DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
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# STATEMENT OF

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# U.S. FOOD AND DRUG ADMINISTRATION

# DEPARTMENT OF HEALTH AND HUMAN SERVICES

# BEFORE THE

# SPECIAL COMMITTEE ON AGING

# UNITED STATES SENATE

# HEARING ON

# OVERSIGHT OF DIETARY SUPPLEMENTS

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**INTRODUCTION**

Mr. Chairman and Members of the Committee, I am Dr. Joshua Sharfstein, Principal Deputy Commissioner at the Food and Drug Administration (FDA or the Agency), an agency of the Department of Health and Human Services (HHS).

Thank you for the opportunity to discuss FDA's role in the regulation of dietary supplements, as well as the findings of the study on botanical dietary supplements by the Government Accountability Office (GAO).

Modern FDA oversight of dietary supplements began with the 1994 enactment of the Dietary Supplement Health and Education Act (DSHEA).[1] This regulatory system now includes the following key elements.

1) Prior to its marketing, the manufacturer of a dietary supplement is responsible for ensuring that the supplement is safe;

[1] The Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act) defines a "dietary ingredient" as a vitamin, a mineral, an amino acid, an herb or other botanical, or a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract, or combination of any of the above dietary ingredients. Dietary supplements must be intended for ingestion and may be found in many forms such as tablets, capsules, powder, liquids, softgels, or gelcaps. Importantly, under the Act, a dietary supplement may not contain an article approved as a new drug or an article authorized for investigation as a new drug for which substantial clinical investigations have been instituted and made public, unless the article was first marketed as a dietary supplement or conventional food. DSHEA defines the term "dietary supplement" as a product that, among other things, is not represented for use as a conventional food or sole item in a meal or diet; is intended to supplement the diet; and contains at least one or more dietary ingredients.

2) Manufacturers are only permitted to make certain types of claims, and may not make false or misleading claims of any kind;
3) Manufacturers must abide by current Good Manufacturing Practices (cGMPs);
4) Manufacturers must submit to FDA all reports that they receive of serious adverse events associated with a product that it manufactures; and
5) A manufacturer must submit a notification to FDA before it markets a dietary supplement containing a "New Dietary Ingredient."

## 1. RESPONSIBILITY FOR SAFETY

FDA does not approve dietary supplements before they reach the consumer. Rather, manufacturers of dietary supplements are responsible for ensuring that the supplement is safe before marketing.

In the case of a new dietary ingredient (described further below), a premarket submission of data and information regarding the safety of the product is required by law. Otherwise, a firm does not have to provide FDA with the evidence on safety before it markets its products.

Generally, manufacturers register their facilities but do not register their products with FDA.

## 2. CLAIMS

Under the law, claims that are allowed to be used on food and dietary supplement labels fall into three categories: health claims, nutrient content claims, and structure/function claims. Disease-related claims are generally not permitted for dietary supplements.

### Health Claims

Health claims describe a relationship between a dietary supplement ingredient and a reduction in the risk of a disease or health-related condition.[2] FDA's oversight has three components:

First, under the Nutrition Labeling and Education Act of 1990 (NLEA), FDA issues regulations authorizing health claims for dietary supplements after FDA's review of the scientific evidence submitted in health claim petitions.

Second, the 1997 Food and Drug Administration Modernization Act authorizes health claims based on an authoritative statement of a scientific body of the U.S. government with official responsibility for public health protection or research directly related to human nutrition, or the National Academy of Sciences. Such claims may be used after submission of a health claim notification to FDA.

[2] A health claim by definition has two essential components: 1) a substance (the dietary supplement or ingredient) and 2) a characterization of its relationship to a disease or health-related condition.

Third, FDA permits some health claims that are not authorized by regulation but are supported by credible evidence and accompanied by a non-misleading disclaimer. Such claims are referred to as "qualified health claims." For example: "One small study suggests that chromium picolinate may reduce the risk of insulin resistance, and therefore possibly may reduce the risk of type 2 diabetes. FDA concludes, however, that the existence of such a relationship between chromium picolinate and either insulin resistance or type 2 diabetes is highly uncertain."

**Nutrient Content Claims**

NLEA permits the use of claims that characterize the level of a nutrient in a food or dietary supplement made in accordance with FDA regulations.

Nutrient content claims describe the level of a nutrient or dietary substance in the product, using terms such as free, high, and low, or they compare the level of a nutrient in a food to that of another food, using terms such as more, reduced, and "lite." Most nutrient content claim regulations apply only to those nutrients or dietary substances that have an established daily value.

The regulations that govern the use of nutrient content claims help ensure that descriptive terms, such as high or low, are used consistently for all types of food products (including dietary supplements) and are meaningful to consumers.

Percentage claims for dietary supplements are another category of nutrient content claims. These claims are used to describe a level of a dietary ingredient for which there is no established Daily Value. Examples include simple percentage statements such as "40% omega-3 fatty acids, 10 mg per capsule," and comparative percentage claims, e.g., "twice the omega-3 fatty acids per capsule (80 mg) as in 100 mg of menhaden oil (40 mg)."

**Structure/Function Claims**

DSHEA established special regulatory procedures for structure/function claims for dietary supplement labels.

Structure/function claims describe the role of a nutrient or dietary ingredient intended to affect normal structure or function in humans. Examples of these claims include "calcium builds strong bones" and "fiber maintains bowel regularity."

Structure/function claims may also describe a benefit related to a nutrient deficiency disease, as long as the statement also tells how widespread such a disease is in the United States.

Manufacturers are responsible for ensuring the accuracy and truthfulness of these claims. Such claims are not pre-approved by FDA. If a dietary supplement label includes a structure/function claim, Section 403(r)(6) of the Act and its implementing regulation at 21 *Code of Federal Regulations* 101.93(b) require that the label state in a "disclaimer" that FDA has not evaluated

the claim. The disclaimer must also state that the dietary supplement product is not intended to "diagnose, treat, cure or prevent any disease," because only a drug can legally make such a claim under the FD&C Act.

Dietary supplement manufacturers that make structure/function claims on labels or in labeling must submit a notification to FDA no later than 30 days after marketing the dietary supplement that includes the text of the claim. FDA has provided industry with guidance on these requirements.

**Generally Not Permitted: Disease-Related Claims**

Dietary supplements are generally not permitted to claim to act as a treatment, prevention or cure for a disease or condition. Such claims are generally reserved for drugs and require pre-approval by FDA. The only exception is that supplements may claim a benefit related to a classical nutrient deficiency disease, provided that they also disclose the prevalence of the disease in the United States.

## 3. CURRENT GOOD MANUFACTURING PRACTICES

DSHEA provides express authority for regulations establishing cGMP requirements for dietary supplements.

In June 2007, FDA promulgated a final rule establishing these cGMPs, under which manufacturers are required to evaluate the identity, purity, quality, strength, and composition of dietary supplements. The final rule aims to avoid wrong ingredients; too much or too little of a dietary ingredient; improper packaging; improper labeling; or contamination problems due to natural toxins, bacteria, pesticides, glass, lead, or other substances.

To limit any disruption for dietary supplements produced by small businesses, the rule has a three-year phase-in for small businesses. The largest firms, with more than 500 employees, were subject to compliance beginning in June 2008; mid-size firms in June 2009; the smallest firms, with fewer than 20 employees, will be expected to be in compliance with the cGMPs this June.

Since the final rule was released, FDA has trained both industry stakeholders and FDA staff on the requirements of the regulations. Violations of the regulations are violations of the law and can lead to both civil and criminal penalties.

Since the rule went into effect in June 2008, we have conducted approximately 55 inspections for compliance with the new regulations. The majority of facilities have been found to be in substantial compliance.

## 4. ADVERSE EVENT REPORTING

As of December 2007, manufacturers, packers, and distributors of dietary supplements must forward to FDA any reports they receive of serious adverse events associated with the use of those products. These firms must also keep records about each adverse event report they receive and provide FDA with access to these records during inspections.

The Agency evaluates the serious adverse event reports, and any other adverse event information reported voluntarily by healthcare providers, firms, or consumers, to identify signals that a product may present safety risks to consumers. FDA received 1,107 serious adverse event reports in 2008 and 1,275 reports in 2009.

## 5. NEW DIETARY INGREDIENTS

The FD&C Act requires that manufacturers and distributors who wish to market dietary supplements that contain "new dietary ingredients" (NDIs) provide FDA with information regarding the safety of such a dietary supplement before marketing.[3] Ingredients marketed in food in the United States prior to passage of DHSEA are not "new dietary ingredients" and are

[3] A "new dietary ingredient" (NDI) is a dietary ingredient not marketed in the United States in a dietary supplement before October 15, 1994. The notification must include information on the basis on which the manufacturer or distributor concluded that a dietary supplement containing a new dietary ingredient will reasonably be expected to be safe. For 75 days after the filing date, the notifier may not market the dietary supplement that contains the NDI. During the 75-day period, FDA may ask the notifier for more information, which may reset the review clock. If FDA has no objection, it can acknowledge the notification but does not issue an "approval" regulation as it does for drugs or food additives.

thus grandfathered out of this requirement, as are many ingredients introduced into the food supply after 1994, such as those introduced for use in conventional foods.

There is no authoritative list of ingredients that were marketed prior to 1994, which creates a significant challenge to FDA in enforcing this provision of the Act.

FDA is developing a guidance document on what should be considered in determining the status of an ingredient as an NDI, what information should be submitted about a dietary supplement containing the NDI, and how a reasonable expectation of safety of the NDI should be established. We expect this guidance document to be ready by the end of this year.

**FDA'S ENFORCEMENT PRIORITIES**

FDA monitors products on the market for safety by reviewing adverse event reports, obtaining information from inspections of dietary supplement manufacturers and distributors, reviewing consumer and trade complaints, performing laboratory analyses of product samples, and monitoring retail outlets, including the Internet.

The Agency also monitors product information, such as labeling, package inserts, and accompanying literature, for potentially false or misleading claims. Our regulatory partners at the Federal Trade Commission (FTC) have authority over dietary supplement advertising.

Currently, the Agency focuses enforcement actions related to dietary supplements on three areas that pose the greatest risk to public health.

**Adulteration with Drug Substances**

Products that are marketed as dietary supplements but contain active ingredients in FDA-approved drugs, analogs of approved drugs, and other compounds that do not qualify as dietary ingredients, present an emerging and expanding challenge.

FDA has found that certain products in the following categories have been illegally represented as dietary supplements: sexual enhancement or erectile dysfunction, weight loss, cholesterol reduction, and body building products. These products have been found to be intended for use as drugs and to contain active prescription pharmaceutical ingredients including PDE-5 Inhibitors (e.g., sildenafil or Viagra), controlled substances for obesity (e.g., sibutramine or Meridia), lovastatin, and synthetic steroids or steroid-like substances.

These products are often sold with misleading labeling and are frequently manufactured without quality controls.

A challenge for enforcement is that some of these chemicals can be difficult to detect. Nonetheless, in the last two years:

FDA has participated in the voluntary recall of dozens upon dozens of tainted supplement products, including:

- More than 50 sexual enhancement supplements, including a rare "FDA-requested" recall;
- More than 40 weight loss supplements; and
- More than 80 body building supplements by two distributors alone.

The Agency has issued multiple consumer alerts and press announcements to warn consumers about hazardous products. These include:

- Four warnings about individual firms marketing sexual enhancement products in cases in which FDA was unable to secure acknowledgement of an appropriate action to remove the products from commerce;
- Multiple consumer alerts concerning more than 70 tainted weight loss supplements; and
- A public health advisory issued about body building products that are represented as containing steroids or steroid-like substances.

We have has participated in seizures and criminal prosecutions to disrupt the distribution of illegal products, including:

- Two civil seizures of illegal sexual enhancement supplements in 2009;
- Two individuals arrested for illegally trafficking weight loss "supplements"; and

- Multiple search warrant affidavits served on firms marketing body building products that are represented as containing steroids or steroid-like substances, with one manufacturer pleading guilty to selling the illegal products.

**Illegal Claims**

Dietary supplements with unsubstantiated and illegal claims may encourage consumers to self-treat for a serious disease without the benefit of a medical diagnosis or treatment. FDA conducts enforcement activities against supplements that make these types of claims.

For example, on March 31, 2010, the United States Marshal for the Western District of Wisconsin seized a range of dietary supplements and other products from a firm that was promoting the products for unapproved uses. The firm promoted its bee-derived products to treat, cure or prevent diseases and conditions such as cancer, asthma, arthritis and hypertension.

In response to the H1N1 flu crisis of 2009, FDA launched an initiative to address the numerous fraudulent products that were promoted to treat, prevent, or cure H1N1 flu. The Agency targeted products that were promoted on the Internet and issued Warning Letters to the owners of the websites. Approximately 70 products were supplements. In addition to the Warning Letters issued solely by FDA, FDA and FTC issued one joint letter to a supplement firm. This was the first joint FDA/FTC advisory letter.

**Unsafe Ingredients**

A dietary supplement is adulterated, and subject to enforcement action, "if it bears or contains any poisonous or deleterious substance which may render it injurious to health" or if it presents a "significant or unreasonable" risk to consumers. DSHEA allows the HHS Secretary to ban a dietary supplement if she finds it to be an "imminent hazard."

Under the current regulatory framework, FDA looks for such problems after marketing through reviewing the medical literature and analyzing adverse event reports. Because many products have multiple ingredients, it is challenging to identify causal connections between specific ingredients and adverse effects.

In 2009, FDA became aware of serious problems associated with a supplement product called Hydroxycut. Many of the reports advised of serious liver injuries, including liver damage that required transplants. After discussion with the Agency, the manufacturer voluntarily recalled Hydroxycut and subsequently reformulated the products.

**GAO STUDY**

Since October 2009, GAO has been conducting an investigation, at the request of this Committee, into the manufacturing and marketing of dietary supplements, particularly botanical

products. GAO has discussed its findings with FDA and we have provided GAO with our comments.

During their inquiry into the marketing of herbal dietary supplements, GAO investigators found a number of claims that appear to cause the products to be illegal. In general, these claims promised cures for diseases and conditions. When FDA identifies such claims in the labeling of products on the market, the Agency takes action.

GAO also analyzed 40 dietary supplements for heavy metal contaminants. All of the products were found to contain trace amounts of lead, cadmium, arsenic and mercury. Given the expected generally small consumption of the supplements, we do not believe these levels represent a significant risk to health. For example, the cadmium levels reached to about 1.4 µg/day (micrograms per day). This compares to FDA's tolerable daily intake level of 60 µg/day.

The lead levels reached to 1.9 µg/day, which is about a third of FDA's tolerable daily intake. While this is a not a dangerous level, it is a significant fraction of daily intake. It is possible that preventive standards of the type authorized by pending food safety legislation could help FDA reduce lead levels in dietary supplements as much as feasible.

Recently, FDA and the New York City Health Department identified lead in a dietary supplement at a level of 1,100 parts per million (ppm) -- more than 10,000 times higher than FDA's maximum recommended level for lead in certain candies. We immediately notified the

public of a potential risk and inspected the facility, and the manufacturer recalled the supplement.

GAO also analyzed supplements for pesticide residues. The 41 residues listed in Appendix IV of GAO's statement of facts fall into four groups.

- Seven residues were found at levels within the Environmental Protection Agency (EPA) tolerances for dietary supplements. For example, two samples of ginseng had residues of metalaxyl at .01 and .03 parts per billion (ppb), while the tolerance level for metalaxyl in ginseng is set by EPA at 3.0 ppb.

- Thirty-one (31) residues were at levels within tolerances used for fruits and vegetables, but there are no tolerances in the law for dietary supplements. For example, the pesticide chlorpyrifos has no set tolerance level for residue in Echinacea, where it was found at a level of .01 ppm. However, residue levels for chlorpyrifos have been set for celery at 15 ppm and for tomatoes at 5 ppm.

- One residue found was a low level of carbofuran, a pesticide that had its tolerances canceled by EPA in 2009.

- Two residues were low levels of pesticides that were either never approved for use in the United States (tolclofos-methyl) or had their use banned in the United States over 40 years ago (hexachlorobenzene, or HCB). These findings are within or very close to the allowable residue levels set by the European Union.

FDA presently analyzes close to two hundred herbal and botanical products annually in our pesticide monitoring program. When violations are found on imported dietary supplements, products are typically put on Detention Without Physical Examination, under which entries of such products are refused admission into United States commerce unless acceptable evidence is provided to the Agency demonstrating compliance with applicable requirements. Likewise, when violations are found on domestically-produced dietary supplements, the product is removed from commerce.

**CONCLUSION**

Thank you for the opportunity to discuss FDA's activities with regard to dietary supplements. FDA looks forward to working with Congress on this important public health issue.

I look forward to your questions.