

# **Guidance for Industry**

## **Questions and Answers Regarding Adverse Event Reporting and Recordkeeping for Dietary Supplements as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act**

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\*See additional PRA statements in Section IV of this guidance

*Contains Nonbinding Recommendations*

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## **Guidance for Industry<sup>1</sup>**

### **Questions and Answers Regarding Adverse Event Reporting and Recordkeeping for Dietary Supplements as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act**

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if such approach satisfies the requirements of the applicable statute and regulations. If you wish to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the telephone number listed on the title page of this document.

#### **I. Introduction**

This guidance document provides guidance to the dietary supplement industry for complying with the adverse event reporting and recordkeeping requirements prescribed for dietary supplement manufacturers, packers, and distributors by the [Dietary Supplement and Nonprescription Drug Consumer Protection Act](#) (Pub. L. 109-462). As required by section 3(d)(3) of this law, FDA (or “we”) issued this guidance document to describe the minimum data elements for serious adverse event reports for dietary supplements. This guidance document also provides guidance on (1) how, when, and where to submit a serious adverse event report for a dietary supplement; and (2) records maintenance and access for serious and non-serious adverse event reports and related documents. Further, this guidance document also provides guidance on how to electronically submit a serious adverse event report for a dietary supplement. (We identify recent changes to the guidance document's questions and answers by identifying the date of the most recent change.) We have issued a separate guidance document on the reporting of serious adverse events for over-the-counter (nonprescription) human drug products marketed without an approved application.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance documents describe our current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA guidance documents means that something is suggested or recommended, but not required.

For purposes of this guidance document, “you” refers to the dietary supplement industry.

## II. Background

On December 22, 2006, the President signed into law the [Dietary Supplement and Nonprescription Drug Consumer Protection Act](#). This law amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) with respect to adverse event reporting and recordkeeping for dietary supplements and non-prescription drugs marketed without an approved application. This guidance document contains questions and answers relating to the [Dietary Supplement and Nonprescription Drug Consumer Protection Act](#)'s requirements concerning the mandatory reporting to FDA of serious adverse events for dietary supplements, the minimum data elements to be submitted in such reports, and records of serious and non-serious adverse events reported to a dietary supplement manufacturer, packer, or distributor. This guidance document also provides guidance to the dietary supplement industry on how to submit a serious adverse event report for a dietary supplement via the FDA Safety Reporting Portal (formerly referred to as the MedWatchPlus investment). Electronic submission is voluntary. A manufacturer, packer, or distributor of a dietary supplement who is unable to or chooses not to submit their mandatory serious adverse event report using the FDA Safety Reporting Portal may continue to submit their report by mail on the paper MedWatch form, Form FDA 3500A. For purposes of this guidance document, in several locations, we refer to Form FDA 3500A as the "paper version" and the FDA Safety Reporting Portal as the "electronic version" of the required "MedWatch form" as prescribed by the [Dietary Supplement and Nonprescription Drug Consumer Protection Act](#).

## III. Questions and Answers

1. **When do the requirements of the [Dietary Supplement and Nonprescription Drug Consumer Protection Act](#) become effective?**

The effective date for compliance with the law was December 22, 2007.

2. **What types of foods are covered by the [Dietary Supplement and Nonprescription Drug Consumer Protection Act](#) requirements?**

The requirements of this law only apply to dietary supplements. No other types of food are covered.

3. **What is FDA's definition of a dietary supplement?**

Dietary supplements are defined, in part, as products (other than tobacco) intended to supplement the diet that bear or contain one or more of the following dietary ingredients:

- a. A vitamin;
- b. A mineral;
- c. An herb or other botanical;
- d. An amino acid;
- e. A dietary substance for use by man to supplement the diet by increasing the total dietary intake; or

- f. A concentrate, metabolite, constituent, extract, or combination of any ingredient mentioned above.

Further, a dietary supplement must be labeled as such and must be intended for ingestion. A dietary supplement must not be represented for use as a conventional food or as a sole item of a meal or the diet. Finally, the dietary supplement category generally does not include articles approved as new drugs, licensed as biologics, or authorized for clinical investigation under an IND, unless the article was previously marketed as a dietary supplement or as a food. The complete statutory definition can be found in section 201(ff) of the FD&C Act (21 U.S.C. 321(ff)).

- 4. **[Updated September 2013] Does the [Dietary Supplement and Nonprescription Drug Consumer Protection Act](#) apply to foods other than dietary supplements, and if not, are there other mandatory reporting requirements for foods other than dietary supplements?**

The requirements of the Dietary Supplement and Nonprescription Drug Consumer Protection Act do not apply to foods other than dietary supplements. However, there are other mandatory reporting requirements in section 417 of the FD&C Act that requires a “responsible party” to inform FDA of “reportable food,” which is defined as an “article of food (other than infant formula or dietary supplements) for which there is a reasonable probability that the use of, or exposure to, such article of food will cause serious adverse health consequences or death to humans or animals.” Also, infant formula manufacturers must comply with notification requirements for violative infant formula under 21 CFR 107.240.

- 5. **What is an “adverse event?”**

An “adverse event” is “any health-related event associated with the use of a dietary supplement that is adverse.” Section 761(a)(1) of the FD&C Act (21 U.S.C. 379aa-1(a)(1)).

- 6. **What is a "serious adverse event?"**

A "serious adverse event" is an adverse event that:

- Results in death, a life-threatening experience, inpatient hospitalization, a persistent or significant disability or incapacity, or a congenital anomaly or birth defect; or
- Requires, based on a reasonable medical judgment, a medical or surgical intervention to prevent an outcome described above.

Section 761(a)(2) of the FD&C Act (21 U.S.C. 379aa-1(a)(2)).

FDA considers inpatient hospitalization to include initial admission to the hospital on an inpatient basis, even if the patient is released the same day, and prolongation of an

existing inpatient hospitalization. Please see the Appendix of this guidance for more information on the criteria for serious adverse events.

**7. [Updated September 2013] What is a "serious adverse event report?"**

A "serious adverse event report" is a report that must be submitted to FDA using the [MedWatch form](#) when a manufacturer, packer, or distributor of a dietary supplement receives any report of a serious adverse event associated with the use of the dietary supplement in the United States. See section 761(a)(3) and (b)(1) of the FD&C Act (21 U.S.C. 379aa-1(a)(3), (b)(1)).

**8. Who must submit the serious adverse event report for a dietary supplement to FDA?**

The manufacturer, packer, or distributor whose name (pursuant to section 403(e)(1) of the FD&C Act)<sup>2</sup> appears on the label of a dietary supplement marketed in the United States is required to submit to FDA all serious adverse event reports associated with use of the dietary supplement in the United States. Section 761(b)(1) of the FD&C Act (21 U.S.C. 379aa-1(b)(1)).

The [Dietary Supplement and Nonprescription Drug Consumer Protection Act](#) usually refers to the entity that is required to submit a serious adverse event report to FDA as the "responsible person." This guidance uses the term "responsible person" as an alternative to "manufacturer, packer, or distributor."

**9. Are retailers required to submit serious adverse event reports for dietary supplements to FDA?**

Usually not, but the answer could be yes in some situations. Whether a retailer is required to submit a serious adverse event report for a dietary supplement it sells will depend on two things: (1) whether the retailer's name appears on the label of the dietary supplement; and (2) if so, whether the retailer has entered into an agreement with the manufacturer or packer of the dietary supplement transferring responsibility for submitting adverse event reports for the product to the other firm.

A retailer whose name appears on the label of a dietary supplement as its distributor may, by agreement, authorize the manufacturer or packer of the dietary supplement to submit the required adverse event reports for such dietary supplement to the FDA so long as the retailer directs to the manufacturer or packer all adverse events associated with such dietary supplement that are reported to the retailer through the address or telephone number on the label of the dietary supplement. Section 761(b)(2) of the FD&C Act (21 U.S.C. 379aa-1(b)(2)). If such an agreement is in place and the retailer complies with its obligation to forward the dietary supplement adverse event reports it receives to the other party (i.e., the manufacturer or packer), the retailer is under no obligation to report to FDA any serious adverse events for the dietary supplements covered by the agreement. Likewise, if the retailer's name does not appear on the label of a dietary supplement, the

retailer is not responsible for reporting any serious adverse events associated with the supplement to FDA.

**10. [Updated September 2013] When must reports of serious adverse events be submitted to FDA?**

Serious adverse event reports received through the address or phone number on the label of a dietary supplement, as well as all follow-up reports of new medical information received by the responsible person within one year after the initial report, must be submitted to FDA no later than 15 business days after the report is received by the responsible person. Section 761(c)(1)-(2) of the FD&C Act (21 U.S.C. 379aa-1(c)(1)-(2)). For the reasons discussed below, FDA recommends that all other serious adverse event reports received by the responsible person also be submitted to FDA within 15 business days of receipt.

Section 761(c)(1) of the FD&C Act, which contains the 15-day deadline for submitting serious adverse event reports to FDA, expressly applies to serious adverse event reports resulting from information received by the responsible person through the address or telephone number on the product label. Although the FD&C Act does not expressly provide a timeframe for serious adverse event reports that the responsible person receives by other means (such as by e-mail or fax), the reporting of such adverse events is required by the plain language of section 761(b)(1) of the FD&C Act (providing that the responsible person "shall submit . . . *any report received* of a serious adverse event associated with such dietary supplement when used in the United States . . . ." (emphasis added)), and we recommend that such reports be submitted to FDA within the same timeframe as reports received by phone or mail, i.e., within 15 business days of their receipt by the responsible person.

Prompt submission of serious adverse event reports is important for public health reasons. Delayed reporting of some serious adverse events to FDA solely because of the medium through which the adverse event was reported to the responsible person would lessen the effectiveness of adverse event reporting as an early warning sign of possible safety problems with dietary supplements. Without prompt notification of all serious adverse events associated with dietary supplements, FDA would be unable to investigate and follow up promptly, which in turn could cause delays in alerting the public when safety problems are found. Therefore, we recommend that all serious adverse event reports received by the responsible person should be reported to FDA within 15 business days of receipt, regardless of the means by which the responsible person received the initial report.

As soon as all of the minimum data elements (i.e., identifiable patient, initial reporter, identity and contact information of responsible person, suspect dietary supplement, and serious adverse event) are known to the responsible person, the 15-business-day time clock begins to run. That date is Day 0 and should be entered in section G, block 4, on the paper version of the MedWatch form. For the electronic version, this is located on the "Introduction" page as "Enter the date you received the initial report". If the

responsible person does not initially receive sufficient data for a serious adverse event report to FDA, but later receives additional information completing the minimum data elements listed in Question 13, then the responsible person should submit the serious adverse event report within 15 business days of the date the additional information was received, with that date entered in section G, block 4, of the paper version of the MedWatch form or on the "Introduction" page for the electronic version as indicated above.

Although the FD&C Act does not expressly require a responsible person to take action in the event that it receives a report of a serious adverse event in which the initial reporter identifies the suspect dietary supplement as one manufactured, packaged, or distributed by another responsible person, we recommend that such reports be promptly forwarded to that other responsible person. In the event that a responsible person receives a report of an adverse event regarding one of its products from another responsible person, the responsible person whose product was involved must submit a serious adverse event report to FDA within the same timeframe applicable to any report received from an initial reporter (i.e., 15 business days from receipt), even if a serious adverse event report has already been submitted to FDA by the first responsible person (see "Suspect Dietary Supplement" discussion in Question 13).

**11. [Updated September 2013] How is a serious adverse event report for a dietary supplement submitted to FDA?**

A serious adverse event report for a dietary supplement is submitted to FDA on either the paper or electronic version of the [MedWatch form](#) (also referred to as [Form FDA 3500A](#) for the paper version and the FDA Safety Reporting Portal for the electronic version). The manufacturer, packer, or distributor of a dietary supplement is required by statute to use a MedWatch form when submitting a serious adverse event report to FDA. The statute permits but does not require FDA to modify the MedWatch form for dietary supplement reporting. We initially determined that the paper [MedWatch form, Form FDA 3500A](#), the form used for mandatory reporting of adverse events for other FDA-regulated products, was also the most appropriate MedWatch form available for mandatory reporting of dietary supplement adverse events. As of September 2013, we are making available an electronic option to submit a serious adverse event report for a dietary supplement via the FDA Safety Reporting Portal, the electronic version of the MedWatch form. We encourage industry to use the electronic version of the MedWatch form to submit a serious adverse event report for a dietary supplement because the electronic version will allow for faster processing of reports and may require less follow up by FDA with the responsible person submitting the paper version.

**12. [Updated September 2013] Are there any instructions available for filling out the paper and electronic version of the [MedWatch Forms](#) to report a serious adverse event for a dietary supplement?**

Yes. Instructions for filling out the paper [MedWatch form, Form FDA 3500A](#), for serious adverse event reports for dietary supplements are in the Appendix of this



guidance. The electronic MedWatch form, the FDA Safety Reporting Portal, provides the user with detailed navigation instructions to include drop-down menus, lists of values, controlled vocabularies, and mouse over help where possible.

**13. [Updated September 2013] What are the minimum data elements that should be included in a serious adverse event report for a dietary supplement, and where should these data elements be entered on the paper and electronic version of the [MedWatch Forms](#)?**

The five data elements listed in the bullets below should be included in any serious adverse event report for a dietary supplement. These elements, at a minimum, are necessary for FDA to avoid duplication in its adverse event reports database, interpret the significance of adverse events, facilitate follow-up, and detect fraud. The section where each element should be entered on the paper version or electronic version of the [MedWatch Forms](#) is given in parentheses at the end of the bullet.

- an identifiable patient (Section A of the paper version/“Problem Summary – Affected Individual Information” of the electronic version);
- an identifiable initial reporter (Section E of the paper version/“Contact Information – Initial Reporter” of the electronic version);
- identity and contact information for the responsible person (i.e., the manufacturer, packer, or distributor submitting the serious adverse event report to FDA) (Section G of the paper version/“Contact Information – Manufacturer, Packer, or Distributor Site Information and Site Point of Contact Information” of the electronic version);
- a suspect dietary supplement (Section C of the paper version/ “Suspect Product(s)” of the electronic version); and
- a serious adverse event or fatal outcome (Section B of the paper version/“Problem Summary – Adverse Event and/or Product Problem Description” of the electronic version).

The responsible person should actively seek information on any minimum data elements that are not initially provided by the reporter and wait to submit a serious adverse event report to FDA until the information is obtained. We do not intend to take enforcement action for failure to report a serious adverse event where, after diligent efforts, the responsible person is unable to obtain all of the five minimum data elements. We recommend that the responsible person document its efforts to obtain the basic elements for a serious adverse event report. As discussed below in the questions and answers about recordkeeping, the responsible person must keep records related to any adverse event report it receives for six years, regardless of whether the event must be reported to FDA. Section 761(e)(1) of the FD&C Act (21 U.S.C. 379aa-1(e)(1)).

During initial contacts with the reporter and subsequent follow-up, the responsible person should make diligent attempts to obtain complete information. To this end, we encourage responsible persons to use trained health care practitioners to elicit information from reporters, computer-assisted interview technology, targeted questionnaires, and/or other

appropriate methods that help focus the line of questioning. When the initial report is from a consumer, we recommend that the responsible person seek the patient's permission to contact the health care practitioner(s) familiar with the diagnosis and treatment of the adverse event to obtain further information and relevant medical records, as needed.

*Identifiable patient:* (Section A - "Patient Information"/"Problem Summary – Affected Individual Information")

To have an identifiable patient means providing enough information to demonstrate that an individual person experienced a serious adverse event. For example, filling in "some consumers" under "Patient Identifier" would not be sufficient; however, a report that listed the patient identifier as "an elderly woman" or "a young man" would be sufficient because there is enough information to assess that a specific person experienced a serious adverse event. One or more of the following automatically qualifies a person as identifiable: age or age category (e.g., adolescent, adult, elderly), sex, initials, date of birth, name, or patient identification number. A report stating that "an elderly woman had anaphylaxis" or "a young man experienced anaphylaxis" would be sufficient. If a report submitted to the responsible person refers to groups of unknown size, such as "some" or "a few" college students got anaphylaxis, the responsible person should follow up to find out the number of patients and then submit a separate report to FDA for each identifiable patient. The responsible person should distinguish each patient so that it is clear that the separate serious adverse event reports are not duplicate reports of a single adverse event.

To protect the privacy of the patient, he or she should not be identified by name or address; instead, the responsible person should assign a code (e.g., the injured person's initials) to each serious adverse event report. The assigned code will permit the responsible person to cross-reference identifying information and contact information for the patient in the event that the responsible person needs to follow up.

*Initial Reporter* (Section E – "Initial Reporter"/"Contact Information – Initial Reporter")

The initial reporter is the person who first notifies the responsible person about the serious adverse event and can be the patient, a family member, or some other person (e.g., doctor, pharmacist). One or more of the following automatically qualifies a reporter as identifiable: a personal identifier (e.g., name), professional identifier (e.g., doctor, nurse, pharmacist), or contact information (e.g., e-mail address, phone number). In addition to the contact information requested on the form, the initial reporter's e-mail address should also be provided, if available.

Individual judgment will be needed at times to decide whether or not a reporter will be considered identifiable for reporting purposes. If the initial reporter is a third party who has only limited information about the serious adverse event (e.g., "my neighbor told me that a friend became seriously ill after taking Product X"), the responsible person should try to obtain contact information (such as a phone number or e-mail address) for someone

with personal knowledge of the adverse event. The responsible person should then follow up with that person to obtain enough information to submit a serious adverse event report to FDA (i.e., the five minimum data elements).

If the initial reporter requests that the responsible person not forward the reporter's name and contact information to FDA, the responsible person can submit a report without identifying the reporter, as long as the responsible person keeps the contact information on file so that it may contact the reporter either upon request by FDA or on its own initiative. For these reports, the responsible person should fill in the initial reporter name and address block in section E of the paper version with a statement such as "Requested Anonymity." The same can be entered in the "Initial Reporter" section of the "Contact Information" page on the electronic version.

*Responsible Person* (Section G - "All Manufacturers"/"Contact Information - Manufacturer, Packer, or Distributor Site Information and Site Point of Contact Information")

This section of the paper and electronic version of the MedWatch forms is for information about the responsible person and the initial report. Per the instructions in Appendix A, blocks 5 and 6 on the paper version are not required for dietary supplement serious adverse event reports. This information is not included on the electronic version.

*Suspect Dietary Supplement* (Section C - "Suspect Product(s)"/"Suspect Product(s)")

With regard to a *suspect dietary supplement*, provide the complete product name, including brand name, and any other known product attributes. The information provided should be sufficient to uniquely identify the suspect product and distinguish it from other similarly named products. For example, "Vitamin C" or "multi-vitamin" would not be considered complete product names. Examples of information that may be needed to uniquely identify the product include the physical form of the product (e.g., tablet, powder, gelcap, bar); strength (e.g., 120 mg); flavor, if any; and packaging form and size (e.g., 120-tablet bottle).

If a serious adverse event involves multiple dietary supplements that are manufactured, packaged, or distributed by the same responsible person, the responsible person should submit only one serious adverse event report to FDA, listing all suspect products in Section C with the same manufacturer report number in section G, block 9 on the paper version and for the electronic version, listing all "suspect products" where indicated.

If the serious adverse event involves a nonprescription drug product marketed without an approved application and a dietary supplement that is also manufactured, packaged, or distributed by the same responsible person, and the initial reporter views each product as suspect, the responsible person should submit the report about the serious adverse event to both CDER and CFSAN. The report should include information about both suspect products either in section C for the paper version or under "suspect products" for the electronic version and should use one manufacturer report number.

If a serious adverse event involves multiple suspect dietary supplements that were manufactured, packaged or distributed by more than one responsible person (e.g., manufacturers A and B), and if the event is reported to one of the responsible persons (manufacturer A), then that responsible person (manufacturer A) must submit a serious adverse event report to FDA that identifies both its own product(s) and manufacturer B's product(s) in the Suspect Product section of either the paper or electronic version including a copy of manufacturer A's product label.<sup>3</sup> In such a case, we recommend that manufacturer A also send manufacturer B a copy of the submitted paper version of the report or a copy of the Individual Case Safety Report generated by the electronic version, including manufacturer A's report number. In the event that manufacturer B receives such a report, manufacturer B must then submit its own serious adverse event report, citing manufacturer A's report number in the "Describe Event or Problem" section of the paper version (i.e., section B.5) or the "Problem Summary" section of the electronic version, and including a copy of manufacturer B's product label. Section 761(b)(1) of the FD&C Act (21 U.S.C. 379aa-1(b)(1)).

If a serious adverse event involves a dietary supplement that has been discontinued, the responsible person must still submit a report to FDA. Responsible persons must submit "any report received" of a serious adverse event associated with their products when used in the United States. Section 761(b)(1) of the FD&C Act (21 U.S.C. 379aa-1(b)(1)). Where a product involved in a serious adverse event has been discontinued, the responsible person may make note of this status in Section B.5 of the paper version or in the "Problem Summary" section of the electronic version of the MedWatch forms.

*Serious Adverse Event or Fatal Outcome* (Section B - "Adverse Event or Product Problem"/"Problem Summary - Adverse Event and/or Product Problem Description")

A *serious adverse event*, as defined in section 761(a)(2) of the FD&C Act (21 U.S.C. 379aa-1(a)(2)), is an adverse event that results in or more of the following patient outcomes or, based on reasonable medical judgment, requires a medical or surgical intervention to prevent one of the following patient outcomes:

- death
- a life-threatening experience
- inpatient hospitalization<sup>4</sup>
- a persistent or significant disability or incapacity
- a congenital anomaly or birth defect.

A *serious adverse event* other than death should, at a minimum, be described in terms of signs (including abnormal laboratory findings), symptoms, or disease diagnosis for purposes of reporting. Thus, a report stating that the patient "experienced unspecified injury," "suffered irreparable damages," or "was ill" would not be specific enough. If the initial reporter does not provide any signs, symptoms, or diagnosis, the responsible person should follow up as necessary to obtain more information from that person, the patient, or (with the patient's permission) medical professionals who treated the patient.

A report of a *fatal outcome* (death) meets the minimum description for a serious adverse event even if the events that led to the death are unknown, but such reports should also include any other available information related to the death (e.g., adverse event(s) associated with the death).

**14. [Updated September 2013] Can a serious adverse event report be submitted to FDA using the MedWatch voluntary reporting form ([Form FDA 3500](#))?**

No. FDA has determined that dietary supplement manufacturers, packers, and distributors must report serious adverse events associated with their products using either the paper [MedWatch form, Form FDA 3500A](#) or the FDA Safety Reporting Portal. Section 761(d) of the FD&C Act (21 U.S.C. 379aa-1(d)). However, voluntary reports of adverse events associated with a dietary supplement may be submitted using either the paper [MedWatch form, Form FDA 3500 \(note the absence of the letter “A”\)](#), or the FDA Safety Reporting Portal. Voluntary reports of dietary supplement adverse events would include:

- any adverse event report submitted by a consumer, health care provider, or any other entity that is not a dietary supplement manufacturer, packer, or distributor;
- a report of a non-serious adverse event submitted by a dietary supplement manufacturer, packer, or distributor for one of its products;
- a report of a serious adverse event submitted by a dietary supplement manufacturer, packer, or distributor for one of its products, where the firm is not the "responsible person" who must report the serious adverse event. For example, the manufacturer of a dietary supplement might choose to submit a report of a serious adverse event to FDA even though the distributor was the "responsible person" because the distributor's name appeared on the dietary supplement label. In such a case, FDA would receive both voluntary and mandatory reports of the same serious adverse event.

**15. a. [Updated September 2013] Must a copy of the label of the dietary supplement that is the subject of the serious adverse event report be submitted with the report?**

Yes. Section 761(b)(1) of the FD&C Act (21 U.S.C. 379aa-1(b)(1)). Wherever possible, responsible persons should submit a copy of the full outer carton/container label and immediate container label from the product the patient used. See 21 U.S.C. 321(k); 21 CFR 1.3(b). Where the patient's product has been specifically identified, but the responsible person does not have a copy of the patient's own label, the responsible person should submit an original or photocopied label that is the same as the label of the product the patient used, or as close as the responsible person can come to that label using all available information.

Where the exact label of the patient's dietary supplement cannot be identified with certainty, such as where a label has changed over time or where the patient's exact product cannot be identified with specificity, the responsible person may submit a copy of the label most likely viewed by the patient, or may submit multiple labels for those

products most likely to be associated with the report. In addition, where the label has changed since the time of the adverse event, the responsible person may also submit a copy of the product's current label.

For responsible persons submitting the paper MedWatch form, Form FDA 3500A, this information should be mailed in with the serious adverse event report. For electronic submissions via the FDA Safety Reporting Portal, responsible persons should attach an electronic image of the label in one of the formats listed on the "Attachments" section.

**15. b. Should anything other than the product label be submitted along with the serious adverse event report**

Yes. As part of the serious adverse event report, we encourage the responsible person to attach the following, as appropriate: (1) hospital discharge summaries, (2) autopsy reports, (3) relevant laboratory data, and (4) other critical clinical data. Please note that this paragraph does not provide an exhaustive list of all the documents or information that may be submitted with the report at the responsible person's option.

**16. Does a sample of the dietary supplement that is the subject of the serious adverse event report have to be submitted to FDA?**

No. There is no requirement that a sample of the dietary supplement be provided to FDA with the adverse event report, and we do not recommend you submit a sample unless requested to do so.

**17. Must new medical information received by the manufacturer, packer, or distributor of a dietary supplement that is related to a previously submitted serious adverse event report also be submitted to FDA?**

Yes, any new medical information received within one year of the initial report must be submitted to FDA. Section 761(c)(2) of the FD&C Act (21 U.S.C. 379aa-1(c)(2)). Even if new medical information is received later than one year after the serious adverse event report and therefore does not have to be reported, you must keep it in your file on the serious adverse event for six years because it is a record related to the serious adverse event report. Section 761(e)(1) of the FD&C Act (21 U.S.C. 379aa-1(e)(1)). Although you are not required to submit to FDA any new medical information that is received later than one year after the serious adverse event report, we encourage the voluntary submission of such information so that we obtain a complete report to evaluate.

**18. When must the new medical information be submitted to FDA?**

This new medical information must be submitted to FDA within 15 business days of being received by the manufacturer, packer, or distributor. Section 761(c)(2) of the FD&C Act (21 U.S.C. 379aa-1(c)(2)).

19. a. **[Updated September 2013] How should the new medical information be submitted to FDA? Should another report be filled out and submitted on the [MedWatch form, Form FDA 3500A](#), or using the FDA Safety Reporting Portal, in addition to the initial serious adverse event report originally submitted?**

No. A new report does not have to be completed on paper [Form FDA 3500A](#) or on the FDA Safety Reporting Portal to submit the new medical information (e.g., medical records). The FDA Safety Reporting Portal allows users to electronically update a serious adverse event report previously submitted via the portal. To submit a follow up report with new medical information, first electronically access the previously submitted report:

Accessing reports submitted as an account holder: Log in from the homepage of the Safety Reporting Portal. Select the appropriate previously submitted report from the "Submitted Reports Available for Follow-up" list.

Accessing reports submitted as a guest: From the Safety Reporting Portal homepage, click "Report as Guest." On the "New Guest Report" screen, choose "Follow-up on a report previously submitted as a guest portal user." Enter the appropriate Report Identification Key in the text box that appears.

Once the appropriate report has been chosen for follow up, attach electronic versions of the new medical information on the Attachments section of the follow up report. If the new medical information cannot be condensed into 5 or fewer files of less than 10 MB each (the limitation of the portal) please submit multiple follow up reports to transmit all of the new information. .

To submit new medical information related to a serious adverse event report previously submitted to FDA on paper [Form FDA 3500A](#), simply attach a copy of the initial serious adverse event report to a copy of the new medical information in the same form you received it. It is not necessary to re-submit any attachments from the initial serious adverse event report.

19. b. **[Updated September 2013] Can FDA provide assurance that the new medical information submitted will be consolidated into a single report by FDA?**

For submission of new medical information related to reports made using the paper version, when a copy of the initial serious adverse event report on [MedWatch Form 3500A](#) is included with the new medical information, we will be able to consolidate the initial submission and the new medical information into a single report. Reports submitted using the electronic version are linked electronically, and the new medical information will be associated with the initial report automatically.

20. **[Updated September 2013] Will FDA confirm receipt of serious adverse event reports submitted and provide a tracking number to use for further submissions of new medical information related to the initial report?**

If the report is submitted using the FDA Safety Reporting Portal, responsible persons will be provided with a confirmation email containing a time stamped copy of their report upon its submission. This copy also contains an Individual Case Safety Report number to identify the report in any subsequent communications.

If the report is submitted using the paper MedWatch form, Form FDA 3500A, no confirmation of receipt or tracking number is provided to the responsible person at this time. We are working to implement processes that will provide a confirmation of receipt and tracking number to the responsible person when a serious adverse event report for dietary supplements is submitted using the paper version. We will revise this guidance when these processes are implemented.

**21. [Updated September 2013] What is the process for getting a copy of [MedWatch Form 3500A](#)?**

[MedWatch Form 3500A](#) is on FDA's Internet web site. If you are unable to access the paper version of the form on-line, request a paper copy of the form by calling 1-800-FDA-1088 or by submitting a written request to:

MedWatch: The FDA Safety Information and Adverse Event Reporting Program  
Office Of The Center Director  
Center for Drug Evaluation and Research  
5515 Security Lane  
Suite 5100  
Rockville, MD 20852

**22. [Updated September 2013] Where are completed paper versions of serious adverse event reports for dietary supplements to be submitted?**

Please mail completed [MedWatch form, Form FDA 3500A](#), along with a copy of the dietary supplement label and any other attachments (see Questions 15a and 15b), to:  
FDA, Center for Food Safety and Applied Nutrition, Office of Food Defense,  
Communication and Emergency Response, CAERS Team, HFS-11, 5001 Campus Drive,  
College Park, MD 20740.

**23. [Updated September 2013] What is the process for submitting serious adverse event reports for dietary supplements electronically?**

The electronic version of the MedWatch form, the FDA Safety Reporting Portal, is accessible at [www.safetyreporting.hhs.gov](http://www.safetyreporting.hhs.gov). A reporter may choose to submit serious adverse event reports as an account holder or as a guest. As noted, the FDA Safety Reporting Portal provides the user with detailed navigation instructions to include drop-down menus, lists of values, controlled vocabularies, and mouse over help where possible.



**24. Can the paper version of the [MedWatch form, Form FDA 3500A](#), for a dietary supplement serious adverse event report be submitted to FDA by facsimile?**

No. Dietary supplement serious adverse events reported on the paper version of [MedWatch form, Form FDA 3500A](#), along with a copy of the dietary supplement label and any other attachments (see Questions 15a and 15b), should be mailed to FDA (see answer to Question 22 for address). We do not accept these reports by facsimile due to concerns about the quality of this form of transmission (i.e., the clarity and readability of faxed documents).

**25. a. How long should records of serious adverse event reports and related medical information be maintained?**

The responsible person must maintain all records related to each report of a serious adverse event for a period of 6 years. Section 761(e)(1) of the FD&C Act (21 U.S.C. 379aa-1(e)(1)). These records should include, at a minimum, copies of the following:

- the responsible person's serious adverse event report to FDA, with attachments;
- any new medical information about the serious adverse event received by the responsible person;
- any reports to FDA of new medical information related to the serious adverse event;
- communications and records of communications between the responsible person and
  - the initial reporter
  - any other person(s) who provided information related to the adverse event

**25. b Should records of non-serious adverse events reported to the manufacturer, packer, or distributor of the dietary supplement involved be maintained?**

Yes. If a report of a non-serious adverse event associated with a dietary supplement for which you are the manufacturer, packer, or distributor, you must keep the report along with any related records (e.g., records of your communications with the person(s) who reported the adverse event to you, records of your assessment of the event as non-serious). All such records of non-serious adverse events must be kept for six years, just as with records of serious adverse events. Section 761(e)(1) of the FD&C Act (21 U.S.C. 379aa-1(e)(1)).

**25. c. Can records of serious and non-serious adverse events reported be maintained electronically?**

Yes. Electronic records created and maintained to meet the requirements of section 761(e)(1) of the FD&C Act (21 U.S.C. 379aa-1(e)(1)) are subject to the requirements of 21 CFR part 11. Therefore, if you maintain your records electronically, you must comply with the electronic record requirements contained in 21 CFR part 11.

**26. Can FDA examine or inspect adverse event report records?**

Yes. During an FDA inspection conducted under the authority of section 704 of the FD&C Act (21 U.S.C. 374), we are authorized to have access to all adverse event report records that dietary supplement manufacturers, packers, and distributors are required to maintain. Section 761(e)(2) of the FD&C Act (21 U.S.C. 379aa-1(e)(2)).

**27. Is submission to FDA of a serious adverse event report an admission that the dietary supplement involved caused the serious adverse event described in that report?**

No. We do not construe submission as an admission that the dietary supplement involved caused or contributed to the adverse event being reported. Any serious adverse event report submitted to FDA, including any new medical information submitted as a follow-up to the initial report, is considered a safety report under section 756 of the FD&C Act (21 U.S.C. 379v) and may be accompanied by a statement, which shall be a part of any report that is released for public disclosure, that denies that the report or the records constitute an admission that the product involved caused or contributed to the serious adverse event. Section 761(f)(1) of the FD&C Act (21 U.S.C. 379aa-1(f)(1)).

Further, we note that both the paper and electronic versions of the [MedWatch form](#) contain the statement "Submission of a report does not constitute an admission that medical personnel, user facility, importer, distributor, manufacturer or product caused or contributed to the event."

**28. [Updated September 2013] If a serious adverse event involves a dietary supplement that has been discontinued, must the responsible person submit a serious adverse event report to FDA?**

Yes. See *Suspect Dietary Supplement* section of Question 13. The responsible person must still submit a report, but may note in Section B.5 of the paper version of the MedWatch form or in the "Problem Summary" section of the electronic version that the product has been discontinued.

## **IV. Paperwork Reduction Act of 1995**

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to maintain the dietary supplement adverse event records recommended in this guidance and required by section 761(e)(1) of the FD&C Act is estimated to average 30 minutes per record, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to:

Office of Nutrition, Labeling, and Dietary Supplements, Division of Dietary Supplement Programs, HFS - 810, Center for Food Safety and Applied Nutrition Food and Drug Administration, 5001 Campus Drive, College Park, MD 20740.

This guidance also refers to previously approved collections of information found in the FD&C Act. Submission to FDA of serious adverse event reports for dietary supplements and follow-up reports of new medical information is required by section 761(c)(1)-(2) of the FD&C Act. The electronic submission of dietary supplement adverse event information to us via the FDA Safety Reporting Portal has been approved under OMB Control No. 0910-0645, while submission of dietary supplement adverse event information to us using the original paper forms (Forms FDA 3500 and 3500A) has been approved under OMB Control No. 0910-0291.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0635 (expires 02/29/2016).

## **V. Appendix: Instructions for Completing the paper version of MedWatch Form 3500A to Report a Serious Adverse Event Associated with a Dietary Supplement**

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<sup>1</sup> This guidance has been prepared by the Division of Dietary Supplement Programs, Office of Nutrition, Labeling and Dietary Supplements in the Center for Food Safety and Applied Nutrition at the U.S. Food and Drug Administration.

<sup>2</sup> Under section 403(e)(1) of the FD&C Act (21 U.S.C. 343(e)(1)) and 21 CFR 101.5, dietary supplements and other foods in package form must bear a label containing the name and place of business of the product's manufacturer, packer, or distributor.

<sup>3</sup> Section 761(b)(1) of the FD&C Act (21 U.S.C. 379aa-1(b)(1)) requires the manufacturer, packer, or distributor of a dietary supplement to submit to FDA "any report received" of a serious adverse event associated with the dietary supplement when used in the United States. Accordingly, where a report is required, responsible persons must provide FDA with the information about the serious adverse event supplied by the initial reporter. Moreover, section 761(d) of the FD&C Act (21 U.S.C. 379aa-1(d)) requires serious adverse event reports to be submitted using the MedWatch form. The MedWatch form, Form FDA 3500A, in existence when the Dietary Supplement and Nonprescription Drug Consumer Protection Act was adopted, includes Section C, which seeks information about "Suspect Product(s)" known to the responsible person. The electronic version of the MedWatch form available via the FDA Safety Reporting Portal also includes a section for "Suspect Product(s)." Therefore, manufacturer A must report information about manufacturer B's products on the MedWatch form in the example above even though manufacturer A did not manufacture, pack or distribute those products.

<sup>4</sup> See Question 6 and Appendix A for guidance on how FDA interprets the term "inpatient hospitalization" and the other criteria defining a serious adverse event.

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This document supercedes the [previous version](#), issued June 2009.