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VICE PRESIDENT
SCIENCE POLICY AND TECHNICAL AFFAIRS

PhRMA

May 10, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane Rm. 1061
Rockville, MD 20857

Re: Docket No. 01D-0056- FDA Draft Guidance for Industry on Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines
(66 Federal Register 14391; March 12, 2001)

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is submitting this set of comments on the "Draft Guidance for Industry on Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines."

PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies. PhRMA member companies are devoted to inventing medicines that allow patients to lead longer, healthier, and more productive lives; our members invest over $30 billion annually in the discovery and development new medicines. For this reason, PhRMA and its member companies are extremely interested in all aspects of the drug development process, including postmarket safety reporting. PhRMA appreciates the opportunity to provide comments on the draft guidance.

PhRMA companies support the Agency's efforts to combine three previously released guidances to both clarify and simplify postmarking reporting. PhRMA companies wish to support the implementation of the draft-combined guidance by offering comments for improvement and clarification of issues.

PhRMA is aware of the role the FDA has had in the CIOMS V initiative, which addresses in considerable detail many of the issues in this draft guidance. The report will be published within the next few weeks. Before finalizing this draft guidance, PhRMA suggests that the agency review the CIOMS V report, which is a result of consensus reached by many regulators, including FDA, and industry representatives.

The following are both general and specific comments. Numbering of the specific comments corresponds to the line-numbering used in the draft guidance.

General Comments:

Many of the draft guidance's recommendations would require re-programming and subsequent validation of the safety database, as well as changes to SOPs; however, it is unclear that they would add any value to the pharmacovigilance process. PhRMA's suggestions, and rationale for these suggestions, are given in the detailed comments.

Throughout the document, the draft guidance mentions "drugs" but not vaccines and/or biologics. PhRMA suggests that wherever "drugs" are mentioned, vaccines and/or biologics should also be mentioned, where applicable.

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PhRMA also recommends that the agency confirm that supplying potentially identifying demographic data is not in conflict with the HHS data protection rule.

The agency is in the process of developing proposed rules to further amend its safety reporting requirements for human drug and biological products. PhRMA commends the agency for basing these proposed rules on recommendations developed by ICH. However, it seems redundant to update this guidance now, and then update it again with the advent of the new regulations. It would seem prudent to wait for the new regulations to go into effect and then update the postmarketing safety reporting guidance. PhRMA respectfully requests that the agency give further thought to consolidating all of the initiatives in the safety reporting area in a more rational order before this particular draft guidance is implemented.

I INTRODUCTION

Section A. What does this guidance discuss? (Line 38-39)
Following the bullet point "15-day reports of Serious, Unexpected Adverse Experiences. PhRMA recommends adding a bullet point specifically stating that this guidance covers both prescription and over the counter products.

(Line 43-44)
In this table, products and regulations the draft guidance addresses are listed, including "Human biological products with approved BLA's." The BLA is a fairly new FDA initiative. PhRMA suggests clarifying whether this guidance covers vaccines licensed prior to the BLA initiative or all currently licensed vaccines.

Section B. What does this guidance not discuss? (Line 59-64)

This section presents a list of products the draft guidance does not cover. PhRMA advocates adding devices to this list.

Section C. Good Guidance Practices (Line 75-77)

The draft guidance states that "use of mandatory language (e.g., must, have to, required) will signify a regulatory requirement while the use of words such as should and recommend will indicate agency policy." Please state that compliance is measured as adherence to regulatory requirements rather than agency policy and guidance.

II BACKGROUND

C. Proposed Rules (Line123-143)

The agency is planning to issue a proposal requiring the electronic submission of postmarketing safety reports consistent with recommendations developed by ICH. Member companies are interested in knowing when the agency will mandate E2B requirements take effect.

III. WHO MUST REPORT

(Line 163-165)
The document states, "Any person whose name...." Company or corporate names are on labels, not individuals. PhRMA recommends that the Agency replace "person" with "Any entity whose name...."

IV. WHAT DO I REPORT?

(Line 189-191)
The definition of adverse experience mentions both drugs and biological products, but not vaccines. Vaccines should be added to the definition.

In addition, the definition includes "whether or not considered product-related by the applicant." The phrase "by the applicant" is new to this definition, and does not appear in the definition of adverse experience in Appendix A. Often the reporter does not consider the event related to the product, and has contacted the manufacturer seeking information regarding the event. Previously, these reports have been treated the same as any other spontaneous report. Please clarify the intent of adding this phrase to the definition. PhRMA recommends that the Agency provide further clarification on the intent of adding this phrase or deletion of the phase "by the applicant" entirely.

A. Type of adverse experience

1. Adverse Experiences that are Serious and Unexpected from All Sources (Domestic and Foreign)

(Line 214-219)
In the glossary of this document, adverse events are defined as events occurring in humans. PhRMA suggests eliminating *in vitro* and animal studies from this section. These would be more appropriately captured in the Annual Report and/or mentioned in the current section IV of the Periodic report (studies involving safety issues).

3. Serious Adverse Experiences

(Line 242)
"Life -threatening adverse experience" is mentioned as a serious criterion, but the draft guidance does not specify that the experience must be life threatening as it occurred to that patient. Please add a paragraph that explains that the AE must be life-threatening as it occurs to the patient, not that the event could be life-threatening had it occurred in a more serious form.

Please clarify whether company medical judgment can be applied when a consumer initial reporter mentions an adverse experience was life-threatening, and the facts do not support this classification. Also please clarify if an initial classification of life threatening may be changed upon receipt of additional information from a health care professional indicating that the event was not life threatening.

(Line 251-258)
"A patient admitted to a hospital for 1 or more days as a result of an adverse experience, even if released on the same day, would qualify for the initial inpatient hospitalization outcome." The language as it stands lacks clarity. PhRMA recommends changing the language to: "A patient admitted to the hospital, even if released on the same day, would qualify for the initial...."

(Line 260-263)
It is unnecessary to include "incarceration because of actions allegedly caused by a drug" within the serious outcome criteria of significant or persistent disability/incapacity. Incarceration is not a medical outcome; it is a result of behavior

modification. This type of event would be considered serious according to "important medical event" criteria. PhRMA recommends removing this paragraph.

(Line 265-269)
This draft guidance implies that the examples of "allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias, or convulsions....." are the only events that would be medically important. Re-wording this sentence to include "important medical events would include events such as allergic....." would indicate other events could be medically important. In addition, not all blood dyscrasias are medically important. A platelet count of 100,000 in a patient with no symptoms is not necessarily medically important. PhRMA recommends to either delete blood dyscrasias or to change it to a specific type of blood dyscrasia, such as agranulocytosis or aplastic anemia. The terms "drug dependency" and "drug abuse" may be used incorrectly by consumers (i.e., without diagnosis from physician). These events should be evaluated on a case by case basis for other serious criteria and for medical importance, and should not be used as an example.

(Line 271-278)
The draft guidance states that the applicant should seek the outcome for a suspected serious adverse experience reported to applicant It is unclear in the document what "outcome " the agency is requesting. Please clarify if it pertains to the outcome of the AE or to the status of the patient.

Companies routinely request permission from consumer reporters to contact health care providers for information regarding suspected serious, unexpected events. If permission is not obtained, it would be a violation of the patient's privacy to attempt to obtain any information from the patient's health care provider. PhRMA proposes that the draft guidance state that if a patient refuses to provide contact information for their health care provider, that refusal be documented in the patient file and no further attempts to collect additional information be made.

(Line 282-286)
PhRMA urges the Agency to provide further guidance on the assessment of expectedness. Specifically, the guidance states that the current "FDA-approved labeling" should be used in the assessment of expectedness. Please clarify that expectedness relates solely to the Package Insert as the reference document.

B. Data Elements to Include in a Postmarketing Individual Case Safety Report

(Line 311-314)
The draft guidance states the applicant should maintain records of its efforts to obtain the basic elements for an individual case in the corporate drug or biological product files. . Companies fulfill the agency's requirement to maintain records of efforts to obtain information according to their individual due diligence guidelines.

(Line 316-325)
The draft guidance states that an applicant actively seeking information on an adverse experience should use direct verbal contact with the initial reporter of an adverse experience. Verbal contact as a routine mechanism of communication is not feasible; such resources should be reserved for serious, unexpected reports. This also contradicts the Agency's guidance in a later section of this document to limit follow-up on non-serious events to the 4 essential elements. PhRMA recommends that direct verbal contact as a method of follow-up be reserved for serious unexpected AE's, The draft guidance should

clarify that written follow-up is sufficient for serious expected reports, and non-serious adverse reports, where any of the four elements are unknown.

Furthermore, written contact is preferred by some reporters and thus results in the ability to obtain better information. It is unreasonable to expect that verbal contact be made since many consumers are not available during working hours and many HCPs prefer not to be contacted during office hours, but have requested communication over the internet, by fax, or by US mail.

The draft guidance states that applicants should use health care professionals for contacts with reporters, because these persons should be able to identify appropriate follow-up questions, and determine the significance of the reports. It is not necessary to limit applicants to utilizing only health care professionals in these roles. Rather than specifying a particular level of education, it is more important that the individuals performing these activities are properly trained and provided with the appropriate tools (e.g., targeted follow-up questions for specific adverse events of interest, etc.) to carry out the activity.

(Line 332-342)
Guidance is provided regarding three of the four essential elements for a valid report (identifiable patient, adverse experience and outcome). Please add guidance regarding what constitutes an identifiable reporter.

IV. TYPES OF REPORTS

A. 15-Day Reports of Serious, Unexpected Adverse Experiences

1. Determination of 15-Day Reporting Period

(Line 368-371)
Clarification by the Agency that the day of receipt of the four data elements is Day 0 for purposes of calculating reporting timeframes is appreciated.

(Line 373-375)
The draft guidance states if the 15th calendar day occurs on a weekend or a US Federal holiday, the 15-day report should be submitted on the first working day after the weekend or US Federal holiday. Additional clarification should be added stating that a report whose "Day 15" falls on a weekend or US Federal holiday will not be considered late if submitted on the first working day after the weekend or Federal holiday. Reports can be submitted prior to Day 15, but the current wording makes it sound as if the report must be submitted on that first working day following the weekend or holiday.

(Line 377-378)
The draft guidance states that the applicant should exercise due diligence to acquire all the information for an individual case safety report immediately upon receipt of a serious, unexpected adverse experience. PhRMA recommends re-wording the sentence to read "The applicant should exercise due diligence to acquire all the information for an individual case safety report subsequent to receipt of a serious, unexpected adverse experience".

(Line 380-383)
The new policy to include in the narrative of FDA form 3500A a chronological description of due diligence efforts if there is a delay in obtaining such information is confusing since "delay" has not been defined. This is also incompatible with Agency instruction later in

this draft guidance to keep narratives as concise as possible because the FDA's database for this section is limited. It would seem to be in the best interest of the public health if this narrative space is used for a description of relevant medical-safety information rather than for administrative purposes. Additionally, in today's global safety systems, the narrative must be suitable for submission to regulators worldwide, and this administrative information would not be acceptable to other regulators. This requirement would also result in duplication of effort, since companies are already required to maintain records of due diligence efforts, most of which are maintained in detail for the individual case outside of the narrative, and these records are available upon request.

(Line 388-390)
The draft guidance states that additional follow-up information should be actively sought and submitted within 15 calendar days after obtaining the new information. PhRMA recommends deleting the word "additional" from this sentence.

2. Supporting Documentation

(Line 399-407)
Submitting copies of discharge summaries and autopsy reports/death certificates for serious, unexpected adverse experiences is redundant. Relevant information from these documents is summarized and included in the appropriate boxes on the FDA 3500A. PhRMA does not understand the rationale for including a list of relevant documents maintained in the applicant's corporate drug or biologic product safety files. These records should be on file, but not included as part of the narrative summary. The narrative section should be limited to pertinent clinical details only. A written request should be submitted to the applicant from the Agency if a copy of any documentation retained by the applicant is required. No other regulatory authority worldwide has requested that this information be submitted routinely. This request is inconsistent with the Paperwork Reduction Act and E2B. Please clarify the rationale for including these documents with each serious unexpected AE.

B. Periodic Reports

2. Content of a Postmarketing Periodic Report

a. Section 1: Narrative Summary and Analysis

(Line 486-495)
This draft guidance changes the ordering of the periodic report sections. While this new ordering does put the most important sections first, it will involve re-programming for all pharmaceutical companies that produce the current sections 1-3 (except narrative) by computer. It also makes programmatically numbering pages difficult, as pages that are produced manually (by word processing vs computer) will be first rather than last. Since sections are tabbed and readily accessible, the benefit of re-ordering sections is far less than the effort and cost of re-programming and validating the database.

Many companies have applied for waivers so they can submit periodic reports in the PSUR format. The subtle changes in the periodic report section, such as the new requirement for a tabulation of reports received from the FDA, will be a significant technological and administrative burden on companies, since this will mean that additional US-specific listings will need to be added to the PSUR for submission to the FDA. This seems to have minimal added value.

(Line 497-498)
The policy states that the names of all involved drugs appear in the tabulations for a product interaction. PhRMA recommends deleting the requirement to list interacting drugs in the tabulation.

b. Section 2: Narrative discussion of actions taken

(Line 538)
"A list of studies initiated" should be changed to the following: A list of studies initiated for safety concerns.

c. Section 3: Index line listing

(Line 548-550)
The draft guidance states that an index line listing of FDA Form 3500As or VAERS forms included in section 4 of the periodic report must be provided. Adverse event term(s) should be included in the line listing. Please clarify whether the "preferred term", level adverse event term, should be used.

d. Section 4: FDA Form 3500A or VAERS form

(Line 583-587)
This draft guidance states that FDA encourages applicants to attach relevant hospital discharge summaries and autopsy reports/death certificates for serious expected adverse experiences, and to include a list of available documents in the narrative section of the FDA 3500A form. Currently, the Agency does not allow submission of reports containing attached documents in the electronic submission pilot program, as this policy is not consistent with the E2B initiative. Since the Agency has consistently lobbied for electronic submission of periodic FDA 3500A data as a means to speed reviewer access to the data and reduce Agency resources spent in entering the data from these forms into the AERS database, PhRMA would be interested to learn how the Agency plans to deal with all these attached documents in the Periodic Reports, and the rationale for this request.

C. Follow-up Reports

(Line 618-620)
The draft guidance states that follow-up information to adverse experiences submitted initially in a Periodic Report can be submitted in the next Periodic Report. PhRMA feels the addition of the wording " provided the new information does not upgrade the case to a 15-Day Report" provides further clarification, and recommends that it be added to this section.

1. Content of Follow-up Reports

(Line 628-631)
The draft guidance states that information from an initial report that is later found to be inaccurate should not be repeated in the follow-up report. Please clarify if elimination of initially reported adverse event terms that were not confirmed on follow-up would be acceptable. Existing guidance states that adverse events be described "using the reporter's own words"; there has been reluctance in industry to delete any terms or information from subsequent follow-up reports.

The draft guidance states that all new information including the correction of previously submitted inaccurate information included in a follow-up report should be highlighted.

Highlighting all new information in the follow-up report is almost impossible in automated computer systems used for production of FDA 3500A forms, especially if new information is combined with relevant information from the initial report. PhRMA urges that the Agency delete this sentence.

(Line 633-635)
The draft guidance states that the narrative of follow-up reports should be concise because FDA's database for this section is limited. The Agency does not provide any information regarding the length to which the section should be limited. The statement is specific to limiting the narrative for follow-up reports. Please clarify that the same statement holds true for narratives in initial reports as well.

(Line 640-641)
The draft guidance mentions that non-serious reports for which the four basic elements are known do not require any follow-up. Please clarify that this includes both non-serious expected and non-serious unexpected events.

2. Reporting Considerations

(Line 669-672)
The draft guidance states that follow-up reports should not be submitted if additional relevant information is not obtained for the adverse experience. Regulations state that follow-up reports should be submitted when "new information" is received, and make no distinction regarding any new information and relevant new information. Please add "relevant" information.

3. Reporting Forms

(Line 679-680)
Item 3G states that "health professional" should be marked if at any time a health professional provided information for the report. Please define health professional as used in the context of this guidance.

(Line 701-702)
The draft guidance states that on the VAERS form for vaccines, Box 27 should be marked Follow-up and indicate whether this is the 1st, 2nd, 3rd ... follow-up. At the present time, the form lacks a space next to the word follow-up to indicate which follow-up (1st, 2nd, 3rd) it is. PhRMA requests that the agency add a space next to the word follow-up on the VAERS form so applicants can comply with this guidance.

B. Distribution Reports for Biological Products Including Vaccines

(Line 731)
The reference in the last paragraph should be changed to section VIII. D.

V. SPECIAL REPORTING SITUATIONS

A. Scientific Literature Reports

(Line 742-745)
The draft guidance states that it is not sufficient to submit only abstracts of articles. In some cases, authors only write abstracts and do not write a comprehensive article. Please clarify if the Agency will accept a literature report based only on an abstract.

(Line 747-753)
The draft guidance states that when multiple identifiable patients are described in an article, a copy of the article should be attached to only one of the FDA 3500As, and the other forms should reference the manufacturer report number of the case that the article is attached to. The narrative is not an appropriate location for this information. The case is submitted to regulatory authorities worldwide, and this is not standard practice worldwide. Please clarify where the Agency would expect to see this reference on the 3500A form.

(Line 762-765)
The policy to submit literature reports for drugs which contain the same active moiety even when the formulation, indication, etc. are different could lead to duplicate reporting. NDA's for these products may be held by different companies in the US, which means all of the different companies might be sending in the same literature reports. PhRMA recommends that if a specific manufacturer's brand can be identified from the article, then only that manufacturer is required to submit a report.

(Line 767-770)
The 15 day requirement for translation of a foreign article discussing a serious, unexpected AE is quite burdensome. Some companies send an initial report based on an informal translation that identifies a serious unexpected adverse event with an association to their product, and send the fully translated article as a follow-up report. PhRMA recommends that translation and submission of only relevant portions of an article that contains a specific case, especially for lengthy articles, be permissible.

B. Postmarketing, Clinical Trial or Surveillance Studies

(Line 776-777)
The draft guidance indicates that studies not involving "monitoring" of adverse experiences should be considered spontaneous reports. Please clarify if the use of the word "monitoring" implies an FDA requirement to conduct such studies under the auspices of GCP (investigator initiation visit, audit of clinical record to ensure accuracy of case report form, etc.).

(Line 783-785)
The draft guidance states that serious, unexpected adverse experiences that occur during a study must be submitted as 15 day reports if there is a reasonable possibility that the drug or biological product caused the adverse experience. Please add "reasonable possibility per the applicant that the drug or biological product caused the adverse experience."

Please clarify that the definition of "reasonable possibility" does not mean "cannot be ruled out," as included in the E2A Guideline. This language is not included in the existing regulations and is a higher standard than that included in 21CRF312.32. Not sure if edits convey the correct comment.

(Line 794-797)
The draft guidance states that the blind should always be broken for each patient or subject that experiences a serious, unexpected adverse experience. PhRMA would recommend the addition of the phrase "possibly related" following the word unexpected so the statement would read "unexpected, possibly related adverse experience".

C. Foreign Reports

(Line 807-813)
This draft guidance states that when a foreign report is submitted on a product that is not identical to a product marketed in the United States, the foreign trade name, generic name and NDA number of the US product with the same active moiety should be included in box C1 of the FDA 3500A form. Box C1 is not large enough to include all this information. The NDA number of the US product appears in box G5; repeating it in box C1 is redundant. Current practice when this occurs is to list the foreign trade name, formulation, and generic name in the narrative (box B5), and the generic name and formulation in box C1, along with the notation "non-US product."

D. Death Reports

(Line 817-821)
The draft guidance states that death is always a serious outcome, whether associated with an unexpected adverse experience, or associated with an expected adverse experience, with labeling that does not specifically state that the adverse experience may be associated with a fatal outcome. Please clarify the timeframe for submitting an adverse experience when the only information received is "outcome-death".

F. Lack of Effect Reports

(Line 834-840)
The definition of adverse experience includes any failure of expected pharmacological action that is synonymous with lack of effect. Please clarify if the reporter has to use the terms "lack of efficacy" in order for the report to be termed "lack of effect". PhRMA does not understand the value in reporting lack of effect in unapproved indications, even if such information were available. PhRMA requests elimination of this item from the draft guidance.

Lot number is not always provided. Please add: The lot number of the suspect product should be included if available in item C6 of FDA form 3500A.

(Line 842-844)
Industry does not consider emergency contraceptive a labeled indication; however, FDA does, and special note of this situation should be made. Specific mention of this point in the draft guidance is requested.

G. Information on the Internet

(Line 848-855)
Please provide guidance regarding what constitutes an identifiable reporter for adverse events encountered via Internet sites (i.e., is an e-mail address sufficient to establish an identifiable reporter?). For either a company sponsored or non-company sponsored chat room, please clarify what constitutes a valid reporter and a valid patient. PhRMA recommends that information received via internet chat rooms not be considered valid as there is no way to conduct confidential follow-up.

H. Pediatric Patients

(Line 859-862)
The FDA is asking that both age and DOB be provided for children <3 years old. This is redundant and inconsistent with E2B recommendations. The draft guidance states that

for all pediatric patients, weight and dose should be included. This information is not always available. Please change the statement to read "for all pediatric patients, weight and dose should be included, if available."

J. Another Applicant's Product

(Line 885-889)
The draft guidance states that reports in which the suspect drug is that of another applicant should be promptly forwarded to that applicant. Please clarify whether this guidance applies to all reports, serious and non-serious, as the regulations address forwarding only serious adverse experiences to the applicant.

(Line 891-894)
The draft guidance states that an applicant should only submit a report of an adverse experience to the FDA for a suspect product marketed by another applicant if the applicant of the suspect product is unknown or the report is for "a serious, unexpected adverse experience occurring during the conduct of a study." Please clarify if this is an option or if it should always be applied when the report is from a clinical study.

K. Multiple Suspect Products

(Line 898-904)
The draft provides guidance regarding various scenarios for reporting multiple suspect drugs. The draft guidance states that when two products are equally suspect, only one FDA Form 3500A should be completed, and the report should be submitted to the product first in alphabetical order. Please clarify if this is by trade or generic name. Please clarify if this draft guidance also applies when a drug product and a licensed non-vaccine biological product are equally suspect. Reports for these products are sent to two different addresses. Please clarify if the Agency will handle the internal processing aspects of this situation, or if the guidance to submit only one FDA Form 3500A does not apply in this situation.

(Line 906-909)
A separate form should be submitted for a non-vaccine biological and a vaccine when both are suspect. PhRMA assumes this also means that there should be separate reports for a drug and vaccine report, drug and device, device and drug, etc. Please clarify this point.

(Line 911-918)
The last paragraph is very confusing. Please indicate whether exchanging copies of FDA 3500As applies only to domestic reports.

M. Two or More Marketers of a Product

(Line 932-936)
The draft guidance discusses the clock start for two companies that co-market a product in the US and for affiliates of the same company outside the US. They do not address international co-marketing agreements. In the 1992 guideline, the definition of affiliate included licensees abroad. This draft guidance is not practical unless there is a licensing agreement between two companies. Please clarify if the agency is referring to two or more companies in a contractual agreement to co-market a product. Please indicate whether this is a change in policy.

P. Reports from the FDA

(Line 963-965)
The draft guidance states that applicants who receive individual case safety reports from FDA are not required to resubmit them to the agency. However follow-up information to these initial reports must be submitted to the FDA. Please clarify what mechanism would be used to link the follow-up information to the information originally received from the agency, as there would be no unique manufacturer control number by which the applicant or the Agency can reference the initial information.

Q Product Defects

(Line 969-972)
Please define product defect. Please clarify if "product defect" would include product tampering.

VIII. REPORTING FORMATS

(Line 1018-1023)
In most computer systems UNK, NA or NI would be a default and re-programming would be needed to manually enter these values. The benefit of these fields does not seem proportional to the work of reprogramming, validation and manual entry. In any event, PhRMA does not believe that three categories are needed; NA (not applicable) and UNK (unknown) should be sufficient, even if the latter refers to temporarily unknown (at the time of submission).

APPENDIX A: GLOSSARY

(Line 1431)
Applicant: Please define "divided manufacturing."

(Line 1498)
Spontaneous Report: Following "It does not include cases identified from information solicited by the applicant such as individual cases or findings derived from a study," please add, "patient assistance programs, and registries."

PhRMA also notes that the definition in this draft guidance is not consistent with that in the E2C document which was published in the *Federal Register* May 16, 1997, and suggests that the Agency use the latter definition.

APPENDIX B: REPORT CHECKLIST

A. For all FDA form 3500A reports

(Line 1530)
1. Add "identifiable" patient.

(Line 1543)
5. Due to patient privacy concerns, it is a fairly common practice to exclude the name and address of the initial reporter from box E1 if the initial reporter is the patient or the patient's relative. This is in keeping with FDA's regulation, which states that the names

and addresses of individual patients should not be included in the reports. Please indicate that this is acceptable.

Definition of the term, "initial reporter", as used in the 3500A, Box E is not correct. For example, if the original reporter is a consumer and a physician gives the applicant follow-up either before the initial report is sent or on follow-up, the physician's name and address is put in Box E. The draft guidance needs to be consistent with actual practice regarding information in Box E is needed.

(Line 1550)

7. PhRMA recommends that the Agency include publications in the list of attachments.

PhRMA appreciates the opportunity to provide comments on this draft guidance document, and would be pleased to discuss these comments with the Agency at your request.

Sincerely,

Alice E. Till, Ph.D.