Gramm
Texas

United States Senate

MEMORANDUM

Date: 5-11-00

DUE DATE
6/13/2000

Department of Health and Human Services
Office of the Congressional Liaison
200 Independence Ave. SW, Room 416G
Washington, DC 20201

A constituent has sent the enclosed communication. A response which addresses his/her concerns would be appreciated.

Please send your response, together with the constituent's correspondence, to the following address:

Office of Senator Phil Gramm
2323 Bryan Street, #2150
Dallas, Texas 75201

Attention: Richard Zientek
(214) 767-5217
(214) 767-8754 (fax)

email: Richard_Zientek@gramm.senate.gov

No. 00-3570

CONST: Rick

FROM: Senat

SUBJECT: re:dj

DATE FO: May 1

ACTION: Direc

STAFF REF: This

PLEA

OCN-1200

C6

No. 00-3

SUMMARY OF IMPORTANT ISSUES WITH RESPECT TO FDA RULEMAKING ON DIETARY SUPPLEMENT PRODUCTS CONTAINING EPHEDRINE

- Request that the FDA allow a one year period for the public to analyze, review and comment on the adverse event reports (AERs) released by the FDA on April 3, 2000, rather than the forty-five day review period currently proposed by the FDA. (For further details, see attachment included with this briefing summary).

- Recommend that the FDA create a process to allow open public input in any future rulemaking concerning dietary supplement products containing ephedrine, and to take into consideration fully independent review and evaluation of the data on the AERs.

- Recommend that the FDA provide a forum during any future rulemaking process to allow the input and viewpoints of the industry, trade associations, consumers and other stakeholders.

- Recommend that the FDA convene a working group comprised of industry, trade associations, consumers and other stakeholders discuss all points of view concerning dietary supplement products so as to determine the best possible regulatory framework to achieve the FDA policy goals that is in the best interests of all parties concerned. If the FDA is unwilling to convene a working group, request that the FDA hold meetings with the industry, trade associations, consumers or other stakeholders to discuss the various respective viewpoints on this important issue.

- Recommend that the FDA delay any rulemaking until the House Science Committee has completed its investigations and hearings on dietary supplement products containing ephedrine.

- Note that FDA has been criticized by several government agencies in its regulation of dietary supplement products containing ephedrine. The FDA has been criticized for having a bias against ephedrine products. The Small Business Administration has criticized the FDA for the numerous delays in releasing the AERs. (See attached SBA letter.) The General Accounting Office (GAO) has issued reports criticizing the FDA for relying on inadequate and incomplete data in its initial round of rulemaking. (See attached report summary.)

WHY THE PUBLIC SHOULD BE GIVEN AN EQUIVALENT PERIOD OF TIME – ONE YEAR – TO RESPOND TO FDA'S LATEST ANALYSIS OF EPHEDRA

- FDA has just published a new Federal Register Notice announcing the availability of extensive new information relating to the consumption of dietary supplements containing ephedrine alkaloids (ephedra products). 65 Fed. Reg. 17510 (April 3, 2000). This Notice establishes a new docket relevant to ephedra products, which Joseph Levitt, FDA's Director of the Center for Food Safety and Applied Nutrition (CFSAN), described as "enormous," "approximately 15 to 20,000 pages of material, about 10 linear feet of documents."

- According to FDA's Notice, this new record contains approximately 270 new adverse event reports (AERs). FDA has separated a group of approximately 140 of these AERs, gathered during the period from June 1, 1997 to March 31, 1999, and has conducted two internal and 7 external expert reviews relevant to this set of 140 AERs. These reviews are extensive both in length and in supporting documentation. FDA's written analyses consist of more than 200 pages of text and tables and over 250 scientific references. The outside reviews are comparable in length. **FDA has taken over one year to review approximately half the AERs in question and to prepare the written analyses.**

- As a result of several Freedom of Information Act (FOIA) requests, FDA has had a legal obligation to provide the 140 AERs that form the basis for the agency's new assessment, as well as the 130 that FDA has yet to review, for almost 2 years. Instead of devoting the relatively minor resources that would have been needed to purge these records to meet its legal obligations to respond to the FOIA requests, FDA has expended enormous resources on its internal review and has also paid external consultants to review these records. FDA has made public statements on numerous occasions that the agency had no resources to purge the records at issue. These statements are contradicted by the record that the agency has just released.

- Mr. Levitt, in a telephone conference on March 31 with the American Herbal Products Association (AHPA), the Consumer Health Products Association (CHPA), the Council for Responsible Nutrition (CRN), and the National Nutritional Foods Association (NNFA), stated that FDA's primary goal between now and the public forum on ephedra products to be held in June is to obtain information from the public that would help the agency assess the safety of ephedra products. Mr. Levitt then confirmed that FDA was providing the public 45 days to obtain, review and analyze the new record.

- Perhaps a 45-day comment period would be reasonable if FDA had complied with its legal obligations under the FOIA and had turned over these documents two years ago. However, given the two years that FDA has withheld these records and the year that

FDA spent reviewing and preparing its own lengthy expert statements, FDA cannot now argue that the public should only have 45 days to accomplish a much larger task.

- In those 45 days, FDA expects the public to obtain copies of this record, and then to analyze and comment on not only the 140 AERs that occupied FDA's experts for over one year, but also FDA's extensive reviews of these original 140 AERs as well as the additional 130 AERs that remain unanalyzed.

- Each of the trade associations on the March 31 telephone conference with FDA strenuously objected to the comment period and asserted that the time permitted was obviously unreasonable. AHPA stressed FDA's failure to meet its legal obligations to respond to requests for the records at issue, and the need to hire experts to review the massive record and respond to FDA's experts. CRN stated that its ongoing review effort with an internationally-recognized toxicology firm, Cantox Health Sciences International, would not be completed until June at the earliest. CHPA said that it would need to retain experts through a bidding process, and then submit draft comments for review to member companies before submitting final comments to FDA. NNFA generally concurred with all of these assessments.

- Mr. Levitt was asked for his reaction to the inadequate comment period and was also asked why FDA could not give industry one year, approximately the time FDA took to compile the new record, to conduct a thorough review of that record. Mr. Levitt declined to comment other than to say that anyone could ask for an extension, and that he perceived that there was a need for rapid closure of the ephedra issue without disclosing what that need was.

- FDA's own delays and handling of the ephedra rulemaking belie the need for urgency. FDA began the process of reviewing ephedra products 6 years ago. Since that time, industry has created a national standard through industry guidance and state laws that industry has sponsored. As the General Accounting Office noted in its 1999 report on FDA's proposed rule, before FDA engages in further rulemaking, the impact of these standards needs to be carefully examined.

- In addition, the public health will benefit from a thorough review of the relevant data, and from the generation of additional data that are necessary to perform a complete health assessment of these widely sold products.

- FDA's latest review of these products again shows that FDA has attempted to use AERs to establish product risk in a manner that is contrary to accepted science and contrary to FDA's policy statement that AERs are not useful to assess product risk. FDA has given no consideration to the amount of ephedra product consumed in the period of time that the 140 AERs were collected. Further, although it is true that

adverse events such as heart attacks and strokes are not expected in young adults, there are published epidemiological papers that have been provided to FDA that establish the background incidence for these and other events in the relevant populations. FDA has made no mention of this information in its new assessment.

- FDA's own Center for Drug Evaluation and Research (CDER) stressed the need for such information prior to completing any health assessment in the Center's review of the 140 AERs that CFSAN provided. In the conclusion of its March 28, 2000 report, CDER stated that "[I]t is possible that the reported serious adverse events are reflective of coincidental background spontaneous occurrences in the population and are not necessarily causally related to [Ephedra] product uses. The availability of additional information, including product market or usage data, would be useful to further characterize the potential risks associated with the use of these products."

- At all costs, FDA must avoid any appearance that the agency is creating a process that will make it difficult or impossible for the public and industry to participate. The 45-day time period combined with FDA's failure to provide the records at issue despite numerous FOIA requests does just that.

- Given the unique history of this rulemaking and the unprecedented tension that it has created between industry and FDA, we propose that FDA allow a one-year comment period. There is precedent in the over-the-counter drug review process for comment periods of one year and even longer to permit the thorough assessment of the safety and use of products, such as ephedra, that are already widely marketed.

- We strongly believe that such a comment period is appropriate here and would have long-term benefits as well. FDA would be giving industry the same period of time to review this information that FDA took for its review. FDA would be assuring that it did not make a decision without all of the available data, as it now appears poised to do.

- Most important, a prolonged comment period would help to restore a working relationship between FDA and industry. The ephedra rulemaking has strained that relationship to the breaking point. FDA has repeatedly stated that it intends to foster a more cooperative relationship with the dietary supplement industry. It is time for FDA to act on its stated goals. A one-year comment period would be a significant step in the right direction.

Dietary Supplements: Uncertainties in Analyses Underlying FDA's Proposed Rule on Ephedrine Alkaloids (Letter Report, 07/02/1999, GAO/HEHS/GGD-99-90).

In 1997, the Food and Drug Administration (FDA) published a proposed rule that would establish a dosing regimen, require warning statements, and affect other aspects of product labeling for dietary supplements containing ephedrine alkaloids, which are promoted as helping individuals lose weight and increase energy levels. GAO is concerned that the proposed dosing level was based on information associated with only 13 adverse event reports and that the proposed duration-of-use limits were based on scientific studies showing problems with extended use well beyond the proposal's seven-day limit. FDA did not establish a causal link between the ingestion of ephedrine alkaloids and adverse events for either of these two aspects of its rule. FDA did not document the basis for its estimate of benefits from the rule sufficiently to allow GAO to determine the estimate's accuracy. FDA has no internal guidance on using adverse events reports for rulemaking related to dietary supplements, and its use of reports for this rule was different from its use in earlier rulemaking. FDA generally complied with statutory and executive order requirements for rulemaking but did not disclose why it made key assumptions in its cost-benefit analysis, the degree of their uncertainty, or alternative assumptions that would have dramatically affected its estimate of benefits.

---------- Indexing Terms ----------

REPORTNUM: HEHS/GGD-99-90
TITLE: Dietary Supplements: Uncertainties in Analyses Underlying FDA's Proposed Rule on Ephedrine Alkaloids
DATE: 07/02/1999
SUBJECT: Nutrition research
Health statistics
Agency proceedings
Food and drug legislation
Proposed legislation
Cost effectiveness analysis
Health hazards
Safety standards
Product safety
Safety regulation
IDENTIFIER: CPSC National Electronic Injury Surveillance System

Medical Device Reporting: Improvements Needed in FDA's System for Monitoring Problems With Approved Devices (Letter Report, 01/29/97, GAO/HEHS-97-21).

Pursuant to a legislative requirement, GAO reviewed user facilities' compliance with the Safe Medical Devices Act of 1990's (SMDA 90) reporting requirements, focusing on whether: (1) the enactment of SMDA 90 has led to an increase in reporting of device-related adverse events to the Food and Drug Administration (FDA); (2) the amount and quality of information from user facilities have enhanced FDA's ability to quickly identify and take action on device problems; (3) manufacturers and FDA have responded to device problems identified in user facility reports; (4) FDA routinely communicates device problem trends and corrective actions taken to user facilities and the public; and (5) changes need to be made to the user facility reporting requirements and FDA's adverse event reporting system to improve medical device problem reporting.

GAO found that: (1) although the amount of information reported to FDA about medical device problems has increased dramatically since SMDA 90 was enacted, FDA does not systematically act to ensure that the reported problems receive prompt attention and appropriate resolution; (2) as a result, FDA's adverse event reporting system is not providing an early warning about problem medical devices as SMDA 90 intended; (3) during fiscal years (FY) 1991 through 1994, FDA received almost four times as many adverse event reports from device manufacturers as it did during FY 1987 through 1990; (4) however, the extent to which user facility reporting under SMDA 90 directly accounted for the increased volume of reports is unclear because, until recently, FDA did not require manufacturers to disclose whether serious injury reports originated from user facilities or from some other source; (5) this increased volume made it difficult for FDA to process and review reports in a timely manner; (6) to address this problem, FDA chose to give priority to death and serious injury reports, which resulted in its delaying for nearly 2 years processing and reviewing almost 50,000 malfunction reports, which are essential in alerting FDA to potentially serious device problems before they result in death or serious injury; (7) to better manage the reporting workload in the future, FDA has initiated several changes to the adverse event reporting system; (8) FDA has received significantly fewer adverse event reports from user facilities than it expected; (9) much of the information that user facilities did provide was of poor quality and incomplete, in part because FDA did not issue the final medical device reporting regulation in a timely manner or periodically educate user facilities about their responsibilities under SMDA 90; (10) although FDA contends that it notifies manufacturers and user facilities about imminent hazards and industrywide safety concerns, it does not routinely document the corrective actions it takes or those taken by manufacturers to address reported medical device problems; (11) FDA does not keep track of the length of time it takes to process, review, and initiate action on serious device-related problems or the time that elapses before manufacturers resolve the problems; (12) manufacturer and user facility representatives told GAO they do not know how FDA uses adverse event reports to protect the public health; and (13) FDA and re-

---------- Indexing Terms ----------

REPORTNUM: HEHS-97-21
TITLE: Medical Device Reporting: Improvements Needed in FDA's System for Monitoring Problems With Approved Devices
DATE: 01/29/97
SUBJECT: Medical equipment
Reporting requirements
Product safety
Consumer protection
Statistical methods
Food and drug law
Hospitals
Government information dissemination

IDENTIFIER: FDA Medical Device Reporting System
FDA Medical Device and Laboratory Problem Reporting Program
FDA Manufacturer and User Device Experience System
FDA Medical Products Reporting Program
FDA MedWatch System
FDA Good Manufacturing Practices Compliance Program

ROUTING SLIP
GENERATED BY: HFW-1
DATE: MAY 24, 2000

FDA CONTROL NUMBER: 00 3570 TRACER #: OS #:

DATE OF CORRESPONDENCE: 05/11/00 DATE INTO FDA: 05/24/00

TO: DHHS

FROM: PHIL GRAMM, SENATE, UNITED STATES SENATE
RICK GREEN, TEXAS HOUSE OF REPRESENTATIVES

SYNOPSIS: (C) CCU#0519200017 RE DIETARY SUPPLEMENTS CONTAINING EPHEDRINE ALKALOIDS

LEAD OFFICE: HFW-1 HOME OFFICE: HFW-1

CONTACT/PHONE#: JULIA D POUNDS 301-827-0290

COPIES:

COORDINATION:

SIGNATURE REQUIRED: ASSOCIATE COMMISSIONER FOR LEGISLATION

REFERRALS FROM HFW-1

ASSIGNED TO	ACTION	DUE DATE
HFW-1 PRINCED	PREPARE DIRECT REPLY	06/13/00

REMARKS: DEPT SETS THE DUE DATE

Congressional Liaison
Correspondence Control Unit
Room 416G HHH Building
Telephone: 690-7452

DUE DATE	CONTROL #	DATE OF INQUIRY
6/13/2000	0519200017	5/11/2000

CONST: Rick Green REF TO: FDA

FROM: Senator Phil Gramm

SUBJECT: re:dietary supplement containing ephedrine alkaloids

DATE FO: May 19, 2000

ACTION: Direct Reply

STAFF REF: This was referred by Richard Zientek of your staff.

PLEASE RETURN A COPY OF THIS CONTROL SLIP
WITH REPLY !!!!!!!!!!!!

No. 00 - 3570