



December 15, 2010

Dear Manufacturer of Dietary Supplements:

This letter addresses the significant public health problems posed by products that are marketed as dietary supplements but that contain the same active ingredients as FDA-approved drugs, analogs of the active ingredients in FDA-approved drugs, or other compounds, such as novel synthetic steroids, that do not qualify as dietary ingredients. These ingredients, generally undeclared in the labeling, can pose considerable dangers to consumers who may take these products without knowing that the ingredients are present, that the ingredients may be associated with serious side effects, or that they may interact in dangerous ways with other products consumers may be taking. FDA has received numerous reports of serious adverse events associated with consumer use of these tainted products including strokes, acute liver injury, kidney failure, pulmonary embolisms (artery blockage in the lung), and death.

Recognizing our shared interest in addressing this problem, FDA is working with the dietary supplement industry's trade organizations to remind companies of their legal obligations and their responsibility to prevent tainted products from reaching the U.S. market.

Undeclared Active Ingredients in Products Marketed as Dietary Supplements

FDA laboratory tests have revealed an alarming variety of undeclared active ingredients in products marketed as dietary supplements, including anticoagulants (e.g., warfarin), anticonvulsants (e.g., phenytoin), HMG-CoA reductase inhibitors (e.g., lovastatin), phosphodiesterase type 5 inhibitors (e.g., sildenafil), nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., indomethacin), and beta blockers (e.g., propranolol). FDA has also identified products marketed as dietary supplements that contain active pharmaceutical ingredients removed from the market for safety reasons (e.g., fenfluramine), as well as new chemical ingredients of unknown safety. Some products marketed as dietary supplements have been found to contain controlled substances (e.g., benzodiazepines and anabolic steroids).

These products are illegal because they are unapproved new drugs under 21 U.S.C. §§ 321(p) and 355(a) and/or adulterated dietary supplements under 21 U.S.C. § 342. When such products contain undeclared ingredients or bear misleading claims (e.g., "100% natural" or misrepresentations about the safety of the product), they are also misbranded drugs under 21 U.S.C. § 352 and/or misbranded dietary supplements under 21 U.S.C. § 343.

FDA has found that products that are marketed as dietary supplements and that contain hidden or deceptively labeled ingredients are often promoted for weight loss, sexual enhancement, and body building. These products not only pose risks to consumers but undermine confidence in legitimately marketed dietary supplements in these and other categories.

To protect consumers from potentially harmful products that are marketed as dietary supplements, FDA must identify and test products that are already on the market, including products offered for sale on the Internet. This testing requires a significant investment of time and resources. In light of the increasing number of products FDA has found that test positive for these ingredients, FDA is focusing its efforts to address this problem.

Warnings, Recalls, Product Seizures and Criminal Consequences

Where FDA investigations have discovered products marketed as dietary supplements that contain the same active ingredients as in FDA-approved drug products, analogs of such drug ingredients, or other compounds of concern, such as novel synthetic steroids, FDA has issued warning letters and conducted seizures and criminal prosecutions. FDA has also worked with industry on the recall of numerous products with such potentially harmful ingredients, including more than 70 products marketed for sexual enhancement, more than 40 products marketed for weight loss, and more than 80 products marketed for body building. The Agency has also issued consumer alerts and press announcements to warn consumers about such products.

Starting today, FDA will establish a RSS feed on its website to alert consumers more rapidly when FDA finds that a product marketed as a dietary supplement is tainted. Following the public alert, FDA's investigation will include contacting the responsible firm to immediately address product that remains on the market or in the hands of consumers. FDA is also developing other communication tools to alert consumers and educate them about tainted products.

In addition to the actions listed above, responsible individuals and companies should be aware that the government may initiate criminal investigations to hold accountable those who violate the Federal Food, Drug, and Cosmetic Act (the Act) and endanger the public health. Responsible individuals, even if the individual did not participate in, encourage, or have personal knowledge of the violation, can be criminally prosecuted under the Act, pursuant to 21 U.S.C. § 331. See United States v. Park, 421 U.S. 658 (1975). When the evidence warrants, felony charges may be appropriate. Manufacturers, ingredient suppliers and distributors should not expect that a warning letter will be issued if FDA discovers potentially harmful violative ingredients in products marketed as dietary supplements. FDA recognizes that active ingredients at meaningful levels do not appear by accident in a product marketed as a dietary supplement – somewhere in the supply chain, the active ingredient is incorporated into the ingredient or the finished product. Actions that pose a risk to public health should expect a swift and strong agency response.

The Role and Responsibility of Industry to Address This Problem

Manufacturers, distributors, importers and others in the supply chain of dietary supplements are responsible for ensuring that their products comply with the statutes and regulations FDA enforces. Therefore, responsible individuals should take appropriate steps to ensure that their products do not contain active ingredients that may cause the product to be an unapproved new drug, a misbranded drug and/or an adulterated or misbranded dietary supplement, such as: those in FDA-approved drugs, analogs of approved drugs, active pharmaceutical ingredients removed from the market for safety reasons, new chemical ingredients that have not been studied adequately in humans, or controlled substances. In addition, companies that manufacture,

process, pack or hold dietary supplements are required to register their facilities under 21 U.S.C. § 350d and 21 CFR 1.225-1.243.

FDA recommends that all firms that manufacture, import, distribute, or sell dietary supplements that may be vulnerable to potential adulteration with undeclared active pharmaceutical ingredients and/or new chemical ingredients understand and investigate their full supply chain and review their manufacturing and quality assurance activities to ensure the lawfulness, quality, and safety of their products. Products in the weight loss, sexual enhancement, and body building categories should receive extra attention and scrutiny from their manufacturers and distributors. FDA issued a fact sheet on retailer and distributor responsibilities in October, available on FDA's website at:

<http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/MedicationHealthFraud/UCM230993.pdf>.

Manufacturers and distributors of dietary supplements must comply with all applicable dietary supplement Current Good Manufacturing Practice (CGMP) requirements in 21 CFR Parts 111 and 110 and are subject to FDA inspection. A dietary supplement manufacturer must have proper controls in place to ensure the quality of the dietary supplement and to ensure that the supplement is processed in a consistent manner. The CGMP requirements in Parts 111 and, as applicable, 110 apply to all domestic and foreign companies that manufacture, package, label, or hold dietary supplements for the U.S. market. Specifically, dietary supplement manufacturers must implement processes to ensure the integrity of their supply chain. For example, a firm that manufactures a dietary supplement must establish specifications for components used in the manufacture of the supplement. These specifications must include limits on those types of contamination that may adulterate or lead to adulteration of the finished batch of dietary supplement, as required by 21 CFR 111.70(b). The firm must verify that such component specifications are met, as required by 21 CFR 111.75(a). A firm must maintain records, including documentation that dietary supplements were manufactured in conformance with written procedures (21 CFR 111.375), that dietary supplement components conform to established product specifications, and, as appropriate, documentation of the qualification of a supplier for the purpose of relying on a supplier's certificate of analysis (21 CFR 111.95).

Raw ingredients arriving at a manufacturer's facility may already be tainted with undisclosed and illegal ingredients that, if present in a finished dietary supplement, would adulterate the dietary supplement, or cause it to be an unapproved and misbranded drug. A manufacturer must qualify its supplier and establish specifications for raw ingredients used in the manufacture of a dietary supplement to ensure that such ingredients are not a source of contamination. A strong program of qualifying your suppliers, testing incoming ingredients, and verifying the contents of finished products – all of which are required by the CGMP regulations – can help minimize those risks.

FDA encourages industry to report any suspected tainted supplement ingredients or finished products and the manufacturers or distributors who market these products to FDA. We have created two tools to receive this information – via email to TaintedProducts@fda.hhs.gov and/or via our anonymous reporting form “Report Suspected Criminal Activity” located at: <http://www.fda.gov/oci>.

In summary, FDA is very concerned about products marketed as dietary supplements that contain the same active ingredients as FDA-approved drugs, analogs of the active ingredients in

FDA-approved drugs, or other compounds, such as novel synthetic steroids, that do not qualify as dietary ingredients. Today, we are asking the dietary supplement industry's trade associations to share this letter widely. FDA is also seeking continued input and collaboration from the trade associations to educate the industry about this problem and to develop strategies to combat it.

Thank you for your efforts to protect the American public from harmful and deceptive products.

Sincerely,

/S/

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs