CHAPTER 63 - HEALTH FRAUD: HUMAN DRUGS

SUBJECT: Fraudulent Drugs	IMPLEMENTATION DATE: June 1, 2007 COMPLETION DATE: June 1, 2012

DATA REPORTING	
PRODUCT CODES	PRODUCT/ASSIGNMENT CODES
Use appropriate product coding for product/operation	63001

FIELD REPORTING REQUIREMENTS:

Submit to CDER, Office of Compliance (HFD-310), with copies to other appropriate agency officials in accordance with the Regulatory Procedures manual (RPM), recommendations for regulatory action concerning suspected health fraud drug products that are not subject to submission to CFSAN under the dietary supplement/foods CDER/CFSAN Intercenter Agreement (Agreement). See Attachment A for a copy of the Agreement. Regulatory actions concerning products that are the responsibility of CFSAN based on this Agreement should be recommended to the appropriate office in CFSAN.

PART I - BACKGROUND

In general, health fraud drug products are articles of unproven effectiveness that are promoted to cure disease or improve health or well being. The rationales used by a firm/individual for selling fraudulent products vary. Some products are distributed by sincere but misguided individuals; others involve promotional schemes by "quick-buck artists" and charlatans. The size and scope of the problem varies from small regional operations to nationwide and international marketers.

For many years, FDA policy in the health fraud area has been primarily aimed at detecting and removing from the market fraudulent products that present consumers with direct health hazards and serious indirect health hazards. As in the past, any product posing a direct health hazard to the user should receive priority agency attention.

This program includes general guidance concerning investigations and the submission of appropriate regulatory actions concerning fraudulent products that are direct or serious indirect health hazards. In addition, the program emphasizes the mutually supporting roles and responsibilities of the Field and Headquarters in achieving the agency's public health protection objectives.

PART II - IMPLEMENTATION

OBJECTIVES:

Consistent with agency priorities and resources, the agency’s objective is to identify, investigate, and take corrective action against fraudulent drug products that are direct or serious indirect health hazards to the consumer.

PROGRAM MANAGEMENT INSTRUCTIONS:

A. General

The protection of the public health using sound risk management principles requires timely communication between the Districts, the Division of Field Investigations, the Division of Field Sciences, the Office of Enforcement/ORA, the Office of Criminal Investigations, and the Office of Compliance/CDER concerning planned and ongoing surveillance and compliance activities. It is the responsibility of each organization involved in these operations to ensure that all appropriate levels of the agency are kept current on the status of potential, emerging, and active investigations.

Health fraud products that pose a direct health hazard to the user are the agency’s highest health fraud enforcement priority. For the purposes of this compliance program, a product presents a direct health hazard if the drug is likely to cause death, injury, or other serious adverse effect when used as labeled or in a customary manner. [See Compliance Policy Guide (CPG) § 120.500, Health Fraud - Factors in Considering Regulatory Action.]

Health fraud products that pose an indirect health hazard are those that do not directly harm the person as a result of their use, but instead deny, delay, or interfere with effective treatment. Those indirect health hazards that may have a significant adverse impact on a patient’s health by directing the user to forego standard, recognized therapy are considered high priority as well. Before devoting significant resources to the investigation of potential health fraud cases that involve indirect health hazards, Districts should contact the Internet and Health Fraud Team

(HFD-310).

This CPGM describes several factors which may influence regulatory action.

B. Specific

CPG § 120.500 describes health fraud and the factors that the agency will consider before initiating regulatory action. Consistent with the CPG, this CPGM has been revised to: (1) include only two categories of health fraud products -- direct health hazard and indirect health hazard; (2) eliminate the "economic cheat" category, since economic fraud is a component of all health fraud products; and (3) provide a current list of factors that influence the initiation of regulatory action for indirect health hazards.

1. Direct Health Hazards

Products in this category present a direct health hazard because they are likely to cause injury, death, or other serious adverse effect when used as directed or in a customary manner. Actions taken against these products will continue to receive the agency's highest health fraud enforcement priority. Products included are those that pose a significant risk of causing serious adverse effects (e.g., based on toxicity or serious/hazardous interactions with other drugs or foods), and those for which there is documentation of injury or death. When these products are encountered, the district shall immediately contact the Internet and Health Fraud Team (HFD-310) to discuss the hazard and determine if investigations have already been initiated by other agency entities, such as OCI. When appropriate and in consultation with the Internet and Health Fraud Team, the district will conduct a thorough investigation as soon as possible. Refer to RPM 7-6-1 for procedures in determining a Health Hazard Evaluation.

2. Indirect Health Hazards

Products in this category may not directly harm persons as a result of their use, but rather cause harm by denying, delaying, or interfering with effective treatment. Products included are those that may have a significant adverse impact on a patient's health due to: (1) promotion of the products for uses for which they are not effective; and (2) the delay or denial of proper medical treatment resulting from reliance on the fraudulent products.

Because of limited resources, enforcement actions against serious indirect hazards must be carefully selected based on the level of risk posed by the products involved. The selection process should focus primarily on those firms or products against which enforcement actions would offer the most public health benefit. The following factors will be considered by CDER in the review of regulatory action recommendations:

1) Whether the marketing of the products is likely to have a significant negative impact on the NDA approval or OTC drug monograph processes;
2) Whether the enforcement action is likely to have widespread effect on other similarly situated fraudulent products and/or have a deterrent effect on the future marketing of similar fraudulent products;
3) Whether the therapeutic claims or conditions to be treated are significant, as interpreted by CDER;
4) Whether there are scientific data or specific pieces of information to support the safety or effectiveness of the product for its intended or customary use;
5) The degree of vulnerability of the prospective user group, e.g., the elderly or persons with illnesses for which there is no recognized effective treatment;

6) The availability of other administrative or regulatory alternatives to bring the product or firm into compliance, e.g., education, referral, or cooperation with local, state, or other federal agencies;
7) The amount of agency resources required and whether those resources are sufficient to pursue the action to its conclusion;
8) The source of the product, size of the industry distributing the same or similar products, and the likely impact of the action on that source and industry;
9) The cost of the product, and the profit (per sale) realized from the sale of the product;
10) The amount (dollar and volume) of product sold, and the geographical scope of its distribution.

Generally, enforcement actions against large firms distributing high volumes of fraudulent products are the most efficient focus of enforcement resources, particularly when the products involved are marketed for the treatment of serious disease conditions and undermine the NDA approval or OTC drug monograph processes.

PART III - INSPECTIONAL

Investigational tactics and strategies will be left to District direction as much as possible. Headquarters will issue assignments to the Field, as appropriate, based upon information obtained by the Internet and Health Fraud Team from field reports, consumer complaints, and other sources. Headquarters may furnish guidance through the issuance of specific assignments, Drug Fraud Bulletins, or through other means. These materials will provide Districts with background and direction for the investigation of classes of fraudulent products and guidance for regulatory follow-up.

The need for the collection of documentary samples to support a Warning Letter will be determined on a case-by case basis. The collection of labeling for each product to support any misbranding or new drug charges in a Warning Letter is essential. The labeling may be submitted as exhibits. Any questions regarding the need to collect documentary samples should be directed to DNDLC.

The Internet

The Internet has become a marketing and promotional tool that gives great visibility and reach to marketers of fraudulent products. It is imperative that information found on the Internet be preserved electronically or by website page printouts when a health fraud enforcement action is being contemplated. Internet websites can be used to document responsibility for fraudulent and illegal products and activities, and to establish the intended uses of a fraudulent product. If a product can be purchased from an Internet website, information contained on that Internet site often can be defined as product labeling.

Therefore, it is imperative that the Internet be considered an integral part of all investigations and recommendations for enforcement actions against health fraud products. The field can contact headquarters for assistance with internet investigative tools. Recommendations for enforcement actions must include a copy of any Internet website that supports the case. If no Internet website can be located concerning the firm or product that forms the basis of an enforcement recommendation, a statement to that effect should be included in the recommendation's cover memo.

Imports

Coverage of imported products will be conducted using the guidance given in this program for domestic products. Imported products that present direct or serious indirect health hazards should be given priority through the issuance of import alerts. Field offices are encouraged to submit recommendations of firms or products for inclusion in import alerts to the Division of Import Operations and Policy (DIOP), HFC-170. Note that coverage of products in domestic commerce should follow Part V below.

PART IV - ANALYTICAL

Specialized laboratory examination may sometimes be required, depending on the product being investigated. This may include characterization of products of unknown composition and possible impurities, as well as the development of new methods of analysis. Consult the Division of Field Science, HFD-141, for advice concerning analytical methodology. In general, when a product will be the subject of an enforcement action based on toxicity/direct hazard, a qualitative and quantitative analysis may be required.

PART V - REGULATORY/ADMINISTRATIVE STRATEGY

To be successful in meeting the Agency's public health responsibilities, efficient use of risk-management strategies is paramount. In this regard, heavy reliance should be placed on communication between the Districts and the Internet and Health Fraud Team (HFD-310).

CPG §120.500 provides guidance concerning when to take regulatory actions. Based upon the type of fraudulent drug product, the regulatory sanction may include a warning letter, seizure, detention, injunction, and/or referral to OCI for possible criminal prosecution. Recall of outstanding stock may also be appropriate. Assistance from other federal agencies and from state and local health authorities should be requested when needed, and the Districts should follow their specific procedures for making contact with these outside entities as appropriate. Whenever possible, inspections should determine whether the subject firm is a down-stream distributor or a significant supplier/manufacturer. If the former, districts should attempt to determine the source of the down-stream distributor's products. Therefore, the more significant firms can be targeted or at least copied on potential warning letters.

Decisions to take regulatory action may be based on factors or initiatives that originate outside CDER, as well as outside the agency. These factors may include international and national (interagency) enforcement and compliance initiatives, and HHS priorities.

It may be appropriate in some cases to supplement regulatory activities with FDA public health advisories and/or warnings to consumers about fraudulent products. For example, when a product poses a direct health hazard, press releases should be considered in consultation with the Internet and Health Fraud Team (HFD-310). When merited, FDA's health fraud activities should include educational and public information programs coordinated by public affairs mechanisms both in field offices and the Commissioner's office.

Direct Health Hazard

FDA will use all available sanctions to assure, to the extent possible and appropriate, that the violative product is removed from the market. Publicity may be used to warn consumers and health professionals about such products. Prosecutions shall be

considered and pursued when merited.

Indirect Health Hazard

FDA's primary objective is to obtain corrective action as swiftly and efficiently as possible.

District offices should consider all available sanctions in dealing with products representing serious indirect health hazards.

Warning letters as a first step can be the most efficient means of achieving correction with minimal use of resources. However, enforcement actions, such as a seizure, may also be considered to remove violative products from the market. Injunctions against manufacturers or major promoters also may be necessary to shut down illegal operations. Typically, when a product poses a serious indirect health hazard, seizures and injunctions follow a determination that a warning letter did not produce the required corrections.

To more efficiently use limited agency resources, enforcement actions should be directed primarily towards firms distributing/manufacturing large volumes of products that would be expected to have a negative impact on the NDA approval or OTC drug monograph process. Field Offices should further consider the criteria outlined in part B.2 of the Program Management Instructions, above.

Field offices should transmit proposed regulatory actions in accordance with current Agency policies and procedures.

Imports

Imported products that present direct or serious indirect health hazards should be given priority through the issuance of import alerts. Field offices are encouraged to submit recommendations of firms and or products for inclusion in import alerts to the Division of Import Operations and Policy (DIOP), HFC-170.

Detain all health fraud products that present a direct health hazard. When a product poses a serious indirect health hazard or solely economic fraud, contact DIOP, HFC-170, the Imports and Exports Team or the Internet and Health Fraud Team in HFD-310 to determine if detention is appropriate.

PART VI - REFERENCES, ATTACHMENTS, AND PROGRAM CONTACTS

REFERENCES

- Compliance Policy Guides: 120.500;
- Drug Fraud Bulletins
- Inspection Operations Manual: 4.4.9-LABELS AND LABELING

ATTACHMENTS

- Attachments A – CDER/CFSAN Intercenter Agreement

CONTACTS

- Linda Silvers, Team Leader, Internet and Health Fraud Team, CDER, (301) 827-8938.
- Gary Coody, Office of Enforcement, (240) 632-6806.
- Ada Irizarry, Team Leader, Imports and Exports Team, CDER, (301) 827-8967.
- John Verbeeten, Division of Import Operations and Programs (HFC-170), (301) 594-3853.
- Tom Savage, Division of Field Science (HFC-141), DFS/ORO/ORA, (301) 827-1026

PART VII - CENTER RESPONSIBILITIES

The Internet and Health Fraud Team, HFD-310, is responsible for:

1. providing guidance to the Districts in headquarters-issued assignments and Drug Fraud Bulletins, and furnishing Districts with information and reports of surveillance concerning health fraud products;

2. assuring that Drug Fraud Bulletins are cleared by the Office of Regulatory Affairs (ORA);

3. assuring that District assignments are cleared through ORA and other entities as appropriate;

4. consulting with and advising the Districts concerning surveillance investigations and candidates for enforcement within the District;

5. approving or disapproving regulatory sanctions and supporting litigation arising from this program; and

6. maintaining contacts with the National Health Fraud Coordinator and other FDA Centers, other state and federal components to assure that consumers are properly advised about fraudulent products in the market.

U. S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Center for Drug Evaluation and Research
June 1, 2005

Intercenter Agreement Between the Center for Drug Evaluation and Research and the Center for Food Safety and Applied Nutrition to Assist FDA in Implementing DSHEA Regarding Products that Bear Structure/Function and/or Disease Claims

This document outlines a working agreement between the Center for Food Safety and Applied Nutrition (CFSAN) and the Center for Drug Evaluation and Research (CDER) of the Food and Drug Administration (FDA). The agreement assigns lead Center status for the regulation of certain products that bear structure/function and/or disease claims. It *is* intended to achieve a more efficient allocation of resources and better coordination of regulatory actions concerning products that purport to be dietary supplements but for which disease claims are made. The agreement does not apply to products purporting to be dietary supplements that are subject to the jurisdiction of other Centers (CBER, CVM, or CDRH).

This agreement is intended to assist FDA in implementing DSHEA and the structure/function rule by clarifying program responsibilities in *light* of overlapping jurisdiction between CDER and CFSAN. The agreement is entirely procedural in nature and is not intended to affect the Agency's approach to the implementation of the structure /function rule or the regulation of dietary supplements. The agreement does not formally bind FDA and creates no new rights or obligations for FDA or any regulated entities.

For further information contact either:

Director
Office of Compliance
Center for Drug Evaluation and Research
11919 Rockville Pike
Rockville, MD 20852

Director
Office of Nutritional Products, Labeling, and Dietary Supplements
Center for Food Safety and Applied Nutrition
5100 Paint Branch Parkway
College Park, MD 20740-3835

I. EFFECTIVE DATE AND REVIEW/RENEWAL

This agreement takes effect on June 1, 2005. CFSAN and CDER will evaluate this agreement on a tri-annual basis and make appropriate modifications.

II. BACKGROUND

CDER is generally the FDA's lead Center for the regulation of human drugs, as defined in Section 201(g) of the Act. CFSAN is the Agency's lead Center for the regulation of human foods, as defined in Section 201(f) of the Act, and dietary supplements, as defined in Section 201(ff) of the Act.

The Dietary Supplement Health and Education Act (DSHEA) added Section 403(r)(6) to the Act. This section provides that the label or labeling of a dietary supplement may bear a claim that, among other things, "describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans" or that "characterizes the documented mechanism by which a nutrient or a dietary ingredient acts to maintain such structure or function." Such statements are generally referred to as "structure/function" claims. In addition, the definition of a drug in Section 201(g) was amended by DSHEA
to establish that a dietary supplement is not a drug solely because the label or labeling makes these structure/function claims.

Accordingly, the label and labeling of dietary supplement products may bear structure/function claims for which no prior FDA review or approval is required. However, DSHEA does not permit any statement in the product's label or labeling that claims to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases. These claims are generally referred to as "disease claims" and cause products associated with these claims to be regulated as drugs under Section 201(g)(l)(B) of the Act. Disease claims may be explicit or implied if such claims refer to identifiable characteristics of a disease from which a disease may be inferred. In order to help define the types of claims that are valid structure/function claims under Section 403(r)(6) of the Act, and to distinguish these claims from disease claims, FDA published a final rule on January 6, 2000 (65 FR 1000), known as "the structure/function rule." This MOU will not affect CDER's lead responsibility, as stated in the joint CDER/CFSAN letter of February 29, 2000, for distinguishing between "disease" and "non-disease" states or conditions in implementing the structure/function rule.

III. CFSAN DESIGNATION AS LEAD CENTER

Under this agreement, CFSAN is designated as the lead Center for regulatory action for certain products for which the labeling includes disease claims if such products also conform to each of the elements of the dietary supplement definition that appears in

section 201(ff) of the Act. Likewise, CFSAN is designated as the lead Center for regulatory action for certain products for which the labeling includes disease claims, but which do not bear the term "dietary supplements," provided that the products conform to all other elements of the dietary supplement definition that appears in Section 201(ff) of the Act and the products are labeled for marketing purposes as dietary supplements. Furthermore, CFSAN will be the lead Center if the *sole* reason for the product being subject to the drug requirements is that its labeling includes a disease claim rather than a structure/function or other appropriate dietary supplement claim.

As the lead Center for the products described above, CFSAN will have the authority to include appropriate drug charges (including sections 502 and 505 of the Act) in any regulatory action concerning a product associated with a disease claim. CFSAN agrees to consult with CDER, as appropriate, to ensure consistency when pursuing regulatory action based upon these drug charges.

CDER will retain concurrent jurisdiction to assert drug charges in pursuing regulatory actions against certain types of products for which CFSAN is the lead Center. In these cases, CFSAN will retain the right of first refusal for regulatory action. In these designated areas, CDER may pursue regulatory action for which CFSAN has declined to exercise its authority as lead Center, CDER agrees to consult with CFSAN and provide adequate advance notice before pursuing regulatory action under the circumstances.

CDER's action in these cases will be limited to drug charges and will not include any food charges. The designated areas are for products with disease claims that otherwise conform to each of the elements of Section 201(ff) of the Act, but raise unique issues for which CDER's historical role or medical expertise adds value to the Agency's regulatory action. The designated areas include the following:

- Products containing hormones, including their metabolites and precursors;
- Products that have ion- use as drugs and are widely recognized as drugs, even though they might be marketed purporting to be dietary supplements; and
- Products for which CDER has identified serious health hazard concerns.

CFSAN will also be the lead Center for regulatory action concerning conventional foods, medical foods, foods for special dietary use, and infant formula, even if disease claims are made for such products.

IV. CDER DESIGNATION AS LEAD CENTER

The following are the type of products, with disease or structure/function claims, for which CDER will serve as lead Center because the products do not qualify as dietary supplements under Section 201(ff):

1. The product is labeled as an over-the-counter or prescription drug and the product is not labeled as a dietary supplement.

2. The product is not "intended to supplement the diet" under Section 201(ff)(l) of the Act (e.g., street drug alternative products, GHB/GBL).
3. The product does not bear or contain any of the designated "dietary ingredients" under Section 201(ff)(l)(A) - (F) of the Act.
4. The product is not "intended for ingestion" under Section 201(ff)(2)(A)(i) (e.g., topicals, inhalants, suppositories, etc.).
5. The product contains a component, under Section 201(ff)(3)(B)(i), that is an article approved as a new drug that was not marketed as a dietary supplement or a food before such approval (e.g., lovastatin).
6. The product contains a component, under Section 201(ff)(3)(B)(ii), that is an article authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, which was not marketed as a dietary supplement before such approval.

CDER will continue to serve as the lead for combination drug and dietary supplement products, such as:

- products that contain a drug and a diem ingredient in a single product (assuming CDER supports a drug charge);
- products that consist of co-packaged individual drug and dietary supplement products; and
- dual labeled products

V. ADMINISTRATIVE PROCESS

CDER and CFSAN agree to promptly establish necessary procedures to ensure adequate communication and a consistent approach to the interpretation and application of this agreement.

/s/

Steven K. Galson, M.D., M.P.H.
Acting Center Director
Center for Drug Evaluation and Research

/s/

Robert E. Brackett, PhD.
Director
Center for Food Safety and Applied Nutrition