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STATEMENT OF

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BEFORE THE
COMMITTEE ON GOVERNMENTAL AFFAIRS

SUBCOMMITTEE ON OVERSIGHT OF GOVERNMENT MANAGEMENT, RESTRUCTURING, AND THE DISTRICT OF COLUMBIA
UNITED STATES SENATE

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Mr. Chairman, thank you for inviting me to appear before you today to discuss dietary supplements and their use for weight-loss purposes. Accompanying me today is Dr. Christine Lewis Taylor, Director of the Office of Nutritional Products, Labeling and Dietary Supplements (ONPLDS) at the Center for Food Safety and Applied Nutrition (CFSAN) and Mr. John Taylor, Director of the Office of Enforcement, Office of Regulatory Affairs (ORA) at the Food and Drug Administration (FDA or the Agency).

Before I address regulatory actions taken against unapproved drug products promoted as weight loss supplements, let me take a moment to explain the regulatory and enforcement programs that FDA uses to implement the Dietary Supplement Health and Education Act (DSHEA or the Act) and Agency efforts to implement DSHEA in the eight years since it became law.

A DIFFERENT TYPE OF FDA PROGRAM

When Congress passed DSHEA, it created a unique regulatory framework for dietary supplements. Its purpose was to strike the right balance between providing consumers access to dietary supplements that they use to help maintain and improve their health and giving FDA the regulatory authority to take action against supplements that present safety problems or have false or misleading labeling.

The DSHEA regulatory framework for dietary supplements is primarily a postmarket program, as is the case for foods in general. Since Congress considered dietary ingredients marketed prior to the passage of DSHEA to be safe, dietary supplements containing these ingredients are permitted to be freely marketed, just like regular foods (e.g., fresh fruits and vegetables, processed foods and beverages, and seafood). Should safety problems arise after marketing, the adulteration provisions of the statute come into play. Under DSHEA, a dietary supplement is adulterated if it or one of its ingredients presents "a significant or unreasonable risk of illness or injury" when used as directed on the label, or under normal conditions of use

(if there are no directions). The burden of proof is on FDA to show that a product or ingredient presents such a risk. In addition, the Secretary of Health and Human Services (HHS) may also declare that a dietary supplement or dietary ingredient poses an "imminent hazard" to public health or safety.

In 1999, in Congressional testimony before the House Government Reform Committee, the FDA Commissioner stated, "It is clear, with the benefit of hindsight, that we still have a way to go both in achieving full implementation of DSHEA and in developing a workable regulatory framework." Based on that assessment FDA decided to take a step back, as if DSHEA had just been enacted, and lay out a long-term comprehensive framework to fully implement the statute. We embarked on a year-long process for FDA to formulate a roadmap of activities to fully implement DSHEA. I personally led this process which included considerable interaction with stakeholders.

STAKEHOLDER INPUT

Obtaining stakeholder input on dietary supplement issues and exchanging ideas with stakeholders on how best to address those issues is a high priority for FDA. To this end, we held two public meetings with stakeholders in the summer of 1999 - one in Washington, DC and one in Oakland, CA - to provide the dietary supplement community the opportunity to identify key issues and how they would like FDA to address these issues. These meetings provided the stakeholders an active role in developing an effective dietary supplement regulatory program. I chaired both meetings.

Overall, the stakeholders' major emphasis was on safety. "Safety first" was a frequent comment. Examples of stakeholders' recommendations include: 1) improving FDA's Adverse Event Reporting System (AERS); 2) publishing regulations on Good Manufacturing Practices (GMPs); 3) creating a stronger scientific foundation for regulating these products; and 4) leveraging outside resources. A number of participants placed a great deal of emphasis on FDA taking stronger action to ensure the safety, composition, and proper labeling of dietary supplement products, with a particular emphasis on safety. Many stakeholders called for greater enforcement of DSHEA.

FDA established five strategy teams to consider the ongoing stakeholder input and to discuss the dietary supplement activities needed to fully implement DSHEA. These teams covered the following topics: safety, labeling, boundaries, enforcement and research. The strategy team members were drawn from several FDA units, including CFSAN, the Center for Drug Evaluation and Research (CDER), ORA, and the Office of the Chief Counsel. A section on outreach was added later and the research category was broadened and renamed "science base." These categories formed the organizational structure of the Dietary Supplement Strategic Plan (DSSP). With the identification of stakeholders' major interests and concerns about DSHEA driving the creation of FDA strategy teams, our process to accomplish a long-term implementation strategy began.

THE DIETARY SUPPLEMENT STRATEGIC PLAN

On January 3, 2000, the Agency launched its DSSP. The plan is designed to be implemented in stages. Its foundation rests on both law and science.

The DSSP goal has four overall themes:

- Fully implement DSHEA. There was considerable concern within the industry that FDA would not "accept" DSHEA. The Agency clearly understands that Congress passed DSHEA and it is FDA's job to implement it as fully as possible.
- Implement DSHEA in a science-based way. This is the underpinning of all of FDA's successful programs, and FDA needs to use that same model here. A science-based model leads to greater objectivity in decision making and greater public confidence in FDA's actions.
- Achieve a high level confidence in the safety, composition, and labeling of dietary supplement products. It is the compass that should guide FDA.
- Engage in a long-term effort. Although implementation is underway, this is an ambitious undertaking. The strategic plan lists 35 issues to address within six broad categories. Moreover, resource availability will play a pivotal role in how long or short the implementation process will be.

Accordingly, the Strategic Plan's Goal Statement reads: "By the year 2010, have a science-based regulatory program that fully implements the Dietary Supplement Health and Education Act of 1994, thereby providing consumers with a high level of confidence in the safety, composition, and labeling of dietary supplement products."

FDA recognizes the success of the strategy will depend on new and continued partnerships with other government agencies, academia, health professionals, industry and consumers. The Agency is committed to continue its outreach to stakeholders by establishing stronger working relationships with them as well as leveraging resources, and communicating accurate dietary supplement information. The DSSP can be accelerated or decelerated, depending on resource availability and safety concerns.

The Strategic Plan is divided into six sections, consistent with the stakeholders' input that FDA received:
1. Safety
2. Labeling
3. Boundaries
4. Enforcement
5. Science Base
6. Outreach

1. <u>Safety - AERS and GMPS</u>

Virtually every stakeholder urged us to address "safety first." Because of DSHEA's postmarketing emphasis, FDA needs an effective AER monitoring system to identify and respond to potential health risks to consumers associated with the use of dietary supplements. FDA's AERS for dietary supplements provides an essential tool for signaling potential safety problems that may be associated with the use of a particular product or type of products that needs to be investigated and critically evaluated.

For example, in March 2002, FDA issued a consumer alert about kava-containing dietary supplement products and the potential risk of serious liver injury. The basis for this alert was a review of adverse event reports involving kava kava from the U.S. and Europe by FDA health care professionals. In the U.S., FDA had received a report of a previously healthy young female, who after using kava, required a liver transplant. In other countries, approximately 25 adverse events had been reported, four of which resulted in liver transplants. In addition, the Europeans had reported a documented case of hepatic toxicity in an individual who retook the kava-containing product even after experiencing an initial reaction. Taken

together, this information warranted a consumer alert. FDA urged persons who have liver disease or liver problems, or persons who are taking drug products that can affect the liver, to consult a physician before using kava-containing supplements.

In April 2001, the Office of the Inspector General (OIG) of HHS provided a number of useful recommendations for enhancing the quality and capability of FDA's AERS for dietary supplements.

CFSAN has embarked on a significant effort to enhance its AERS through the development of the new CFSAN Adverse Event Reporting System (CAERS). Inherent in the design of CAERS is the capture and analysis of all reports of consumer complaints and adverse events related to CFSAN-regulated products, particularly dietary supplements. This system will incorporate all existing Center adverse events reporting systems into one state-of-the-art reporting and monitoring system. The CAERS staff will work closely with program experts throughout FDA and other governmental agencies, and with industry, professional organizations, and other interested parties. CAERS is in its developmental stages. With new funding of 2.5 million dollars provided in the Fiscal Year (FY) 2002 budget, FDA will be able to pilot-test the new system this fiscal year.

There is broad public support for dietary supplements GMPs to enhance public confidence in these products. As a preventative measure, DSHEA grants FDA explicit authority to establish GMP regulations for dietary supplements. Such regulations are critical to assuring quality, purity, and consistency in dietary supplement products. FDA has made the publication of a GMP proposed rule a high priority and we are in the final stages of that process. We will conduct an outreach program after the publication of the proposed rule. Instituting a credible GMP system will require that FDA have enough field investigators for inspections to ensure that industry is manufacturing products in accordance with the GMPs.

2. Labeling

One of the challenges FDA faces is to strike the right balance between preserving consumers' access to products and information, and assuring the safety and proper labeling of all these products. At the public meetings we held in 1999, the stakeholders clearly expressed the view that labeling was a major problem and an area that FDA should emphasize as it worked to ensure public confidence in these products. When products are not labeled accurately or are labeled in a misleading way, consumers do not readily know what they are getting when they take these products.

For example, stakeholders raised concerns that consumers do not understand that dietary supplements can interact in a harmful way with medications they may be taking, such as prescription or over-the-counter (OTC) drugs, and that it is important to discuss dietary supplement consumption with their healthcare providers. In addition, certain populations such as pregnant or lactating women, infants and young children, and the elderly are more vulnerable to potential adverse effects from dietary supplements. Many stakeholders want labels to include information that addresses potential drug/dietary supplement interactions and to discuss concerns related to specific, potentially more vulnerable populations.

FDA heard concerns from some stakeholders about labeling claims and substantiation of claims. Many stakeholders believe that there are products on the market with false or misleading claims, and that the line between labeling and advertising/marketing increasingly has become blurred through direct-to-consumer

advertising and through the Internet. Stakeholders also believe that FDA had not used its authority to enforce DSHEA with respect to labeling claims and substantiation.

DSHEA allows the use of certain claims (often called structure/function claims) of general well being from consumption of a dietary ingredient, and claims of benefits related to classical nutrient deficiency diseases. These claims require the manufacturer to notify FDA within 30 days of marketing. Manufacturers must have substantiation that the claims are truthful and not misleading, and the product label must bear the statement "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." FDA published a final "structure/function" regulation in January 2000.

FDA reviews proposed health claims for dietary supplements under the provisions of the Nutrition Labeling and Education Act of 1990 (NLEA), implementing regulations and relevant case law. A number of dietary supplement health claims are authorized by regulation, including claims for calcium and reduced risk of osteoporosis and for psyllium and reduced risk of heart disease. By law, claims that a dietary supplement treats or mitigates a disease may not be made unless the supplement is approved for that use under the new drug provisions of the Federal Food, Drug, and Cosmetic (FD&C) Act.

DSHEA also contains a "premarket" provision which covers dietary supplement manufacturers that wish to market certain new dietary ingredients. New dietary ingredients are those that were not marketed in the U.S. before 1994, and that have not been in the food supply as articles used for food without chemical alteration. Dietary supplement manufacturers must submit to FDA, at least 75 days before the product is expected to go on to the market, information that supports the conclusion that a supplement containing the ingredient will reasonably be expected to be safe. After the 75-day period has expired, there is no requirement that the manufacturer receive FDA approval or clearance before marketing the product. It is essential for public health protection that FDA have the resources to review the notifications in a timely manner. So far, we have been able to meet our review deadlines. However, our workload may increase as, with the passage of time, the industry seeks to market more new dietary ingredients.

Finally, stakeholders pointed to recommendations made by the Commission on Dietary Supplements Labels on November 24, 1997. Stakeholders wanted FDA to use those recommendations as a blueprint for addressing many of the labeling concerns that still exist today.

3. Boundaries

The boundaries section highlights one of the profound challenges of DSHEA - determining the regulatory category of a product. It is important to draw boundaries between dietary supplements, drugs, and conventional foods and to give manufacturers notice of the regulatory regime that applies to their products. FDA's "structure/function" rule, referenced above, began to address the drug/supplement boundary issues.

4. Enforcement

The plan also outlines FDA's enforcement priorities, with safety as a top priority. This section also includes activities devoted to improving FDA's internal capacity in the enforcement area.

Industry clearly was concerned that FDA had not been sufficiently proactive in taking action against violative products on the market. They said the whole industry is affected by the few "bad actors"

marketing unsafe products or products with misleading and untruthful claims, and this undermines consumer confidence. Industry wanted FDA to take enforcement action, where appropriate, so there is a "level playing field" and so consumers will have confidence in the dietary supplement products that do provide benefits. In addition, industry wanted FDA to especially focus its enforcement action on those products whose claims are most egregious.

Consumers also wanted stronger FDA enforcement action. These stakeholders wanted FDA to be more assertive with respect to challenging product claims for substantiation, both in cases where the products presents safety issues and in cases where the products may not provide the benefits they allege they can.

Some specific enforcement activities are discussed later.

***Pearson v. Shalala* Health Claims Policy**

The U.S. Court of Appeals for the District of Columbia, in *Pearson v. Shalala*, ordered FDA to clarify its Significant Scientific Agreement (SSA) standard, reevaluate four claims the Agency had previously denied, and permit health claims that do not meet the SSA standard if a disclaimer can ensure that the claim will not mislead consumers.

The Agency has made considerable progress here. After issuing guidance clarifying the SSA standard and holding a public meeting, FDA published (in the *Federal Register* of October 6, 2000) its current strategy for implementation of the decision. This strategy includes providing enforcement discretion for qualified claims that meet designated criteria.

There have been 14 dietary supplement health claims considered by FDA subsequent to the *Pearson* court case. Of these, six claims were considered for qualified claims; six claims were denied or withdrawn prior to Agency consideration of permitting qualified claims; and two more claims are still under initial review.

5. Improving the science base

The science base section is the most important component of the plan because, like all FDA-regulated products, public credibility comes with knowing there is an adequate scientific foundation to the products and their claims. However, it is also the least well-developed section of the plan. Unlike conventional foods, FDA has limited experience and expertise with dietary supplement ingredients.

Stakeholders emphasized the importance of creating a stronger scientific foundation for regulating dietary supplements. FDA believes this to be the most important factor in the success of this program over the long-term if consumers are to have sustained confidence in these products. Accordingly, strengthening the science base is a critical element in the DSSP, just as it is with all of FDA's programs. The science base for a number of dietary supplements is starting to increase. FDA needs to take advantage of available science while promoting research to continually enhance its knowledge in this area. FDA believes very strongly that there needs to be a strong science base underpinning the regulatory program.

Stakeholders encouraged FDA to leverage outside resources to improve the science base. FDA is developing a broad dietary research agenda because we recognize the long-term success of the dietary supplement program is dependent on the strength of the scientific underpinning for these products. FDA will need to work very closely with the National Institutes of Health (NIH), industry, academia, and other Federal, State, and local agencies to ensure that the goal is met through leveraging and partnerships. We need to make sure the right research is undertaken and the right questions are answered. For example, we

are working closely with the Office of Dietary Supplements and the National Center for Complementary and Alternative Medicine at NIH.

In FY 2001, Congress appropriated one million dollars in FDA's budget for collaborative research between FDA and the National Center for Natural Products Research (NCNPR) at the University of Mississippi. NCNPR is nationally and internationally recognized for its expertise and research experience in botanicals used for health purposes. The NCNPR mandate is to bring government, academia, industry, consumers, health professionals and industry together to solve scientific problems in this area. We are enthusiastic about this new partnership and hope to be able to expand it in future years. An additional one million dollars has been appropriated for FY 2002.

Last year FDA entered into a contract with the Institute Of Medicine (IOM) at the National Academy of Sciences entitled, "Framework for Evaluating the Role of Dietary Supplements in Health." The IOM will develop a protocol for the Agency to use in reviewing the safety of dietary supplements. The contract requires that the IOM constitute a committee that will:

- Develop a proposed framework for categorizing and prioritizing dietary supplement ingredients based on safety issues;
- Describe a process for developing a review system with specifications for evaluating the safety and role in health of dietary supplement ingredients; and
- Develop at least six prototypes as examples of using the proposed framework.

The framework will include a methodology to examine the available peer-reviewed literature with regard to the role of dietary supplement ingredients in health. Methods that other expert bodies have used to categorize and review issues related to safety and the possible roles of dietary supplements and their ingredients in health will also be taken into consideration. The IOM process includes opportunities for public input. On
July 24, 2002, the Academy released the draft framework for public comment. Comments will be taken through September 30, 2002. The Agency now expects the final report in March 2003.

6. <u>Outreach</u>

Finally, the Outreach section of the plan reflects FDA's continued commitment to a two-way dialogue with the dietary supplement community. Communication with the general public, FDA field offices, health care professionals, and industry in an appropriate and timely manner is critical, particularly when information relates to potential adverse effects associated with dietary supplements. FDA will continue its commitment to establish a stronger working relationship with organizations interested in promoting two-way communication and cooperation. As a result of input from FDA's stakeholders and the increasing scope of the scientific questions concerning dietary supplements, a standing Dietary Supplement Subcommittee was recently added to FDA's restructured Food Advisory Committee. We are in the process of scheduling the subcommittee's first meeting.

CHALLENGES SINCE DSHEA

There have been many changes in the size and scope of the industry and in consumer use of dietary supplements since the 1994 enactment of DSHEA.

Dietary Supplement Consumption

A survey by PREVENTION Magazine on Consumer Use of Dietary Supplements in 2000 shows that over 158 million consumers use dietary supplements. The same survey states that "an estimated 115.3 million consumers buy vitamins and minerals for themselves, and 55.8 million purchase them for other members of their family, including children."

The basic reason cited for dietary supplement growth is the desire for self-care. According to the PREVENTION Magazine survey, consumers use dietary supplement products to help them achieve their self-care goals, which arise out of a sense of alienation from the established health care system. Results from a national survey conducted in 1999 by Men's Health magazine show that consumers use dietary supplements as a means of ensuring good health. They also use supplements for very specific, medicinal purposes such as treating and preventing serious illnesses, colds, and the flu; increasing mental sharpness; and alleviating depression (PREVENTION Survey).

The consumer's desire for self-care and the widespread use of dietary supplements may cause problems for public health. Many consumers put themselves at risk from misuse of dietary supplements and the possibility of interaction effects with prescription and OTC products. An estimated 22.8 million consumers use herbal remedies instead of prescription medicine, and an estimated 19.6 million use them with a prescription product, according to the same PREVENTION Magazine survey. According to the National Business Journal, 2000, dialog File No. 93, herbals and botanicals incorporate 32 percent of the estimated 17.1 billion dollars dietary supplement market for the year 2000, with vitamins slightly higher at 38 percent, as referenced in Illustration 3 (National Business Journal, 2000, Dialog File No. 93, San Francisco: The Dialog Corporation, 2000).

Size and Scope of the Industry

The dietary supplement industry is one of the fastest growing industries in the world consisting of 1,566 establishments, as referenced in Illustration 1 ("Survey of Manufacturing Practices in the Dietary Supplement Industry: Final Report," RTI Task Order No. 6, May 17, 2000). Dietary supplement sales reached 14.1 billion dollars in 1998 and are estimated to reach 15.5 billion dollars for 1999 and 17.1 billion dollars for 2000, as referenced in Illustration 2 ("US Dietary Supplements Market Size Expressed as Dollar Sales by Top Six Product Categories for 1994 to 1998 and Forecast for 1999 and 2000"; National Business Journal, 2000, Dialog File No. 93, San Francisco: The Dialog Corporation, 2000). In 1999, consumers spent nearly double the amount spent in 1994, and sales continue to grow at more than 10 percent a year (Nutrition Business Journal, San Diego, 1998).

Scope and Access to the Products

In the past, except for vitamin and mineral products, dietary supplements, particularly botanical products, were mainly sold to adults in health food stores. In contrast, such products are now available in supermarkets, other retail stores, and on the Internet, making these products readily accessible to children and other vulnerable populations. The Nutrition Business Journal estimated that in 1999 U.S. consumer sales of supplements over the Internet amounted to 142 million dollars, almost three times the previous

year's total of 48 million dollars ("E-Commerce in the Nutrition Industry," Nutrition Business Journal, Volume No. 4, April 2000).

REPORT TO CONGRESS

Congress asked FDA to identify the level of funding that would be necessary to fully implement DSHEA as outlined in the DSSP. In May 2002, FDA provided Congress with a "Dietary Supplement Strategic Plan Cost Out."

In this report, FDA estimates the initial investment cost to implement the goals in the Strategic Plan would be a range from 25 million to 40 million dollars by Year 3, increased to 30 million to 55 million dollars by Year 4, and completed at 40 million to
65 million dollars by Year 5. These estimates are reported in FY 2002 current dollars.

ENFORCEMENT

Congress defined the term "dietary supplements" in DSHEA. A dietary supplement is a product that is ingested, is intended to supplement the diet and, among other requirements, contains a "dietary ingredient." The "dietary ingredients" in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and dietary substances such as enzymes. Dietary ingredients also can be metabolites, constituents, extracts, concentrates, or combinations of the preceding types of ingredients. Dietary supplements may be found in many forms, such as tablets, capsules, liquids, or bars. Information on their label must not represent the product as a conventional food or a sole item of a meal or diet. Instead, DSHEA placed dietary supplements in a special category under the general umbrella of "foods" and requires that every supplement be labeled as a dietary supplement.

Agency Actions Based on Dietary Supplements Definition

When a problem arises with a product regulated by FDA, the Agency can take a number of actions to protect the public health. For dietary supplements, as with other products, initially, the Agency works with the marketer of the product to correct the problem voluntarily. If that fails, the Agency can also ask the marketer to recall a product voluntarily. The Agency can also seek, through the courts, seizure of violative products and/or injunction against firms or individuals who market violative products, and detain or refuse entry of products presented for import at U.S. ports. When warranted, criminal penalties - including prison sentences - are sought through the courts, as well as against those who violate the law.

The Agency's ORA works in close cooperation and coordination with all of FDA's Centers (the Centers) in enforcing the law. With regard to health fraud specific to dietary supplements, CFSAN has the lead and is responsible for the oversight of dietary supplements. CDER also has a role to play, as many of the most successful cases the Agency has brought concerned products purporting to be dietary supplements that were actually drugs within the meaning of the FD&C Act and failed to meet the regulatory requirements for drugs prior to their introduction into interstate commerce. The Agency has a number of ongoing activities directed at combating health fraud.

FDA has taken several enforcement actions pertaining to dietary supplements. These include actions related to products containing aristolochic acid and comfrey, obtaining injunctive relief in the case of products containing tiratricol, and actions against LipoKinetix. FDA took action against these products

because they did not contain dietary ingredients identified in DSHEA and/or because they were promoted to treat a disease or presented safety concerns. In FY 2002, Congress appropriated 500,000 dollars for dietary supplement enforcement efforts.

United States v. Syntrax Innovations, Inc., et al.

This case involved a drug called Triax Metabolic Accelerator, marketed by Syntrax as a dietary supplement for the treatment of obesity and to promote weight loss. FDA scientists determined that Triax posed a serious health hazard to those who consumed the product. The product contained triatricol, a potent thyroid hormone, that FDA medical review identified as a hazardous compound that could cause heart attacks and strokes. FDA alleged that Triax could not be a dietary supplement because it was promoted to treat a disease (obesity) and because it did not contain any of the dietary ingredients identified in the definition set forth in DSHEA.

This case began as a seizure by the Department of Justice (DOJ), but the government amended the complaint to request injunctive relief. Syntrax originally contested the case, but later conceded that Triax is a drug. On February 14, 2001, a District Court Judge entered an order of injunction to prevent the distribution of Triax by Syntrax Innovations. In 1999 and 2000, the Agency brought seizure actions against three other weight loss products that contained tiratricol.

E'OLA International, Inc.

At the request of FDA, U. S. Marshals seized unapproved drug products from Biogenics Inc., of St. George, Utah, doing business as E'OLA International, and at its contract manufacturer, Nature's Energy, Inc., of Pleasant Grove, Utah. About 140,000 bottles of AMP II Pro Drops valued at 2.8 million dollars were seized, along with the bulk ephedrine hydrochloride (HCl) used in its manufacture. Although the finished products
contained the drug, ephedrine HCl, they were labeled as dietary supplements for use in weight loss. The products, however, do not meet the definition of a dietary supplement because ephedrine HCl is not a dietary ingredient under the Act. FDA inspections of E'OLA revealed that the firm purchased raw materials and ephedrine HCl, had other firms produce AMP II Pro Drops on contract, and then had them ship the finished product back to E'OLA for distribution.
Ephedrine HCl has been approved as a drug by FDA since 1948 and, therefore, cannot be legally marketed as a dietary supplement. In addition, E'OLA marketed AMP II Pro Drops as a treatment for obesity. Dietary supplements cannot be marketed to treat obesity, a disease. These products also were misbranded because their labeling fails to bear adequate directions for use as is required of all drug products.

In April 2002, a District Court Judge signed a Consent Decree that prohibited Biogenics, Inc., from doing business as E'OLA from holding, manufacturing, processing, packing, labeling, promoting, or distributing AMP II Pro Drops or any other product containing ephedrine HCl or synthetic ephedrine.

Nature's Nutrition Formula One

FDA determined that this pre-DSHEA product, which was marketed between 1992 and 1994, as an all natural "nutritional supplement" that contained plant ingredients, was actually made with two pharmaceutical-grade chemicals, ephedrine hydrochloride and caffeine anhydrous. FDA received more than 100 reports of injuries and adverse reactions related to the product, ranging from serious and life-threatening conditions, such as irregular heartbeat, heart attack, stroke, seizures, hepatitis and psychosis, to

relatively minor and temporary conditions such as dizziness, headache and gastrointestinal distress. At least one death was associated with the use of this product.

This case was developed by the alerts provided from the adverse event reports, by ORA's field staff, and by the work of the Office of Criminal Investigation (OCI) with DOJ. FDA learned that the Chemins Company, Inc., which manufactured the product, went to great lengths to hide its actions from the Agency and concealed the actual ingredients of Formula One. As a result, the government launched a criminal prosecution against the company and its president, James Cameron.

On July 7, 2000, a Federal judge sentenced James Cameron to 21 months in jail and fined him and this corporation 4.7 million dollars. In his plea agreement, Mr. Cameron admitted that he and his company labeled Formula One as "all natural" but secretly spiked the product with synthetic ephedrine hydrochloride and caffeine anhydrous. He also admitted that the product's labeling failed to disclose the use of the chemicals on the list of ingredients, and that he and his employees had misled FDA investigators and hindered inspections of Chemins. The sentence marked the culmination of a three-year investigation. Mr. Cameron, whose company continues to make dietary supplements, began serving the sentence in September 2000.

Other Enforcement Actions

In addition, FDA and DOJ have pursued seizures of a number of unapproved drugs that have been promoted on the Internet as dietary supplements, including GBL and 1, 4 butanediol. FDA also has sought product recalls and achieved the voluntary destruction of 18 products containing these substances.

Other Activities to Combat Health Fraud

Health Fraud Working Groups

In 1992, FDA began sponsoring a National Health Fraud Working Group. The Working Group is currently comprised of representatives from the Association of Food and Drug Officials, State Attorneys General, Federal Trade Commission (FTC), Health Canada, and FDA representatives from the Center and field offices. This group meets on a regular basis to facilitate the coordination of regulatory activities, information exchange, and leveraging of each member agency.

Health Fraud Workshops

In July 2001, FDA, FTC and the Association of Food and Drug Officials sponsored a "Health Products Fraud Investigations and Law Enforcement: Building Partnerships Workshop" in San Antonio, TX.

The workshop provided an opportunity for attendees from Federal, State, and local regulatory and law enforcement agencies in the U.S., Canada, and Mexico to share their methods for regulating and prosecuting deceptive and fraudulent promotion of health products and services. The workshop helped the participants identify and leverage methods of enforcement. The workshop helped participants identify areas for coordination and cooperation with other agencies.

Building on the successful outcomes of the San Antonio workshop, FDA and FTC sponsored a "Health Fraud Summit" in Washington, DC on May 29, 2002. This meeting provided more than thirty management-level participants from twelve Federal/State regulatory and law enforcement agencies in the U.S. and Canada with an opportunity to come together to develop procedures to improve and strengthen interagency cooperation. The regulation of dietary supplements and the fraudulent marketing of dietary supplements were discussed at both meetings.

"Operation Cure.All"

FDA also has enhanced its cooperation with FTC, through "Operation Cure.All" and other efforts. In 1997, FTC, FDA, Health Canada, and various State Attorneys General organized and implemented an ongoing and comprehensive law enforcement and consumer education campaign against the fraudulent marketing of supplements and other health products on the Internet. The agencies have moved to stop Internet scams for supplements and other products that purport to cure cancer, HIV/AIDS, and countless other life-threatening diseases.

FDA has made Internet surveillance an enforcement priority. The Agency's partnership with FTC, and others, in "Operation Cure.All" further demonstrates FDA's commitment to monitoring violative conduct on the Internet. Collaboration on all "Operation Cure.All" activities maximizes FDA's effectiveness in communicating to the Internet community that the various regulatory and law enforcement agencies are working together to combat health fraud. All activities are coordinated in order to ensure consistent results in areas where FTC, FDA, the States, and Health Canada have jurisdiction.

Since the inception of the original Operation Cure.All campaign there have been three Internet surfing campaigns. In October 2001, a coordinated FDA and FTC Internet "surf" found Internet sites touting products and therapies that claim to prevent, treat, or cure anthrax, smallpox, and other health hazards. The Internet search focused on products claiming to protect against, detect, prevent, or treat biological and chemical agents, including anthrax.

The campaign was based on information gathered by FTC and FDA, more than 30 State Attorneys General, and the California Department of Health Services. More than 200 sites marketing bioterrorism-related products were uncovered. Included were 50 sites selling dietary supplements such as colloidal silver, zinc mineral water, thyme, and oregano oil as treatments for contamination by biological agents. FTC sent e-mail warnings to these operators telling them to pull the misrepresentations that any diet supplement could be used to cure anthrax. FDA sent warnings to nine Internet sites selling the antibiotic ciprofloxacin for the treatment or prevention of anthrax.

Since its inception, "Operation Cure.All" has resulted in hundreds of advisory letters directed at sites selling products with egregious claims as well as many enforcement actions directed against the marketing of fraudulent products. FDA sent cyber-letters to 48 sites selling colloidal silver products with egregious disease claims. And FDA sent a letter to manufacturers of products containing comfrey, which is associated with liver damage and other health hazards, advising them not to use this ingredient in dietary supplements.

The Agency has engaged in several consumer education efforts with FTC including a "Miracle Health

Claims: Add a Dose of Skepticism" health fraud brochure. The brochure helps the consumer in spotting false and unsubstantiated claims and has suggestions on how to avoid being the target of health fraud.

Other Internet Activities

Over the past several years, FDA has sharpened its focus on the issue of Internet promotion and sale of drugs as online activity has expanded. In 1996, and again in 1999, FDA held public meetings to discuss and examine the issue of promoting, prescribing, and dispensing drugs online.

In January and February 2002, an Internet surf was conducted as part of an International Internet surf, led by the Australian Competition and Consumer Commission and with participation by 19 members of the International Marketing Supervision Network, an organization made up of consumer protection agencies worldwide. As a result of the surf, FTC has sent over 280 advisory letters to domestic and foreign sites that were identified as making questionable claims for health-related products or services including dietary supplements. FDA also is making initial contact with Internet sites and alerting them to potential legal problems. The websites FDA visited promote dietary supplement products for treatment of diseases to include arthritis, cancer, and HIV/AIDS. As a follow up, CFSAN will be revisiting these sites to verify whether the website operators made corrective actions. FDA is planning follow up as appropriate. In addition, FDA and FTC are evaluating the responses to these advisory letters and they will coordinate appropriate enforcement actions if they are necessary.

In July 1999, FDA adopted, and has since been implementing, an Internet Drug Sales Action Plan to expand and improve its activities in addressing the unlawful sale of drugs over the Internet. The illegally marketed drugs targeted by the plan include a variety of fraudulent products, including counterfeit drugs, drugs marketed with fraudulent health-related claims, and unapproved new drugs masquerading as dietary supplements. The plan is based on internal deliberations, meetings with Federal and State regulatory and law enforcement bodies, as well as organizations representing customers, health care practitioners, and the pharmaceutical and pharmacy industries. The elements of the plan include, among others:

- **Public Outreach:** FDA Talk Papers, articles in the FDA Consumer magazine, and information on FDA's website to help educate consumers about safely purchasing drugs online.
- **Professional Outreach and Partnering:** Periodic meetings with State and Federal regulatory and law enforcement bodies, consumers, health care practitioners, and industry to share information and strategize about how to address the challenges the Internet presents.
- **Coordinating Activities with other State and Federal Agencies:** Established cooperative working relationships with DOJ, the Drug Enforcement Administration, the Federal Bureau of Investigation, FTC, U.S. Postal Service, U.S. Customs Service, and other appropriate Federal and State law enforcement agencies.
- **International Cooperation:** FDA and other Federal agencies must work with foreign governments to bring action against foreign-based sellers.

Under DSHEA, FDA will take appropriate action against unsafe products, inaccurate and misleading labeling and consumer fraud. FDA will also conduct marketplace surveillance and monitoring activities. FDA will establish partnerships with Federal, State, and local agencies to enhance enforcement efforts by sharing data, heightening communication, and utilizing resources.

FDA is committed to identifying and taking action on products that present safety hazards. In September 2001 testimony before the Senate Committee on Aging, FDA's Director of the Office of Enforcement stated, "While we are first and foremost a science-based public health agency, we also are a law enforcement agency… Strong law enforcement tools - including a cadre of seasoned law enforcement agents and sufficient statutory authority - coupled with a strong base of medical and scientific expertise to evaluate marketed health products are vital to the Agency's ability to meet its mission of protecting the public health."

Recent Developments

On June 14, 2002, HHS Secretary Tommy Thompson announced plans to expand scientific research on the safety of ephedrine alkaloids and to aggressively pursue the illegal marketing of non-herbal synthetic ephedrine alkaloid products. As part of these efforts, FDA sent six warning letters to firms unlawfully selling non-herbal ephedrine-containing products over the Internet. Six letters went to manufacturers of products that contain the drug ephedrine or norephedrine hydrochloride (a synthetic, non-herbal, version of the herbal ingredient ephedra) labeled as dietary supplements for use in weight loss, suppression of appetite, enhanced libido, and the like. These products violate the law because they are not legal dietary supplements and are illegal drugs. Also, FDA warned another company for illegally promoting its ephedrine product as an alternative to street drugs.

HHS recently funded the RAND Corporation to conduct a comprehensive review of the existing science on ephedrine alkaloids, particularly those in dietary supplements. The review should be completed this fall. NIH will use this information, which will clarify the existing state of the science on ephedrine alkaloids, to guide an expanded research effort to better understand the safety of ephedrine alkaloids.

CONCLUSION

FDA will continue to work collaboratively with other governmental agencies, academia, health professionals, industry, and the Congress so that we all can be assured that we are doing what is best for the American consumer with regard to the safety of dietary supplements. In support of that effort, the Agency firmly believes that its DSSP will provide the necessary blueprint, using a phased-in approach, for a comprehensive program that will implement the additional regulatory responsibilities required of FDA by DSHEA.

FDA fully understands that it operates in a world of limited resources and competing priorities and is sensitive to the amount of resources that will be required to fully implement its DSSP. The Agency also understands the discipline required to manage and utilize these resources in the most effective and economical way possible, while at the same time achieving maximum results for the taxpayer. The Agency is committed to utilizing all resources in a manner consistent with the goals and activities delineated in DSHEA and the Strategic Plan in order to achieve success.

Mr. Chairman, there are some specific questions in your invitation letter that I did not address in my written testimony. I would be happy to respond to those or any other questions the Committee may have. Thank you.