressed air or other gases mechanically introduced into a dietary product or used to clean equipment or utensils shall be treated in such a way that dietary ingredients or dietary supplements are not adulterated.
§ 110.35 Sanitary operations	(b) Sanitation of equipment and utensils.
... Cleaning and sanitizing of utensils and equipment shall be conducted in a manner that protects against contamination of food, food-contact surfaces, or food-packaging materials.	(1) Cleaning and sanitizing of utensils and equipment shall be conducted in a manner that protects against adulteration of raw materials, in-process or finished dietary product, processing equipment, utensils or packaging materials.
(d) Sanitation of food-contact surfaces. All food-contact surfaces, including utensils and food-contact surfaces of equipment, shall be cleaned as frequently as necessary to protect against contamination of food.	(2) All utensils and processing equipment shall be cleaned as frequently as necessary to protect against product adulteration.
(1) Food-contact surfaces used for manufacturing or holding low-moisture food shall be in a dry, sanitary condition at the time of use. When the surfaces are wet-cleaned, they shall, when necessary, be sanitized and thoroughly dried before subsequent use.	(3) Utensils and processing equipment used for manufacturing or holding of dry dietary products shall be in a dry, sanitary condition at the time of use. When the surfaces are wet-cleaned, they shall, when necessary, be sanitized and thoroughly dried before subsequent use.

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(2) In wet processing, when cleaning is necessary to protect against the introduction of microorganisms into food, all food-contact surfaces shall be cleaned and sanitized before use and after any interruption during which the food-contact surfaces may have become contaminated. Where equipment and utensils are used in a continuous production operation, the utensils and food-contact surfaces of the equipment shall be cleaned and sanitized as necessary.	(4) In wet processing, when cleaning is necessary to protect against the introduction of microorganisms into a dietary product, all utensils and processing equipment shall be cleaned and sanitized as appropriate before use and after any interruption during which the utensils or processing equipment may have become contaminated. Where equipment and utensils are used in a continuous production operation or in back-to-back operations involving different batches of the same products, the utensils and product-contact surfaces of the equipment shall be cleaned and sanitized as appropriate.
(3) Non-food-contact surfaces of equipment used in the operation of food plants should be cleaned as frequently as necessary to protect against contamination of food.	(5) Nonproduct-contact surfaces of equipment should be cleaned as frequently as necessary to protect against product adulteration.
(4) Single-service articles (such as utensils intended for one-time use, paper cups, and paper towels) should be stored in appropriate containers and shall be handled, dispensed, used, and disposed of in a manner that protects against contamination of food or food-contact surfaces.	(6) Single-service articles (such as utensils intended for one-time use, paper cups, and paper towels) should be stored in appropriate containers and shall be handled, dispensed, used, and disposed of in a manner that protects against adulteration of dietary products, and contamination of utensils and processing equipment.
(5) Sanitizing agents shall be adequate and safe under conditions of use. Any facility, procedure, or machine is acceptable for cleaning and sanitizing equipment and utensils if it is established that the facility, procedure, or machine will routinely render equipment and utensils clean and provide adequate cleaning and sanitizing treatment.	(7) Sanitizing agents shall be adequate and safe under conditions of use. Any facility, procedure, or machine is acceptable for cleaning and sanitizing equipment and utensils if it is established that the facility, procedure, or machine will routinely render equipment and utensils clean and provide adequate cleaning and sanitizing treatment.
(e) Storage and handling of cleaned portable equipment and utensils. Cleaned and sanitized portable equipment with food-contact surfaces and utensils should be stored in a location and manner that protects food-contact surfaces from contamination.	(8) Cleaned and sanitized portable equipment with product-contact surfaces and utensils should be stored in a location and manner that protects product-contact surfaces from contamination.
<p>§ 110.80 (b) Manufacturing operations.</p> <p>(1) Equipment and utensils and finished food containers shall be maintained in an acceptable condition through appropriate cleaning and sanitizing, as necessary. Insofar as necessary, equipment shall be taken apart for thorough cleaning.</p>	(9) Equipment and utensils and finished product containers shall be maintained in an acceptable condition through appropriate cleaning and sanitizing, as necessary. Insofar as necessary, equipment shall be taken apart for thorough cleaning.
	(10) Written procedures shall be established and followed for cleaning and maintaining equipment and utensils used in the manufacture of dietary products.
	(11) A written record of major equipment cleaning and use shall be maintained in individual equipment logs that show the date, product and lot number of each batch processed. The persons performing the cleaning shall record in the log that the work was performed. Entries in the log should be in chronological order.
(7) Equipment, containers, and utensils used to convey, hold, or store raw materials, work-in-process, rework, or food shall be constructed, handled, and maintained during manufacturing or storage in a manner that protects against contamination.	(12) Equipment, containers, and utensils used to convey, hold, or store raw materials, in-process material, rework, or finished product shall be constructed, handled, and maintained during manufacturing or storage in a manner that protects against contamination.
<p>§ 110.80 Processes and controls.</p> <p>Appropriate quality control operations shall be employed to ensure that food is suitable for human consumption and that food-packaging materials are safe and suitable.</p>	<p>Quality Control and Laboratory Operations</p> <p>Appropriate quality control operations shall be employed to assure that dietary products conform to appropriate standards of purity, quality and composition, and that packaging materials are safe and suitable for their intended purpose.</p>
	(a) Quality control unit. (1) There shall be a quality control unit that has the responsibility and authority to:
	(i) Approve or reject all procedures, specifications, controls, tests and examinations, or deviations from them, that impact the purity, quality and composition of a dietary ingredient or dietary supplement;
	(ii) Approve or reject all raw materials, packaging materials labeling, and finished dietary products, including products manufactured.

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	<p>processed, packed, or held under contract by another company, based on adequate determination of conformance to established specifications; and</p> <p>(iii) Assure that completed production records are reviewed as appropriate. Quality control shall be responsible for evaluation of errors committed in the manufacture of a product and shall have the final authority to determine if the error may be corrected in such manner that the product can be approved for distribution or must be destroyed. Such evaluations and their resolution must be documented and maintained with and/or cross referenced in the batch production record.</p>
	<p>(2) Adequate laboratory facilities should be available, as needed, to the quality control unit.</p>
	<p>(3) The responsibilities and procedures applicable to the quality control unit shall be established in writing and followed.</p>
	<p>(b) Laboratory records. Laboratory records shall be maintained and shall include complete data derived from all specified tests.</p>
	<p>(c) Expiration dating.</p>
	<p>(1) Whenever a shelf life or an expiration date for a dietary ingredient or dietary supplement, whichever is appropriate, bears an expiration date, such date shall be supported by data and rationale to reasonably assure that the product meets established specifications at the expiration specified date. Testing or inspection of the product shall be appropriate to the particular dietary ingredient or dietary supplement product.</p>
	<p>(2) Appropriate accelerated stability studies or data from similar product formulations may be used for an initial determination of shelf life. Product shelf life shall be confirmed and may be extended on the basis of real time studies on product stored under labeled storage conditions.</p>
	<p>Production and Process Controls (a) Master production and control records.</p>
	<p>(1) To assure uniformity from batch to batch, a master production and control record shall be prepared for the manufacture of each dietary ingredient and dietary supplement, and shall be reviewed and approved by the quality control unit.</p>
	<p>(2) Master production and control records shall include, as appropriate.</p> <p>(i) A complete list of raw materials used in the manufacture of a dietary product, designated by names or codes sufficiently specific to indicate any special quality characteristic(s).</p> <p>(ii) An accurate statement of the weight or measure of each raw material used in the manufacture of a dietary product. Each batch shall be formulated with the intent to provide not less than 100 percent of each claimed dietary ingredient.</p> <p>(iii) For dietary supplements, the name and weight or measure of each dietary ingredient per unit or portion or per unit of weight or measure of the supplement.</p> <p>(iv) A statement concerning any calculated excess of dietary ingredient contained in a <u>dietary supplement finished product intended for consumption by a consumer</u>.</p> <p>(v) A statement of the total weight or measure of any dietary supplement unit.</p> <p>(vi) A statement of theoretical weight or measure of a dietary ingredient or dietary supplement expected at the conclusion of manufacture, including the maximum and minimum percentages of theoretical yield beyond which investigation is required.</p> <p>(vii) A description of the product container(s), closure(s), and other packaging materials, including positive identification of <u>all finished product packaging labeling used</u>.</p>

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	(viii) Manufacturing and control instructions, designed to assure that the dietary product has the purity, composition, and quality it is represented to possess.
	(b) Batch production and control records.
	(1) Individual batch production and control records shall be prepared and followed for each batch of dietary product produced and shall include complete information relating to the production and control of each batch.
	<p>(2) These records shall be an accurate reproduction of the appropriate master production and control record and shall include documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished, including:</p> <ul style="list-style-type: none"> (i) Dates; (ii) Identity of individual major equipment and lines used; (iii) Specific identification, including lot number, of each raw material or in-process material used; (iv) Weight or measure of each raw material used in the course of processing; (v) Quality control results; (vi) Inspection of the packaging and labeling area; (vii) A statement of the actual yield at the conclusion of manufacture and a statement of the percentage of theoretical yield, as appropriate or possible; (viii) Label control records, including specimens, copies, or records of all labels used; (ix) Description of product containers and closures used; and (x) Any special notes of investigations or deviations from the described process.
	(3) Any deviation from written, approved specifications, standards, test procedures, or other laboratory control mechanisms shall be recorded and justified.
<p>§ 110.80 (a) Raw materials and other ingredients.</p>	(c) Handling and storage of raw materials, in-process materials and rework
<p>(1) Raw materials and other ingredients shall be inspected and segregated or otherwise handled as necessary to ascertain that they are clean and suitable for processing into food and shall be stored under conditions that will protect against contamination and minimize deterioration.</p> <p>... Containers and carriers of raw materials should be inspected on receipt to ensure that their condition has not contributed to the contamination or deterioration of food.</p> <p>(7) Liquid or dry raw materials and other ingredients received and stored in bulk form shall be held in a manner that protects against contamination.</p>	<p>(1) Raw materials, in-process materials and rework shall be inspected and segregated or otherwise handled as necessary to ascertain that they are clean and suitable for processing into dietary products and shall be stored under conditions that will protect against adulteration and minimize deterioration.</p> <p>Containers of raw materials should be inspected on receipt to assure that their condition has not contributed to the adulteration or deterioration of the contents.</p> <p>Liquid or dry raw materials and other ingredients received and stored in bulk form shall be held in a manner that protects against contamination.</p>
<p>Raw materials shall be washed or cleaned as necessary to remove soil or other contamination. Water used for washing, rinsing, or conveying food shall be safe and of adequate sanitary quality. Water may be reused for washing, rinsing, or conveying food if it does not increase the level of contamination of the food.</p>	<p>(2) Raw agricultural materials that contain soil or other contaminants shall be washed or cleaned as necessary. Water used for washing, rinsing, or conveying raw agricultural materials shall be safe and of adequate sanitary quality. Notwithstanding the general requirement for potable water, water may be reused for washing, rinsing, or conveying raw agricultural materials, if it does not increase the level of contamination of the such materials.</p>
<p>(5) Raw materials, other ingredients, and rework shall be held in bulk, or in containers designed and constructed so as to protect against contamination and shall be held at such temperature and relative humidity and in such a manner as to prevent the food from becoming adulterated within the meaning of the act. Material scheduled for rework shall be identified as such.</p>	<p>(3) Raw materials, in-process materials, and rework shall be held in bulk, or in containers designed and constructed so as to protect against adulteration and shall be held at such temperature and relative humidity and in such a manner as to prevent a dietary ingredient or dietary supplement from becoming adulterated within the meaning of the act. Material scheduled for rework shall be identified as such.</p>
<p>(6) Frozen raw materials and other ingredients shall be kept frozen. If</p>	<p>(4) Frozen raw materials and other ingredients shall be kept frozen. If</p>

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thawing is required prior to use, it shall be done in a manner that prevents the raw materials and other ingredients from becoming adulterated within the meaning of the act.	thawing is required prior to use, it shall be done in a manner that prevents the raw materials and other ingredients from becoming adulterated within the meaning of the act.
	(5) Written procedures shall be established and followed describing the receipt, identification, examination, handling, sampling, testing and approval or rejection of raw materials.
	(6) Each lot of raw material shall be identified with a distinctive lot number and shall be appropriately controlled according to its status (e.g., quarantined, approved, rejected).
<p>(4) Raw materials, other ingredients, and rework susceptible to contamination with pests, undesirable microorganisms, or extraneous material shall comply with applicable Food and Drug Administration regulations, guidelines, and defect action levels for natural or unavoidable defects if a manufacturer wishes to use the materials in manufacturing food. Compliance with this requirement may be verified by any effective means, including purchasing the materials under a supplier's guarantee or certification, or examination of these materials for contamination.</p> <p>(2) Raw materials and other ingredients shall either not contain levels of microorganisms that may produce food poisoning or other disease in humans, or they shall be pasteurized or otherwise treated during manufacturing operations so that they no longer contain levels that would cause the product to be adulterated within the meaning of the act. Compliance with this requirement may be verified by any effective means, including purchasing raw materials and other ingredients under a supplier's guarantee or certification.</p>	<p>(7) Raw material samples shall be examined and tested as follows:</p> <p>(i) Each lot of raw material, in-process material, and rework that is liable to adulteration with filth, insect infestation, or other visually evident extraneous material shall be examined against established specifications for such adulteration, and shall comply with any applicable Food and Drug Administration regulations and guidelines. In lieu of such examination by the manufacturer, a guarantee or certification of examination may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's examination.</p> <p>(ii) Each lot of a raw material that is liable to microbiological contamination that is objectionable in view of its intended use shall be subjected to microbiological tests before use. Raw materials shall either not contain levels of microorganisms that may produce food poisoning or other disease in humans, or they shall be otherwise treated during manufacturing operations so that they no longer contain levels that would cause the product to be adulterated within the meaning of the act. In lieu of such testing by the manufacturer, a guarantee or certification of analysis may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's analyses.</p>
<p>(3) Raw materials and other ingredients susceptible to contamination with aflatoxin or other natural toxins shall comply with current Food and Drug Administration regulations, guidelines, and action levels for poisonous or deleterious substances before these materials or ingredients are incorporated into finished food. Compliance with this requirement may be accomplished by purchasing raw materials and other ingredients under a supplier's guarantee or certification, or may be verified by analyzing these materials and ingredients for aflatoxins and other natural toxins.</p>	<p>(iii) Raw materials and other ingredients susceptible to adulteration with aflatoxin or other natural toxins shall comply with current Food and Drug Administration regulations, guidelines, and action levels for poisonous or deleterious substances before these materials or ingredients are incorporated into a finished dietary ingredient or dietary supplement. Compliance with this requirement may be accomplished by analyzing these materials and ingredients for aflatoxins and other natural toxins or, in lieu of such testing by the manufacturer, a guarantee or certification of analysis may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's analyses.</p> <p>(iv) Each lot of raw material shall undergo at least one test by the manufacturer to verify its identity. Such tests may include any appropriate test with sufficient specificity to determine identity, including chemical and laboratory tests, gross organoleptic analysis, microscopic identification, or analysis of constituent markers.</p> <p>(v) Each lot of raw material shall be tested for conformity with all other established specifications. In lieu of such testing by the manufacturer, a guarantee or certification of analysis may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's analyses.</p>
	(8) Approved raw materials shall be rotated so that the oldest approved stock is used first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.
	(9) Raw materials subject to degradation shall be retested or reexamined and approved or rejected by the quality control unit after a specified time in storage or after exposure to air, heat, or other conditions that are likely to adversely affect the purity, quality, or composition of the raw material.
	(10) Rejected raw materials, shall be identified and controlled under a

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	system that prevents their use in manufacturing or processing operations for which they are unsuitable.
§ 110.80(b) Manufacturing operations.	(d) Manufacturing operations.
	(1) All operations in the receiving, inspecting, transporting, segregating, preparing, manufacturing, packaging, and storing of dietary products shall be conducted in accordance with adequate sanitation principles.
	(2) All reasonable precautions shall be taken to assure that production procedures do not contribute adulteration from any source. Chemical, microbial, or extraneous-material testing procedures shall be used where necessary to identify sanitation failures or possible product adulteration.
	(3) All product that has become contaminated to the extent that it is adulterated within the meaning of the act shall be rejected, or if permissible, treated or processed to eliminate the contamination.
<p>(2) All food manufacturing, including packaging and storage, shall be conducted under such conditions and controls as are necessary to minimize the potential for the growth of microorganisms, or for the contamination of food.</p> <p>One way to comply with this requirement is careful monitoring of physical factors such as time, temperature, humidity, aw, pH, pressure, flow rate, and manufacturing operations such as freezing, dehydration, heat processing, acidification, and refrigeration to ensure that mechanical breakdowns, time delays, temperature fluctuations, and other factors do not contribute to the decomposition or contamination of food.</p>	<p>(4) All product manufacturing, including packaging and storage, shall be conducted under such conditions and controls as are necessary to minimize the potential for the growth of microorganisms, or for the adulteration of raw materials, in-process materials and finished product.</p>
<p>(3) Food that can support the rapid growth of undesirable microorganisms, particularly those of public health significance, shall be held in a manner that prevents the food from becoming adulterated within the meaning of the act. Compliance with this requirement may be accomplished by any effective means, including:</p> <p>(i) Maintaining refrigerated foods at 45 °F (7.2 °C) or below as appropriate for the particular food involved.</p> <p>(ii) Maintaining frozen foods in a frozen state.</p> <p>(iii) Maintaining hot foods at 140 °F (60 °C) or above.</p> <p>(iv) Heat treating acid or acidified foods to destroy mesophilic microorganisms when those foods are to be held in hermetically sealed containers at ambient temperatures.</p>	
<p>(4) Measures such as sterilizing, irradiating, pasteurizing, freezing, refrigerating, controlling pH or controlling a_w that are taken to destroy or prevent the growth of undesirable microorganisms, particularly those of public health significance, shall be adequate under the conditions of manufacture, handling, and distribution to prevent food from being adulterated within the meaning of the act.</p>	<p>(5) Measures such as sterilizing, irradiating, pasteurizing, freezing, refrigerating, controlling pH or controlling water activity (a_w) that are taken to destroy or prevent the growth of undesirable microorganisms, particularly those of public health significance, shall be adequate under the conditions of manufacture, handling, and distribution to prevent dietary products from being adulterated within the meaning of the act.</p>
<p>(5) Work-in-process shall be handled in a manner that protects against contamination.</p>	<p>(6) Work-in-process shall be handled in a manner that protects against adulteration.</p>
<p>(6) Effective measures shall be taken to protect finished food from contamination by raw materials, other ingredients, or refuse. When raw materials, other ingredients, or refuse are unprotected, they shall not be handled simultaneously in a receiving, loading, or shipping area if that handling could result in contaminated food. Food transported by conveyor shall be protected against contamination as necessary.</p>	<p>(7) Effective measures shall be taken to protect finished dietary ingredients and dietary supplements from adulteration by raw materials, in-process materials or refuse. When raw materials, in-process materials or refuse are unprotected, they shall not be handled simultaneously in a receiving, loading, or shipping area if that handling could result in adulterated dietary products. Dietary ingredients and dietary supplements transported by conveyor shall be protected against adulteration as necessary.</p>
	<p>(8) All raw material containers, compounding and storage containers, processing lines and major equipment used during the production of a</p>

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	batch shall be properly identified at all times to indicate their contents and when necessary, the phase of processing of the batch.
(8) Effective measures shall be taken to protect against the inclusion of metal or other extraneous material in food. Compliance with this requirement may be accomplished by using sieves, traps, magnets, electronic metal detectors, or other suitable effective means.	(9) Effective measures shall be taken as necessary to protect against the inclusion of metal or other extraneous material in product. Compliance with this requirement may be accomplished by using sieves, traps, magnets, electronic metal detectors, or other suitable effective means.
(9) Food, raw materials, and other ingredients that are adulterated within the meaning of the act shall be disposed of in a manner that protects against the contamination of other food. . .	(10) Dietary products, raw materials, and in-process materials that are rejected or adulterated within the meaning of the act shall be identified, stored and disposed of in a manner that protects against the adulteration of other products.
	(11) Written procedures shall be established and followed that describe appropriate tests, and/or examinations to be conducted that may be necessary to assure the purity, composition, and quality of the finished product.
(9) . . . If the adulterated food is capable of being reconditioned, it shall be reconditioned using a method that has been proven to be effective or it shall be reexamined and found not to be adulterated within the meaning of the act before being incorporated into other food.	(12) Written procedures shall be established and followed prescribing the method for reprocessing batches or operational start-up materials that do not conform to finished goods standards or specifications. Finished goods manufactured using such materials shall meet all established purity, composition, and quality standards.
(10) Mechanical manufacturing steps such as washing, peeling, trimming, cutting, sorting and inspecting, mashing, dewatering, cooling, shredding, extruding, drying, whipping, defatting, and forming shall be performed so as to protect food against contamination. Compliance with this requirement may be accomplished by providing adequate physical protection of food from contaminants that may drip, drain, or be drawn into the food. Protection may be provided by adequate cleaning and sanitizing of all food-contact surfaces, and by using time and temperature controls at and between each manufacturing step.	(13) Mechanical manufacturing steps such as cutting, sorting, inspecting, shredding, drying, grinding, blending, and sifting shall be performed so as to protect dietary ingredients and dietary supplements against adulteration. Compliance with this requirement may be accomplished by providing adequate physical protection of dietary products from contact with adulterants. Protection may be provided by adequate cleaning and sanitizing of all processing equipment between each manufacturing step, as necessary.
(11) Heat blanching, when required in the preparation of food, should be effected by heating the food to the required temperature, holding it at this temperature for the required time, and then either rapidly cooling the food or passing it to subsequent manufacturing without delay. Thermophilic growth and contamination in blanchers should be minimized by the use of adequate operating temperatures and by periodic cleaning. Where the blanched food is washed prior to filling, water used shall be safe and of adequate sanitary quality.	(14) Heat blanching, when required in the preparation of a dietary product, should be effected by heating the product to the required temperature, holding it at this temperature for the required time, and then either rapidly cooling the material or passing it to subsequent manufacturing without delay. Thermophilic growth and contamination in blanchers should be minimized by the use of adequate operating temperatures and by periodic cleaning. Where the blanched product is washed prior to filling, potable water shall be used.
(12) Batters, breadings, sauces, gravies, dressings, and other similar preparations shall be treated or maintained in such a manner that they are protected against contamination. Compliance with this requirement may be accomplished by any effective means, including one or more of the following: (i) Using ingredients free of contamination. (ii) Employing adequate heat processes where applicable. (iii) Using adequate time and temperature controls. (iv) Providing adequate physical protection of components from contaminants that may drip, drain, or be drawn into them. (v) Cooling to an adequate temperature during manufacturing. (vi) Disposing of batters at appropriate intervals to protect against the growth of microorganisms.	
(14) Food such as, but not limited to, dry mixes, nuts, intermediate moisture food, and dehydrated food, that relies on the control of a_w for preventing the growth of undesirable microorganisms shall be processed to and maintained at a safe moisture level. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices: (i) Monitoring the a_w of food. (ii) Controlling the soluble solids-water ratio in finished food. (iii) Protecting finished food from moisture pickup, by use of a moisture barrier or by other means, so that the a_w of the food does not increase to	(15) Intermediate or dehydrated dietary products that rely on the control of water activity (a_w) for preventing the growth of undesirable microorganisms shall be processed to and maintained at a safe moisture level. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices: (i) Monitoring the water activity (a_w) of the material. (ii) Controlling the soluble solids-water ratio in finished product. (iii) Protecting finished product from moisture pickup, by use of a moisture barrier or by other means, so that the water activity (a_w) of the

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an unsafe level.	product does not increase to an unsafe level.
<p>(15) Food such as, but not limited to, acid and acidified food, that relies principally on the control of pH for preventing the growth of undesirable microorganisms shall be monitored and maintained at a pH of 4.6 or below. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices:</p> <p>(i) Monitoring the pH of raw materials, food in process, and finished food.</p> <p>(ii) Controlling the amount of acid or acidified food added to low-acid food.</p>	<p>(16) Dietary ingredients and dietary supplements that rely principally on the control of pH for preventing the growth of undesirable microorganisms shall be monitored and maintained at an appropriate pH. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices:</p> <p>(i) Monitoring the pH of raw materials, in-process material, and finished product.</p> <p>(ii) Controlling the amount of acid added to the product.</p>
<p>(16) When ice is used in contact with food, it shall be made from water that is safe and of adequate sanitary quality, and shall be used only if it has been manufactured in accordance with current good manufacturing practice as outlined in this part.</p>	<p>(17) When ice is used in contact with dietary products, it shall be made from potable water, and shall be used only if it has been manufactured in accordance with current good manufacturing practice as outlined in 21 CFR part 110.</p>
<p>(17) Food-manufacturing areas and equipment used for manufacturing human food should not be used to manufacture nonhuman food-grade animal feed or inedible products, unless there is no reasonable possibility for the contamination of the human food.</p>	
	(e) Packaging and labeling operations.
<p>(13) Filling, assembling, packaging, and other operations shall be performed in such a way that the food is protected against contamination. Compliance with this requirement may be accomplished by any effective means, including:</p> <p>(i) Use of a quality control operation in which the critical control points are identified and controlled during manufacturing.</p> <p>(ii) Adequate cleaning and sanitizing of all food-contact surfaces and food containers.</p> <p>(iii) Using materials for food containers and food-packaging materials that are safe and suitable, as defined in § 130.3(d) of this chapter.</p> <p>(iv) Providing physical protection from contamination, particularly airborne contamination.</p> <p>(v) Using sanitary handling procedures.</p>	<p>(1) Filling, assembling, packaging, and other operations shall be performed in such a way that dietary products are protected against adulteration. Compliance with this requirement may be accomplished by any effective means, including:</p> <p>(i) Adequate cleaning and sanitizing of all filling and packaging equipment, utensils, and product containers, as appropriate.</p> <p>(ii) Using materials for product containers and packaging materials that are safe and suitable.</p> <p>(iii) Providing physical protection from adulteration, particularly airborne contamination.</p> <p>(iv) Using sanitary handling procedures.</p>
	<p>(2) Written procedures shall be established and followed describing in sufficient detail the control procedures employed for the receipt, storage, handling, sampling, examination, and/or testing that may be necessary to assure the identity of labeling and the appropriate identity, cleanliness and quality characteristics of packaging materials for dietary products.</p>
	<p>(3) For dietary supplements, labels and other labeling materials for each different product type, strength, or quantity of contents shall be stored separately with suitable identification.</p>
	<p>(4) Obsolete labels, labeling, and other packaging materials for dietary products shall be destroyed.</p>
	<p>(5) Written procedures shall be established and followed to assure that correct labels, labeling, and packaging materials are issued and used for dietary products.</p>
	<p>(6) Dietary ingredient and dietary supplement packages shall be identified with a lot number that permits determination of the history of the manufacture and control of the batch.</p>
	<p>(7) Packaged and labeled dietary supplements shall be examined to provide assurance that containers and packages in the lot have the correct label and lot number. Products not meeting specifications shall be rejected by the quality control unit.</p>
<p>§ 110.93 Warehousing and distribution</p>	<p>Warehousing, Distribution and Post-Distribution Procedures</p> <p>(a) Storage and distribution.</p>

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Storage and transportation of finished food shall be under conditions that will protect food against physical, chemical, and microbial contamination as well as against deterioration of the food and the container.	(1) Storage and transportation of finished product shall be under conditions that will protect product against physical, chemical, and microbial adulteration as well as against deterioration of the product and the container.
	(2) Adequate distribution records shall will be maintained and retained by the manufacturer at least 1 year beyond expected product's shelf life or expiration date, whereby an effective product recall can be achieved should one become necessary.
	(b) Reserve samples. An appropriately identified reserve sample that is representative of each batch of a dietary product should be retained and stored under conditions consistent with the product labeling until at least 1 year after the product's shelf life or expiration date, or if no expiration date is identified on the product, for at least 3 years after the date of manufacture. The reserve sample should be stored in the same immediate container-closure system in which the finished product is marketed or in one that provides similar protection. The reserve sample shall consist of at least twice the quantity necessary to perform all the required tests.
	(c) Records retention.
	(1) Any laboratory, production, control or distribution record specifically associated with a batch of product shall be retained for at least 1 year after the product's shelf life or expiration date of the batch, or if no expiration date is identified on the product, for at least 3 years after the date of manufacture.
	(2) Raw material records shall be maintained for at least 1 year after the product's shelf life or expiration date of the last batch of product incorporating the raw material, or if no expiration date is identified on the product, for at least 3 years after the date of manufacture of the finished product.
	(d) Complaint files.
	(1) Written procedures describing the handling of all written and oral complaints regarding a dietary product shall be established and followed. Such procedures shall include provisions for review by the quality control unit of any complaint involving the possible failure of a product to meet any of its specifications and, for such products, a determination as to the need for an investigation.
	(2) A written record of each complaint shall be maintained, until at least 1 year after the expiration date of the product, or 1 year after the date that the complaint was received, whichever is longer.
	(3) The written record shall include, where known: The name and description of the product, lot number, name of complainant, nature of complaint, and reply to complainant, if any.
	(4) Where an investigation is conducted, the written record shall include the findings of the investigation and followup action taken.
	(e) Returned products. Returned dietary products shall be identified as such and held. If the conditions under which returned dietary products have been held, stored, or shipped before or during their return, or if the condition of the product, its container, carton, or labeling as a result of storage or shipping, casts doubt on the purity, composition or quality of the product, the returned product shall be destroyed unless examination, testing, or other investigations prove the product meets appropriate standards of purity, composition, and quality. A product may be reprocessed provided the subsequent product meets appropriate specifications. Records pertaining to returned products that are subsequently reprocessed and/or redistributed shall be maintained and shall include the name and description of the product, lot number, reason for the return, quantity returned, date of disposition, and ultimate

Current Food GMPs	Proposed Dietary Supplement GMPs, Including CHPA Comments*
	disposition of the returned product.
	(f) Product salvaging. Dietary products that have been subjected to improper storage conditions including extremes in temperature, humidity smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace. Whenever there is a question whether products have been subjected to such conditions, salvaging operations may be conducted only if there is: (1) Evidence from laboratory tests that the products meet all applicable standards of purity, quality, and composition; and (2) evidence from inspection of the premises that the products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident. Records including name, lot number, and disposition shall be maintained for products subject to this section.
<p>Subpart G Defect Action Levels § 110.110 Natural or unavoidable defects in food for human use that present no health hazard.</p>	(g) Defect action levels.
<p>(a) Some foods, even when produced under current good manufacturing practice, contain natural or unavoidable defects that at low levels are not hazardous to health. The Food and Drug Administration establishes maximum levels for these defects in foods produced under current good manufacturing practice and uses these levels in deciding whether to recommend regulatory action.</p>	<p>(1) Some dietary ingredients and dietary supplements, even when produced under current good manufacturing practice, contain natural or unavoidable defects that at low levels are not hazardous to health. The Food and Drug Administration establishes maximum levels for these defects in dietary products produced under current good manufacturing practice and uses these levels in deciding whether to recommend regulatory action.</p>
<p>(b) Defect action levels are established for foods whenever it is necessary and feasible to do so. These levels are subject to change upon the development of new technology or the availability of new information.</p>	<p>(2) Defect action levels are established for dietary products whenever it is necessary and feasible to do so. These levels are subject to change upon the development of new technology or the availability of new information.</p>
<p>(c) Compliance with defect action levels does not excuse violation of the requirement in section 402(a)(4) of the act that food not be prepared, packed, or held under unsanitary conditions or the requirements in this part that food manufacturers, distributors, and holders shall observe current good manufacturing practice. Evidence indicating that such a violation exists causes the food to be adulterated within the meaning of the act, even though the amounts of natural or unavoidable defects are lower than the currently established defect action levels. The manufacturer, distributor, and holder of food shall at all times utilize quality control operations that reduce natural or unavoidable defects to the lowest level currently feasible.</p>	<p>(3) Compliance with defect action levels does not excuse violation of the requirement in section 402(a)(4) of the act that dietary products not be prepared, packed, or held under unsanitary conditions or the requirements in this part that dietary product manufacturers, distributors, and holders shall observe current good manufacturing practice. Evidence indicating that such a violation exists causes a dietary product to be adulterated within the meaning of the act, even though the amounts of natural or unavoidable defects are lower than the currently established defect action levels. The manufacturer, distributor, and holder of a dietary product shall at all times utilize quality control operations that reduce natural or unavoidable defects to the lowest level currently feasible.</p>
<p>(d) The mixing of a food containing defects above the current defect action level with another lot of food is not permitted and renders the final food adulterated within the meaning of the act, regardless of the defect level of the final food.</p>	<p>(4) The mixing of a dietary ingredient or dietary supplement containing defects above the current defect action level with another lot of dietary ingredient or dietary supplement is not permitted and renders the final product adulterated within the meaning of the act, regardless of the defect level of the final product.</p>
<p>(e) A compilation of the current defect action levels for natural or unavoidable defects in food for human use that present no health hazard may be obtained upon request from the Center for Food Safety and Applied Nutrition (HFS-565), Food and Drug Administration, 200 C St. SW., Washington, DC 20204.</p>	<p>(5) A compilation of the current defect action levels for natural or unavoidable defects in dietary products that present no health hazard may be obtained upon request from the Industry Programs Branch (HFF-326), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 C St. SW., Washington, DC 20204.</p>

* Recommended changes to the proposal published by FDA 2/6/97 are noted as follows:
 Deletions are marked by strikeouts;
 Additions are marked by underlines.



*Producers of Quality
Nonprescription Medicines and
Dietary Supplements for Self-Care*

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

Formerly Nonprescription Drug Manufacturers Association

**CFSAN's Public Meeting on Regulations on
Statements for Dietary Supplements
Concerning the Effect of the Product
on the
Structure or Function of the Body**

[Docket No. 98N-0044]

R. William Soller, Ph.D.
Senior Vice President and
Director of Science & Technology
Consumer Healthcare Products Association

August 4, 1999

Consumer Healthcare Products Association

Representing producers of quality nonprescription medicines and dietary supplements

Founded 1881

**CFSAN's Public Meeting on Regulations on
Statements for Dietary Supplements Concerning the Effect of the Product
on the Structure or Function of the Body [Docket No. 98N-0044]
August 4, 1999**

**R. William Soller, Ph.D.
Senior Vice President and
Director of Science & Technology
Consumer Healthcare Products Association¹**

Executive Summary

CHPA recommends that CFSAN:

1. Amend its proposed definition of disease for structure/function claims to incorporate the distinguishing concepts of "adverse" and "natural state or process," so as to ensure natural states/processes are a domain for dietary supplement claims:
 - "a disease is any adverse deviation from, or impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by one or more signs or symptoms that are not characteristic of a natural state or process."
 - "a natural state or process is a life change or physiologic manifestation expected in the normal course of life progression."
2. Unlike the definition of disease in 101.14(a)(6) or FDA's proposed definition, the concept of natural state should be distinguished from the concept of disease within the definition itself -- as is done in CHPA's proposed re-definition of disease. The demarcation line is defined by the "adverse" nature of the deviation from normal.
3. The statutorily required disclaimer is intended to explicitly and effectively eliminate the potential for structure/function claims to be interpreted as implied disease claims. Hence, there is no need for FDA to seek additional regulatory constructs to address the subject of implied disease claims.
4. CHPA requests that the comment period be extended for 30 days after this open meeting on structure/function claims.

¹ The Consumer Healthcare Products Association (CHPA, formerly known as the Nonprescription Drug Manufacturers Association (NDMA), is the 118-year-old trade organization representing the manufacturers and distributors of national and store brand dietary supplements and nonprescription medicines. CHPA's membership includes over 200 companies involved in the manufacture and distribution of these self-care products and their affiliated services (e.g., raw material suppliers, research testing companies, contract manufacturing companies, advertising agencies, etc.).

Detailed Oral Comments

Introduction

We have been asked to comment on common conditions associated with natural states. However, FDA has posed three issues for discussion: The definition of disease; common conditions associated with natural states; and implied disease claims. As these issues are so interrelated, it is unrealistic to propose that groups presenting today address only one issue independent of their views on the other two. I will therefore provide CHPA's consolidated approach to all three issues.

Definition of Disease

First, the definition of disease under NLEA in 101.14(a)(6) is insufficient in its particulars to ensure that the intent of Congress is met to permit structure/function claims for dietary supplements intended to promote and maintain health and to beneficially affect signs and symptoms associated with natural states.

21CFR 101.14(a)(6): "Damage² to an organ, part, structure, or system of the body such that it does not function properly (e.g., cardiovascular disease), or a state of health leading to such dysfunctioning (e.g., hypertension); except that disease resulting from essential nutrient deficiencies (e.g., scurvy, pellegra) are not included in this definition."

"A state of health leading to such dysfunctioning" is overly broad and might include, for example, a healthy state despite high fat intake or toxic exposure leading to damage of the body.

Second, FDA's proposed definition of disease for structure/function claims for dietary supplements is overly broad.

FDA's Proposed Definition: "Any deviation from, impairment of, or interruption of the normal structure or function of any part, structure, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms, including laboratory or clinical measurements that are characteristic of a disease."

² "Damage" is an appropriate concept to include in the definition of disease, as noted by FDA in the preamble to the proposed rule. In the preamble to the proposed rule on structure/function label claims, FDA states its rationale for proposing a definition of "disease," as follows: "Diseases, by definition, *adversely* affect some structure or function of the body, and it is possible to describe most products intended to treat or prevent disease in terms of their effects on the structure or function of the body" (63 Fed. Reg. 23624, 1998; emphasis added).

Unlike the definition in 101.14(a)(6), FDA's proposed definition for structure/function claims omits the concept of "damage." Under FDA's proposed definition, "any deviation ... from normal" could include "aging well" as a disease state.

Therefore, CHPA recommends amending FDA's proposed definition to more clearly distinguish structure/function claims for dietary supplements from drug claims on the basis of the adverse nature of diseases for which drugs are used, on the one hand, and the non-adverse nature of natural states for which dietary supplements are used. Specifically, CHPA proposes the definition of disease for structure/function claims should be:

CHPA's Proposed Definition of Disease: "... a disease is any adverse deviation from, or impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms, ~~including laboratory or clinical measurements~~ that are not characteristic of a ~~disease~~ natural state or process."

(Note: underlined portions are additions and strikeouts are deletions from FDA's proposed definition of disease.)

"Any deviation" is too broad; "any **adverse** deviation" appropriately defines the nature of the deviation; "laboratory or clinical measurements" are redundant and included under the concept of "signs;" and "not characteristic of a natural state or process" appropriately encompasses Congress' intent to allow health promotion/maintenance claims.

CHPA also recommends natural state or process be defined by regulation, as follows:

"A natural state or process is a life change or physiologic manifestation expected in the normal course of life progression."

In summary, CHPA recommends including the concept of a natural state or process into the definition of disease to exclude natural states from being considered diseases, thus ensuring that Congress' intent for health promotion/maintenance is not undermined. The concept of natural states/processes in the CHPA definition of disease is balanced by the concept of "adverse" to create the appropriate basis for regulating structure/function claims. Hence, under the CHPA-proposed definition, drug claims would address such specific diseases as, by way of example:

- Heart disease
- Diabetes
- Cancer
- Migraine headache
- Alzheimer's disease
- Viral and bacterial diseases
- Obesity

- Depression

And, under the CHPA-proposed definition of disease, structure/function claims would address such conditions as, by way of example:

- Conditions characteristic of the menstrual cycle
- Hair loss associated with aging
- Stress, frustration
- Pregnancy
- Cholesterol management
- Premenstrual syndrome (PMS)³
- Menopause (e.g., hot flashes)
- Decreased sexual functioning with aging
- Weight management
- Benign prostatic hypertrophy

Common Conditions Associated with Natural States

FDA suggests that non-diseases (i.e., certain common conditions associated with natural states) might be explicitly considered diseases for the purposes of structure/function claims, drawing the line based on the severity of the disease.

Unlike the definition of disease in 101.14(a)(6) or FDA's proposed definition, the concept of natural state should be distinguished from the concept of disease within the definition itself -- as is done in CHPA's proposed re-definition of disease. The demarcation line is defined by the "adverse" nature of the deviation from normal.

First, natural states are not diseases. "Natural states or processes":

- Have a characterized expression of events (e.g., menstrual period, menopause).
- Are often self-limiting, such as fatigue, sleeplessness, PMS³, pregnancy, graying hair, male pattern baldness, etc.
- Have consequences that are most often not harmful to the human body if they go without effective treatment. For example, graying of the hair, male patterned baldness, benign prostatic hypertrophy, and the menstrual period are not necessarily harmful to the body.
- In general, are not normally associated with adverse consequences that are potentially harmful, such as the toxemia of pregnancy, severe postpartum depression.
- Can often be reversed by normal physiological/biological/biochemical functions (e.g., weight control through exercise and dieting).

³ Although the agency uses the menstrual cycle as an example of normal function, "premenstrual syndrome" currently is proposed as a disease state. However, if the hormonal fluctuations of the menstrual cycle are normal, then so should be their effects, as experienced, to varying degrees, by at least an estimated 75% of women. It is not reasonable that this percentage of the female population be characterized as "diseased." More appropriately, the disease state is "Premenstrual Dysphoric Disorder" per DSM-IV (estimated incidence, 3%-5% of women).

Second, the issue of inclusion of such conditions as hypertension and toxemia of pregnancy are handled in CHPA's proposed amendments to FDA's proposed definition of disease, which is again restated below:

“a disease is any adverse deviation from, or impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by one or more signs or symptoms that are not characteristic of a natural state or process.”

“a natural state or process is a life change or physiologic manifestation expected in the normal course of life progression.”

Specifically, the phrase “any adverse deviation from, or impairment of, or interruption of” would include such things as:

- Cancer, as an adverse deviation from normal structure and/or function;
- Hypothyroidism, as an interruption or impairment of normal function;
- Toxemia of pregnancy, as an impairment of the normal function of the body;
- Hypertension, generally considered to be an adverse deviation of normal function.

Third, the exclusionary phrase “that are not characteristic of natural states” avoids creating a definition of disease that runs counter to the intent of Congress in establishing structure/function claims for health promotion and maintenance.

As stated earlier, such conditions as the following would not be considered diseases, provided the associated symptomatology is “not an adverse deviation from normal...” in the context of what constitutes a “natural state” (for example):

- Conditions characteristic of the menstrual cycle;
- Hair loss associated with aging;
- Stress, frustration;
- Pregnancy;
- Cholesterol management;
- PMS;
- Menopause (e.g., hot flashes);
- Decreased sexual functioning with aging;
- Weight management;
- Benign prostatic hypertrophy.

Implied Disease Claims

The line should be drawn based on the law.

- Under DSHEA claims may not be made about the use of a dietary supplement to diagnose, prevent, mitigate, treat, or cure a specific disease (unless approved under the new drug provisions of the FD&C Act).
- Under DSHEA, claims may describe the supplement's effects on "structure or function" of the body or the "well-being" achieved by consuming the dietary ingredient.
- To use these claims, manufacturers must have substantiation that the statements are truthful and not misleading and the product label must bear the statement, or disclaimer:

"This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."

CHPA's definition of a disease amends FDA's proposed definition by incorporating the distinction between natural states and processes (i.e., a claims domain for dietary supplements) and adverse consequences to the body (i.e., a claims domain for drugs and other medical treatments). Thus, CHPA's proposed redefinition of disease would represent the fundamental regulatory standard against which structure/function claims for dietary supplements would be judged in conjunction with the required disclaimer.

The statutorily required disclaimer is intended to explicitly and effectively eliminate the potential for structure/function claims to be interpreted as implied disease claims. Hence, there is no need for FDA to seek additional regulatory constructs to address the subject of implied disease claims.

In the proposed rule, FDA proposed that claims of an effect on symptoms that are recognizable as characteristic of a specific disease or diseases would constitute disease claims (i.e., such symptoms in a claim would constitute an implied disease claim). Whether or not a specific set of signs or symptoms is recognizable as related to a disease is irrelevant, since the statutorily required disclaimer is the self-correcting aspect of DSHEA that avoids an implied disease claim from being made.

Conclusion

In addition to amending the definition of disease and relying on the disclaimer to address the issue of implied disease claims, FDA should identify explicitly the following elements in regulation for determining whether a reference to a sign and/or symptom (or set thereof) constitutes a claim about a "specific disease or class of diseases," using the CHPA-proposed definitions of "disease" and "natural state or process" as the standard:

1. The words "diagnose," "prevent," "treat," "cure," "mitigate" (or other grammatical forms of these verbs) should not be used in a statement of nutritional support (i.e., a structure/function claim), since statements permitted under 403(r)(6) of the Act "may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases;"
2. The words "stimulate," "maintain," "support," "regulate," or "promote" (or other words of this nature or other grammatical forms of these verbs) may be used in a structure/function claim to distinguish the claim from a specific disease claim:
3. Recognizability of endpoints as being related to a disease and therefore constituting an implied disease claim is irrelevant in relation to structure/function claims because of the required disclaimer.

Request for a Post-Meeting Comment Period

CHPA notes that the comment period relating to submissions pertaining to CFSAN's overall strategy on dietary supplements, including claims, is open until August 20, 1999.

CHPA requests that the comment period on FDA's three questions relating to structure/function claims remain open at least as long, and preferably for 30 days after this meeting.

- # # -

TRAINING AND COMMUNICATIONS

**FORMAL MEETINGS BETWEEN CDER AND
CDER'S EXTERNAL CONSTITUENTS**

CONTENTS

**PURPOSE
BACKGROUND
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EFFECTIVE DATE**

Attachment A - Monthly Sample Meetings Report

Attachment B - Suggested Format for Meeting Agenda

Attachment C - Suggested Format for Meeting Minutes

PURPOSE This MaPP describes the Center's policies and procedures for scheduling and conducting formal meetings between CDER staff and those outside CDER requesting such formal meetings. Among other things, it describes a maximum time after a request by which a meeting will be scheduled, the need for prompt preparation and sharing of minutes, and the need for a summary of major points and agreements at the end of every meeting.

BACKGROUND

- Formal meetings serve a beneficial purpose for both the Center and its external constituents to provide clarity and resolve issues related to the drug development and review processes, compliance actions, and policy development.
 - This MaPP provides a consistent and transparent approach to scheduling and conducting formal meetings (face-to-face, teleconference, and videoconference) between individuals from CDER and CDER's external constituents outside FDA.
-

REFERENCES

- MaPP 4510.3 "Telecommunications"
-

DEFINITIONS

- **Formal Meeting.** A planned meeting that occurs through a face-to-face interaction, scheduled teleconference, or scheduled videoconference with a person(s) from outside FDA. Unscheduled meetings, such as "drop-in visits" and unscheduled teleconferences, are not included in this definition and are beyond the scope of this policy. In addition, this document does not address "emergency meetings." Meetings dictated by emergency situations shall be handled on a case-by-case basis, although meeting minutes should be prepared as described below.
 - **External Constituents.** Individual(s) outside the FDA organizational structure.
 - **Pre-Meeting.** An internal meeting of FDA personnel to discuss a strategy and/or meeting approach in anticipation of a formal meeting with external constituents.
 - **Week.** Seven calendar days.
 - **Day.** One calendar day.
-

POLICY

- The Center will respond to requests for scheduling a formal meeting from external constituents consistently and promptly and will agree to such meetings unless they are clearly unnecessary or premature.
- All formal meetings will be conducted in an appropriate business-like manner according to a pre-determined agenda appropriate to the purpose of the meeting, with specified objectives, and accurate summarization of key points and action items at the end of the meeting.
- Accurate minutes ("official minutes") will be prepared promptly by CDER for all formal meetings with external constituents. Official minutes shall be promptly distributed to all Center participants and to the external constituents (unless not appropriate, such as minutes from formal meetings held for Compliance investigatory purposes).
- The Center will work with its external constituents to identify and resolve any inconsistencies, discrepancies, or disagreements between participants with respect to understandings of the outcome of the meeting.
- Letters described in this MaPP may generally be sent or received by facsimile. Hardcopies of all letters must be placed in the product's (or otherwise appropriate) administrative file.

RESPONSIBILITIES**Division Directors, or the appropriate higher manager, shall be responsible for:**

- ensuring that external constituents' requests for meetings are answered in a manner consistent with this policy,
- instituting procedures to insure the policies established in this MAPP are implemented,
- ensuring that formal meetings are conducted in a facilitative, business-like manner and in accordance with this policy,
- ensuring that accurate minutes are prepared, circulated, and distributed in accordance with this policy,
- ensuring that disagreements with respect to understandings concerning the outcome of the meeting are resolved.
- ensuring that any policy or procedural issues that arise from a meeting that cannot be resolved within the division should be dealt with by involving supervisors, other divisions or offices as appropriate or the CDER Ombudsman, if necessary,
- ensuring the production of a monthly report on formal meetings with CDER's external constituents. [Data for these reports can be gathered and maintained in whatever method or format is most convenient for the reporting unit. However, the data reported monthly should be in the attached format. (Attachment A). These monthly reports shall be sent to: the appropriate Office Director, the Director of the Office of Training and Communications, and the Center Senior Project Manager.]

Office Directors shall be responsible for:

- ensuring that the divisions for which they are responsible have instituted meeting procedures and indeed are conducting their formal meetings with external constituents in accordance with this policy.
- reviewing their divisions' monthly reports and deciding whether further input from the office director is needed to assure conformity with this policy.

The Director of the Office of Training and Communications and the Center Senior Project Manager shall be responsible for:

- ensuring that the divisional monthly reports are assessed for evidence of further training needs in meeting management or minuting practices.

-
- compiling (OTCOM) all Center meeting statistics to have available for the Center and for external requests.
-

PROCEDURES

Meeting scheduling:

- Requests for a formal meeting with a Center component shall be made in writing to the appropriate CDER component (organizational work unit - most commonly, division).
- The written request should provide the following elements: 1) a brief statement of the purpose of the meeting; 2) a listing of the specific objectives/outcomes the requester expects from the meeting; 3) a proposed agenda, including estimated times needed for each agenda item; 4) a listing of planned external attendees; 5) a listing of requested participants from CDER; and 6) the approximate time at which supporting documentation for the meeting will be sent to CDER (i.e., "x" weeks prior to the meeting, but should be received by CDER at least 2 weeks in advance of the scheduled meeting).
- The responsible director for the CDER component, based on the information provided in the written meeting request, shall determine if such a meeting is clearly unnecessary or premature (not reasonably likely to be useful). If necessary the requester can be contacted for clarification of the purpose of the meeting.
- Information and/or supporting documentation necessary for a productive meeting does not need to be submitted before a meeting will be scheduled. This supporting documentation should be submitted and received by the applicable CDER component at least two (2) weeks prior to the agreed meeting date. If essential supporting documentation needed to conduct a productive meeting has not been received by the CDER component within this time frame, the meeting may be canceled and/or postponed, as determined by the Division Director. However, the meeting may take place if the component believes it would still be useful, even with a shorter time to review the package.
- If the meeting request is granted, details may be confirmed with the sponsor via the telephone. In addition, within 14 days of the meeting request, the division (usually the assigned Consumer Safety Officer (CSO)/Project Manager(PM)) shall notify the requestor, in writing (either by letter or fax), of the date, time, and place for the meeting to be held, as well as expected CDER participants. The meeting date shall reflect the next available date on which all applicable Center personnel are available to attend, consistent with the component's other business, but shall not exceed 75 days from the date of the external constituent's initial dated meeting request.
- If a commercial development program is stalled and cannot proceed until a meeting with FDA is held and agreement on issue(s) reached, the sponsor shall contact the

appropriate Office of Drug Evaluation director and request a "Special Considerations Meeting." If the Office Director agrees that the development program is stalled pending resolution of issue(s) with the FDA, the Office Director shall be responsible for insuring that a meeting with the appropriate FDA staff is scheduled and occurs within 30 days of the "Special Considerations Meeting" request. It is understood that scheduling of such meetings may require unusual times for the meeting.

- If scheduling conflicts make it impossible for certain requested CDER participants to attend a meeting scheduled within 75 days, the component shall consult with the requestor to decide whether the requestor prefers that the meeting be held without this person or delayed.
- The assigned CSO/Project Manager is responsible for ensuring that a meeting room appropriate for the projected number of participants is reserved. In addition, he/she should insure that all appropriate audiovisual equipment is reserved and available. This person shall also insure that all logistics are reconfirmed the day prior to the meeting.
- In the event that a request to schedule a meeting is denied (no meeting), the director responsible for the CDER component is responsible for assuring that the requestor is notified of the denial in writing (letter or fax) or by telephone with clear documentation of the telecon to the file within fourteen (14) days from receipt of the request. The notification shall include a clear explanation of the reasons for the denial. In addition, CDER's notification shall provide information detailing the appeal process.

Meeting:

- A "pre-meeting" of FDA personnel who will be attending the formal meeting should generally be held to brief FDA participants on the background and critical issues, to develop initial responses to questions specifically posed by the requestor (but recognizing that the discussion may modify these responses), and to consider the overall meeting strategy/plan. The objectives and agenda for the meeting should be discussed and understood by all. (See Attachment B) The agenda will generally be submitted by the external constituent. If any additional items for discussion are identified by FDA which might require preparation on the part of the constituent, the constituent should be notified prior to the meeting and any FDA materials should be provided to the constituent. Additionally, key persons should be identified (from those scheduled to attend the meeting) at the pre-meeting to: 1) chair/ facilitate the meeting for the FDA; 2) keep track of time; and 3) record minutes. The pre-meeting should preferably be held at least one day before the scheduled meeting with the external participant.
- The CDER chair/facilitator of the meeting shall provide initial structure to the meeting by welcoming the external constituents and clearly stating CDER's

understanding of the purpose and goals of the meeting. At the beginning of the meeting, the CDER chair/facilitator shall insure: that participants are introduced; that the person recording minutes for FDA is noted to the external constituent; that, if necessary, the timekeeper is noted to the external constituent; and that a decision is made between CDER and the external constituent as to who shall be the lead chair/facilitator (CDER or external constituent) for the discussion portion of the meeting. It is recognized that meetings are, and should be, highly interactive and that many meeting participants will participate in the discussions and respond to issues. The CDER chair/facilitator shall be responsible for assuring appropriate participation by FDA staff present.

- At the end of the meeting, the CDER chair/facilitator shall insure key points and/or decisions made are summarized and insure that all participants (FDA and external constituents) concur with the summarization and that any differences are resolved. The recorder shall note these summarized key points in the official FDA minutes of the meeting.
- The meeting timekeeper shall monitor the time dedicated to each agenda item. The timekeeper will notify the chair when discussions exceed the amount of time allocated on the agenda. A decision will then need to be made by the participants on how to utilize the remaining time allotted to the meeting.
- The senior management attendee is responsible for determining who should be the final signatory for the minutes and should inform the recorder. Generally it is expected that the senior management attendee will either be the final signatory or will indicate his/her concurrence with the minutes by initialing them.
- The recorder will accurately prepare minutes of the meeting, including the summarized key points as follows: 1) draft meeting minutes should be written and circulated (for review and comment) to all FDA personnel who attended the meeting within one week of the meeting date; 2) review and incorporate comments and finalize minutes within three (3) weeks after the meeting. (See suggested minute format at Attachment C.)
- Meeting participants will review draft minutes and return to recorder within one week of receiving the draft minutes.

Post-Meeting (follow up):

- Minutes of formal CDER meetings with external constituents shall include the appropriate "CC" (IND, NDA, ANDA, or other file as appropriate) and distribution list to ensure meeting minutes are incorporated into the appropriate administrative file.
- All agency personnel attending the meeting shall receive a copy of the final meeting minutes within four (4) weeks of the meeting.

- The CDER component shall send the external constituents a copy of the final meeting minutes within four (4) weeks of the meeting. The external constituents are responsible for notifying CDER of any significant differences in their understanding of the meeting outcomes (as reflected in the minutes). The CDER component shall notify the external constituent of this responsibility in the CDER letter accompanying the minutes.
- The division director (in consultation with meeting chair, if different from division director) shall be responsible for resolving differences identified by the external constituent between the FDA minutes and their understanding of the meeting outcomes. This negotiation may be accomplished by the project manager, but the division director has ultimate first-line responsibility for a successful resolution. If policy issues or requirements related to a particular application that emerge during or after a formal meeting cannot be resolved at the level of the component holding the meeting, the usual appeals mechanisms can be invoked by the external constituent, including requesting the mediation services of the CDER Ombudsman.
- All correspondence regarding meeting minutes, from FDA or external constituents, shall be submitted to the appropriate product administrative file.
- Monthly reports on formal meetings should include the information contained in the sample format outlined in Attachment A for each meeting (meeting date, company name, meeting chair, IND/NDA/ANDA#, drug name, date minutes issued to sponsor, recorder), and shall be submitted to the following, as defined under "Responsibilities:" appropriate Office Director; Director, Office of Training and Communications; and the Center Senior Project Manager. Copies of minutes of meetings at which policy decisions are made that affect more than one division or component shall be sent to the Associate Director for Policy, CDER.

Appeals

The appeals process shall be in accordance with CDER's appeals policies and procedures (CDER Appeals Procedures MAPP).

FORMAT

- Monthly Meetings Report (see Attachment A)
- Meeting Agenda (see Attachment B)
- Meeting Minutes (see Attachment C)

EFFECTIVE DATE

This MaPP is effective upon date of publication.

**Division Monthly Meetings Report
(Formal Face-to-Face, Teleconference, and Videoconference)**

Division:

Month of _____

Report preparer:

	Mtg Date	Cmpy Name	Frmt	Type	IND/NDA ANDA/ #	Drug Name	Chair	Recorder	Date	Minutes Issued
1.										
2.										
3.										
4.										
5.										
6.										

Format: F=face-to-face; V=videoconference; T=teleconference
 Type: R=RTF; PI = Pre-IND; EP2 = end of P2; PN=Pre-NDA; C=compliance, A=Advertising/promotion;
 S= major safety concern; O= other
 Attach copies of meeting agendas for above meetings.
 Also attach copies of meeting minutes finalized that month.

Copies to:

Appropriate Office Director(s)
 Director, Office of Training and Communications
 Center Senior Project Manager

Suggested Format for Meeting Agenda (if prepared by FDA)

Meeting Date: Location: Time:

External participant:

IND/NDA # and name of product, if appropriate:

Meeting Chair (FDA) Sponsor lead:

Introductions:

Meeting Objective(s):

Meeting Discussion Items:

	Name of Presenter	Discussion Item	Time Allocated
1.			
2.			

Summarize Agreed-upon Points/Unresolved issues

Discuss any necessary follow-up

Close meeting

Attachments/Handouts

Suggested Format for Meeting Minutes

Meeting Date: Time: Location:

IND/NDA/ANDA # (If Applicable) and Drug Name:

External participant (External meeting requestor - sponsor):

Type of meeting (45 day, RTF, pre-IND, End of P2, Pre-NDA, compliance, promotion, etc.)

Meeting Chair: External participant lead:

Meeting Recorder (CSO/Project Manager):

FDA Attendees, titles and offices:

External constituent and titles:

Meeting Objectives:

- 1.
- 2.
- 3.

Discussion Points (bullet format):

- 1.
- 2.
- 3.

Decisions (agreements) reached:

- 1.
- 2.
- 3.

Unresolved issues or issues requiring further discussion:

- 1.
- 2.
- 3.

Action Items:

Item	Responsible person	Due Date
1.		
2.		
3.		

Signature, minutes preparer: _____

Concurrence Chair (or designated signatory): _____

Attachment/Handouts