approximately 17 of the 270 adverse event reports the agency put in the docket after publication of the ephedrine alkaloids proposal. Consequently, FDA has reorganized these 17 reports to include the additional documentation that the agency has received, and it has redacted the files. FDA is now placing the 17 reorganized and redacted adverse event charts in the ephedrine alkaloids proposal's docket.

Should FDA receive additional information on the adverse events that are part of the administrative docket for the ephedrine alkaloids proposal, the agency will include it in that docket.

This updated information may be seen by interested persons at the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

Dated: March 28, 2000.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 00–8112 Filed 3–31–00; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00N–1200]

Dietary Supplements Containing Ephedrine Alkaloids; Availability

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of certain new adverse event reports (AER's) and related information, the vast majority of which were received after publication of the proposed rulemaking on dietary supplements containing ephedrine alkaloids. The agency is also announcing its intention to participate in a public forum to address this new information. This document is being issued to ensure that interested persons are aware of the new information the agency has available on these products and its plans to seek public input on this new information. Elsewhere in this issue of the **Federal Register**, FDA is withdrawing certain provisions of the proposed rule on dietary supplements containing ephedrine alkaloids and making available certain documents to update the administrative docket of that proposal.

DATES: Submit written comments by May 18, 2000.

ADDRESSES: Submit written comments on the information in this docket to the Dockets Management Branch, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments are to be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Marquita B. Steadman, Center for Food Safety and Applied Nutrition (CFSAN) (HFS–007), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852, 301–827–6733. A contact person for the public forum will be announced in the near future.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of June 4, 1997 (62 FR 30678), FDA published a proposed rule on dietary supplements containing ephedrine alkaloids (hereinafter referred to as ''the ephedrine alkaloids proposal''). FDA proposed to establish a finding that a dietary supplement is adulterated if it contains 8 milligrams (mg) or more of ephedrine alkaloids per serving within a 6-hour period or a total daily intake of 24 mg or more of ephedrine alkaloids (''dosing level'' or ''dietary ingredient level''), and to require the label of such supplement state that the product is not to be used for more than 7 days (''duration of use limit''). In addition, FDA proposed to require certain warning statements, and to affect other aspects of labeling for such products. FDA proposed this action after receiving over 800 adverse events associated with the use of dietary supplements that contained, or were suspected to contain, ephedrine alkaloids, and reviewing scientific literature and other data concerning ephedrine alkaloids. FDA received approximately 14,775 comments in response to the ephedrine alkaloids proposal.

The House Committee on Science requested that the Government Accounting Office (GAO) examine the scientific bases for the ephedrine alkaloids proposal, and the agency's adherence to the regulatory analysis requirements for Federal rulemaking. On August 4, 1999, GAO publicly released its report entitled ''Dietary Supplements: Uncertainties in Analyses Underlying FDA's Proposed Rule on Ephedrine Alkaloids.'' A copy of this report is available in Docket No. 95N–0304.

Generally, the GAO concluded that FDA was justified in determining that the number of AER's relating to dietary supplements containing ephedrine alkaloids warranted the agency's attention and consideration of steps to address safety issues. In addition, the GAO concluded that the available scientific information suggests that the use of products containing synthetic ephedrine alkaloids can result in adverse experiences for some individuals. However, GAO expressed concerns about the use of the adverse events in supporting the proposed dosing level and duration of use limit, and concluded that the agency needed additional evidence to support these restrictions.

GAO also concluded that FDA's economic analysis contained the basic elements expected in a Federal agency's cost-benefit analysis and that the ephedrine alkaloids proposal complied with regulatory flexibility analysis requirements under the Regulatory Flexibility Act. GAO noted, however, that FDA's cost-benefit analysis was not always transparent regarding why certain key assumptions were made, the degree of uncertainty involved in those assumptions, or the effect that alternative assumptions would have had on the agency's estimates of the costs and benefits of the proposed action.

GAO recommended that FDA ''provide stronger evidence on the relationship between the intake of dietary supplements containing ephedrine alkaloids and the occurrence of adverse reactions that support the proposed dosing level and duration of use limits.'' In addition, GAO recommended that FDA improve the transparency of its cost-benefit analysis in its final rulemaking.

Before the GAO report was released, FDA had already begun accumulating and evaluating data on additional adverse events reported to the agency since the publication of the ephedrine alkaloids proposal as well as initiating a process to obtain outside scientific input and review. Since publication of the ephedrine alkaloids proposal and following release of the GAO report, FDA has continued to receive reports of adverse events, conducted its own independent evaluations and analyses, and continued to seek input from outside experts on these issues. FDA is now making available new information, the vast majority of which it has received since publication of the ephedrine alkaloids proposal.

II. New Information—Docket No. 00N–1200

To gain a better perspective on the significance of the public health concern and public health problems associated with the current use of dietary supplements containing ephedrine alkaloids, CFSAN applied its available resources towards conducting

an analysis of 140 AER's with a report date (date the adverse event form was completed) period of June 1, 1997, through March 31, 1999, (''New Case Series''). CFSAN chose the June 1, 1997, date because it was close to the publication date of FDA's ephedrine alkaloids proposal. CFSAN chose the March 31, 1999, cut-off date so that it could have a closed set of data to analyze and prepare for public release. These adverse events, reported during the time period June 1, 1997, through March 31, 1999, had not previously received a comprehensive clinical analysis by the agency. All AER's received by FDA within that timeframe were included in the analysis. CFSAN's evaluation included an initial screening to determine whether the quality of the evidence available was sufficient to support a more comprehensive clinical evaluation of those adverse events that met the screening criteria. These criteria are identified in a document entitled ''Assessment of Public Health Risks Associated with the Use of Ephedrine Alkaloid-Containing Dietary Supplements'' which is available in this docket. (See section IV of this document for a more detailed outline of this document.) CFSAN used only those adverse events judged to have sufficient information for further evaluation. Following the initial screening of these reports, eight were eliminated from further review. The remaining 132 cases were subjected to an in-depth clinical review. CFSAN has also obtained a clinical review of 139 of the 140 adverse events in the New Case Series from FDA's Center for Drug Evaluation and Research (CDER). (One of the adverse events in the New Case Series reviewed by CFSAN was not identified as being within the designated time period for the New Case Series until after CDER's review began.)

As part of FDA's overall evaluation, it also contracted with outside scientific and clinical experts to obtain additional evaluation on dietary supplements containing ephedrine alkaloids, including the same 139 adverse events that CDER reviewed. FDA also conducted a market review covering August 1999 through March 2000 to determine whether there have been changes in the marketplace, including identification of new products containing ephedrine alkaloids.

A listing of this new information is provided in section IV of this document.

III. Pre-case and Post-case Series

FDA has received additional new AER's that have not been placed in any docket, and fall outside of the New case series timeframe (e.g., June 1, 1997, through March 31, 1999). Of these adverse events, 14 were reported before May 31, 1997, (''Pre-case series''). Moreover, 119 were reported beginning from April 1, 1999, and received by FDA by December 31, 1999, with any additional followup information received by February 15, 2000 (''Post case series''). Neither FDA nor its outside experts have conducted a comprehensive clinical analysis of the AER's in the Pre-case and Post-case series. FDA is announcing the availability of the Pre-case and Post-case series in this document.

IV. Public Docket

FDA is establishing a new docket [Docket No. 00N–1200] and making available at the Dockets Management Branch (address above) for public inspection the following documents:

1. One hundred and Fourty redacted AER's with a report date during the time period June 1, 1997, through March 31, 1999, (''New Case Series'') associated with dietary supplement products that were known or suspected to contain ephedrine alkaloids.

2. A document entitled ''Assessment of Public Health Risks Associated with the Use of Ephedrine Alkaloid-containing Dietary Supplements,'' which includes the following sections:

a. Section One: Overview/ Background

b. Section Two: CFSAN's Evaluation of New Case Series. This evaluation included an initial screening to determine whether the quality of evidence available was sufficient to support a more comprehensive clinical evaluation. CFSAN subjected only those adverse events judged to have sufficient information to further evaluation. Following the initial screening of these reports, 8 of the 140 were eliminated from further review. The clinical evaluation of the remaining reports resulted in the following classifications: (1) Adequate information to evaluate the relationship of product use to the adverse event and (2) insufficient data to further assess clinically or nonsupportive of a relationship between dietary supplements containing ephedrine alkaloids and the adverse event. Each of the reports with adequate information was reviewed and classified further into ''attributable'' and ''supporting''. The criteria for ''attributable'' and ''supporting'' are explained in the document.

c. Section Three: CFSAN's Review of the Published Literature on the Physiological, Pharmacological and Toxic Effects of Ephedrine Alkaloids.

d. Section Four: Bibliography of Scientific References/citations for documents a through c above.

e. Section Five: Appendices to Section Two above.

3. FDA's Center for Drug Evaluation and Research's review of AER's associated with dietary supplements containing ephedrine alkaloids, including a clinical review of 139 of the adverse events evaluated in CFSAN's New Case Series.

4. Reports from Outside Consultants concerning the following clinical/ scientific reviews:

a. Raymond Woosley, M.D., Ph.D., Review of 139 of the adverse events in the New Case Series and the likelihood of the events being associated with ephedrine alkaloids.

b. Neal Benowitz, M.D., Review of 139 of the adverse events in the New Case Series and the likelihood of the events being associated with ephedrine alkaloids.

c. Andrew L. Stoll, M.D., Review of specific neuropsychiatrically-related adverse events from the New Case Series and the likelihood of the events being associated with ephedrine alkaloids.

d. George A. Ricaurte, M.D., Ph.D., Review of specific nerologically-related adverse events from the New Case Series and the likelihood of the events being associated with ephedrine alkaloids.

e. Ka Kit Paul Hui, M.D., Opinion on the use of ephedra by practitioners trained in Traditional Chinese Medicine, including conditions, dosages, interactions, and duration of use.

f. Mario Inchiosa, Ph.D., Scientific literature search and evaluation of the pharmacokinetics of naturally-occurring ephedrine alkaloids and synthetic ephedrine alkaloids.

g. Alexander Walker, M.D., Dr. P.H., Statement concerning the likely reporting rate of adverse events involving dietary supplements.

5. Fourteen redacted AER's with a report date before May 31, 1997, which have not been placed in any docket (''Pre-case series'') concerning dietary supplements containing ephedrine alkaloids. These AER's have not received an extensive clinical analysis by FDA.

6. One hundred and nineteen redacted adverse events with report dates beginning April 1, 1999, and received by FDA by December 31, 1999, with followup information received by February 15, 2000 (''Post-case series'') concerning dietary supplements containing ephedrine alkaloids. These

AER's have not received an extensive clinical analysis by FDA.

7. CFSAN Market Review—FDA review covering the period August 1999 through March 2000 to determine whether there have been changes in the types of ephedrine alkaloid containing dietary supplement products available in the marketplace since the agency's review in 1995–1996.

Several parties have informed the agency that, since the issuance of the ephedrine alkaloids proposal, there is new usage data, and new scientific information, including clinical trials sponsored by manufacturers, that supports the safety of dietary supplements containing ephedrine alkaloids. FDA has not been provided this information to date and encourages interested persons to submit this information and any other information the submitter believes is relevant to assessing the safety of dietary supplements containing ephedrine alkaloids. FDA encourages interested persons to submit this information to this docket by May 18, 2000, so that it will be available to the public and the agency for review.

Interested persons may submit to the Dockets Management Branch (address above) written comments on the availability. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. These documents and any received comments may be seen by interested persons at the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

V. Public Forum

A public forum for discussion of the documents being made available in this document will be held at a date and location to be announced. A contact person for the public forum will also be announced.

Written comments received in response to this document, and participation at the public forum, will assist the agency in determining appropriate next steps regarding dietary supplements containing ephedrine alkaloids.

Dated: March 30, 2000.

William K. Hubbard,

Senior Associate Commissioner for Policy, Planning, and Legislation.

[FR Doc. 00–8283 Filed 3–31–00; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00D–1119]

Guidance for Industry on Street Drug Alternatives; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled ''Street Drug Alternatives.'' The guidance is intended to inform industry and the public that FDA considers any product that is promoted as a street drug alternative to be an unapproved new drug and a misbranded drug in violation of two sections of the Federal Food, Drug, and Cosmetic Act (the act). Such violations may result in regulatory action, including seizure and injunction.

DATES: Submit written comments on agency guidances at any time.

ADDRESSES: Copies of this guidance for industry are available on the Internet at http://www.fda.gov/cder/guidance/index.htm. Submit written requests for single copies of this guidance to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: William Nychis, Center for Drug Evaluation and Research (HFD–310), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–7363.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a guidance for industry entitled ''Street Drug Alternatives.'' FDA is issuing this guidance in response to the proliferation of various products that are being manufactured, marketed, or distributed as alternatives to illicit street drugs. FDA is concerned that these products are being abused by individuals, including minors, and pose a potential threat to the public health.

These street drug alternatives are generally labeled as containing botanicals, and some are also labeled as containing other ingredients, such as vitamins, minerals, or amino acids. They are marketed under a variety of brand names with claims implying that these products mimic the effects of controlled substances. These products are intended to be used for recreational purposes to effect psychological states.

This guidance is intended to inform industry and the public that FDA considers any product that is promoted as a street drug alternative to be an unapproved new drug and a misbranded drug in violation of sections 505 and 502 of the act (21 U.S.C. 355 and 352). Such violations may result in regulatory action, including seizure and injunction.

Moreover, FDA is also aware that some of these street drug alternatives are being promoted as dietary supplements. FDA does not consider street drug alternatives to be dietary supplements because they are not intended to supplement the diet.

This Level 1 guidance is being issued consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). The guidance is being implemented immediately without prior public comment because of the potential hazard to the public health. The guidance represents the agency's current thinking on street drug alternatives. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Interested persons may, at any time, submit written comments on the guidance to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: March 28, 2000.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 00–8110 Filed 3–31–00; 8:45 am]

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