DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

The Honorable John D. Dingell
Chairman
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

AUG 13 2007

Dear Mr. Chairman:

Thank you for the letter of July 27, 2007, co-signed by Representative Bart Stupak, Chairman of the Subcommittee on Oversight and Investigations, regarding your investigation of the adequacy of the efforts of the Food and Drug Administration (FDA or the Agency) to protect the safety of the nation's food and drug supplies. Your letter expressed concerns about the safety of dietary supplements, particularly the safety of dietary supplements and their ingredients imported into the United States from certain countries including China and India. You requested information regarding FDA's regulation of dietary supplements.

We have repeated your questions in bold, followed by FDA's response.

1. The contaminated wheat gluten imported by ChemNutra was never inspected by the agency because the Operational and Administrative System Import Support did not designate wheat gluten as a high-risk product. Given that ChemNutra is primarily a dietary supplement provider and that wheat gluten can be used as an ingredient in dietary supplements, as soon as you learned about the contaminated wheat gluten, why did you fail to issue an import alert on all dietary supplement ingredients coming from China?

FDA's investigation did not show that the contaminated wheat gluten ingredients were used in dietary supplements. FDA's investigation showed that the contaminated wheat gluten was used as a pet food. Accordingly, the Agency did not have a basis for imposing an import alert for *all* dietary supplements and dietary ingredients from China.

2. Why, given the recent scandals involving Chinese imports of vegetable proteins, fish, and toothpaste, does FDA not require all importers of dietary supplements to test a scientifically valid sample of each shipment either before shipping such products for retail sale or as intermediary goods for inclusion in products intended for human consumption or animal feed?

FDA imposes import restrictions and testing requirements for foods including dietary supplements based on the identification of specific risks for which testing would provide

an effective mitigating response. Dietary supplements comprise a very diverse universe of products (e.g., vitamins, minerals, amino acids, herbs, extracts, and concentrates). Under the recently published Dietary Supplement Current Good Manufacturing Practice (CGMP) regulation, a dietary supplement manufacturer, foreign or domestic, will be required to ensure the quality of a finished dietary supplement by implementing processes throughout the manufacturing process. A manufacturer of a dietary supplement manufactured for the U.S. market will be required to verify that its finished batch of the dietary supplement meets specifications for identity, purity, strength, composition, and limits established by the firm for those types of contamination that may adulterate or that may lead to adulteration of the finished batch. The firm may verify this by either testing or examining (1) every finished batch, or (2) a subset of finished batches for the dietary supplement. The subset of batches tested must be identified using a sound statistical sampling plan. These requirements will help ensure the safety and quality of dietary supplements.

3. Does the agency think imports or untested dietary supplements and dietary supplement ingredients from countries with minimal safeguards such as China and India are safe for Americans to consume?

Manufacturers of dietary supplements for the U.S. market are subject to the dietary supplement CGMP regulation. FDA acknowledges that knowing the identity of what is being imported is the first step in ensuring the safety of dietary supplements. The CGMP regulation will require dietary supplement manufacturers, whether domestic or foreign, to test or examine every finished batch or a subset of finished batches using a sound statistical sampling plan to ensure that the specifications, including identity, purity, strength, composition and any limits established by the manufacturer for those types of contamination that may adulterate or may lead to adulteration of the finished batch, are met. Dietary ingredients that a manufacturer uses in producing a dietary supplement, whether the ingredients are produced domestically or by a foreign firm, must be tested or examined by the manufacturer to ensure that the use of such ingredient will result in a finished dietary supplement that meets its specifications for identity, purity, strength, composition, and any contaminant limits.

Manufacturers will be required to adequately evaluate the quality of product from each supplier of raw materials. In order to accomplish this, firms must establish specifications for each component of a dietary supplement. Then, if a component is a dietary ingredient, the manufacturer must perform at least one test or examination to verify the identity of the ingredient. The firm may rely on the supplier's analysis for other component specifications provided that it has first qualified a supplier by establishing the reliability of the supplier's certificate of analysis through confirmation of the results of the supplier's testing. The certificate must provide descriptions of the method(s) of analysis, the manufacturer must periodically confirm the supplier's certificate of analysis, and the manufacturer's quality control personnel must review and approve all of the documentation setting forth the basis for qualification or re-qualification.

As you are aware, FDA also has issued an interim final rule (IFR) which will allow firms that are subject to CGMP requirements to petition FDA for exemption from the requirement of 100% identity testing for dietary ingredients and request a reduced frequency of identity testing. A

manufacturer who petitions the Agency would have to provide data and information to FDA for why such a reduced frequency of identity testing would result in no material diminution of assurance of the identity of the dietary ingredient, as compared to the assurance provided by 100% identity testing. The petition is specific to a product from a specific supplier and must include a sound scientific basis for FDA to grant the exception. We have no preconceived notions of what these petitions will contain. FDA is soliciting public comment on the IFR. The public comment period will remain open through September 24, 2007.

Moreover, FDA expects that, within its resource constraints, the Agency's overall regulatory strategy for dietary supplement and dietary ingredient safety will provide an assurance that imports from countries with standards that differ from ours will meet U.S. quality and safety requirements prior to their distribution or use. The Agency's approach to ensuring the overall safety of all dietary supplements relies on several complementary actions:

- implementation of CGMP regulations intended to ensure the identity and quality of dietary supplements;
- application of FDA's farm-to-fork approach to food safety, an approach which systematically applies risk management principles at each step as foods move from producers to consumers;
- monitoring the marketplace and identifying and responding to potential safety concerns as rapidly and effectively as permissible; and
- post-market inspection and testing of products.

The answer to question four below gives a more in-depth discussion of FDA's overall approach to ensuring the safety of all dietary supplements.

4. How will the agency determine if untested dietary supplements and dietary supplement ingredients are safe?

Safety evaluation of dietary supplement products is based on the requirements established in the Food, Drug, and Cosmetic Act (the FD&C Act) as amended by the Dietary Supplement Health and Education Act (DSHEA). Although dietary supplements containing only dietary ingredients that were marketed in the U.S. before October 15, 1994, do not require a pre-market review for safety, dietary supplements may only be marketed in the U.S. if they comply with the safety requirements of the FD&C Act for dietary supplements and food. Moreover, for dietary supplements that contain dietary ingredients not marketed before October 15, 1994, the manufacturer of a dietary supplement that contains such ingredient must notify FDA 75 days before marketing and submit evidence that consumption of the dietary supplement containing the new dietary ingredient is reasonably expected to be safe. FDA objects if the Agency believes inadequate evidence has been presented to demonstrate that the product can reasonably be expected to be safe under the conditions of use recommended or suggested in labeling.

In addition, the Agency's approach to ensuring the overall safety of all dietary supplements relies on several complementary actions that we enumerated in our response to question three above.

If a contaminant were accidentally or intentionally added to a dietary supplement, FDA can expeditiously analyze samples of the dietary supplement product and perform a safety/risk assessment of the amount of the substance being used in the product.

5. If dietary supplements are not tested, how will the agency determine if the product is labeled correctly?

As noted above, dietary supplements marketed in the U.S. must comply with the safety requirements of the FD&C Act and must bear truthful and non-misleading labeling. To fully protect public health and meet consumer expectations that what is on the label is what is in the bottle, FDA has published and will enforce a dietary supplement CGMP regulation that requires testing to confirm labeled dietary supplement identity and potency. The regulation requires a firm to verify that its finished batch of the dietary supplement meets specifications for identity, purity, strength, composition, and limits established by the firm for those types of contamination that may adulterate or that may lead to adulteration of the finished batch. The firm may verify this by either testing or examining (1) every finished batch, or (2) a subset of finished batches for the dietary supplement. If a subset of batches are tested, they must be identified using a sound statistical sampling plan. The manufacturer's quality control personnel are responsible for final assurance that what is claimed on the label is actually what is in the product.

The regulation provides more accountability in the manufacturing process so that consumers can be confident that the products they purchase contain what is on the label. Some problems the CGMPs help prevent are inclusion of the wrong ingredients, too much or too little of a dietary ingredient, contamination (for example, by bacteria, pesticides, and glass), and improper packaging and labeling.

FDA will monitor compliance with these requirements through examination of records during inspections and limited compliance testing of samples of finished products in the marketplace.

6. If dietary supplements are not tested, how will the agency determine if the product is as potent as claimed?

As noted above, dietary supplements marketed in the U.S. must comply with the safety requirements of the FD&C Act and must bear truthful and non-misleading labeling. To protect public health and meet consumer expectations on labeled potency, FDA has published and will enforce the dietary supplement CGMP regulation that requires testing to confirm labeled supplement potency. We have described these testing requirements in our response to numbers three and five above.

In addition, dietary supplement quality control personnel must confirm, through appropriate testing, that the dietary supplement is as potent as claimed. FDA will monitor compliance with these requirements through examination of records during inspections and limited compliance testing of samples of finished products in the marketplace.

Thank you again for your letter. If you have further questions or concerns, please let us know. A similar response is being sent to Chairman Stupak.

Sincerely,

Stephen R. Mason
Acting Assistant Commissioner
for Legislation