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Dockets Management Branch (IIFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 03D-0412, CDER 2003138. International Conference on Harmonisation (ICH); Draft Guidance on E2D Postapproval Safety Data Management: Definitions and Standards for Expedited Reporting.

Abbott Laboratories (Abbott) is very pleased to have the opportunity to comment on the ICH - Draft Guidance on E2D Postapproval Safety Data Management: Definitions and Standards for Expedited Reporting, published in the Federal Register on September 15, 2003.

We thank the Agency for their consideration of our attached comments. Should you have any questions, please contact Ivone Takenaka, Ph.D. at (847)-935-9011 or by FAX at (847) 938-3346.

Sincerely,

Doug Sporn /jrs
Douglas L. Sporn

Abbott

October 20, 2003

Comments on
ICH E2D - Postapproval Safety Data Management:
Definitions and Standards for Expedited Reporting, Draft Guidance

Docket No. 03D-0412

The following comments on the "E2D-Postapproval Safety Data Management: Definitions and Standards for Expedited Reporting" Draft Guidance are provided on behalf of Abbott Laboratories.

2.3. Unexpected Adverse Drug Reactions (ADR)

Lines 171-172
Regarding *"In the absence of specific documentation and in the face of uncertainty."*

Comment:

Abbott recommends that FDA/ICH clarify what documentation is being referred to, e.g., the official product information (as referred to in the preceding two paragraphs), the documentation provided by the reporter or other. Furthermore, it is not clear whose "uncertainty" is applicable to, e.g., that of the reporter, of the company, or other's.

2.5.1.1. Spontaneous Reports

Lines 194-197
The guidance includes *"notification by 'A Dear Healthcare Professional' letter, a publication in the press, or questioning of healthcare professionals by company representatives, as ways to stimulate reporting."*

Comment:

Abbott believes these examples are not consistent with the FDA concept, in which stimulated reports may also be from patient programs and direct to consumer advertising.

2.5.1.2. Literature

Abbott requests that the Agency clarify what constitutes lack of efficacy in the literature, i.e., whether lack of effect (or diminished effect) is attributable to changes in drug integrity, such as potency only. The FDA/ICH should provide guidance as to how these cases should be reported when the brand or trade name is not specified in the report.

Lines 207-209
The guidance states *"Marketing Authorization Holder (MAH) is expected to regularly screen the worldwide scientific literature, by accessing widely ..."*

Comment:

The term "regularly" is vague. To improve clarity, we recommend that the sentence *"MAHs should search the literature according to local regulation or at least once a month" (Lines 219-220)* be moved to the beginning of this section.

In addition, the use of the phrase "local regulation" may lead to some confusion. For example, in Europe, a monitoring frequency of at least once a week is stipulated in a guidance document (*Volume 9 of the Rules governing medicinal products in the European Union*). We suggest that the phrase "local requirements" may be more appropriate.

2.5.1.3. Internet

Lines 229-232

The guidance recommends *"MAHs and regulators to consider utilizing their websites to facilitate ADR data collection, e.g., by providing ADR forms for direct reporting or by providing appropriate contact details for direct communication."*

Comment:

We disagree with this proposal of providing ADR forms on MAHs websites. Use of forms on the company website may hinder the pharmacovigilance staff of the company from interacting with the reporter to ask clarifying questions about the adverse event. Follow-up with the initial reporter could be difficult, resulting in more incomplete, poor-quality reports. We agree, however, that contact details for direct communication with the company should be provided via the company website.

2.5.2. Solicited Sources

Lines 240-244

The guidance describes as *"solicited sources, reports derived from organized data collection systems, including clinical trials, post-approval names patient use programs, other patient support and disease management programs, surveys of patients or healthcare provides or information gathering on efficacy or patient compliance."*

Comment:

It is not clear whether reports from other initiatives, such as patient registries, are to be regarded as "solicited". Clarification should be provided.

2.5.3. Licensor-Licensee Interaction

Lines 262-264
The guidance states *"the time frame for expedited regulatory reporting should normally be no longer than 15 calendar days from the first receipt of a case meeting minimum criteria by any of the partners, unless otherwise specified by local regulation."*

Comment:

Abbott believes that the proposed expedited reporting timeframe of 15 days from the first receipt by any of the partners "of a case meeting minimum criteria" is unreasonable. Companies may have many agreements, both international and local, involving multiple partners and products. They must meet the global communication requirements associated with these agreements. No standard co-licensing agreement exists, and each agreement has unique aspects, depending on whether it involves in-licensing, out-licensing, co-promotion, or co-development. Although the MAH is ultimately responsible for reporting, the reporting arrangement may be included as part of the agreement.

Moreover, we recognize the need for prompt exchange is important. However, in situations (such as Japanese agreements) where the reports must be translated to English prior to exchange is unfeasible within this timeframe. Exchanging follow-up in this manner would also be unmanageable.

Requiring a 15-day timeframe would result in companies exchanging raw case data, rather than processed reports, with minimal time for follow-up of the reports. The ultimate result would be a decline in the quality of reports among partner companies.

3.1.2. Reporting Guidelines for Other Observations

Abbott recommends that the Agency provide some guidance on the format to be used for reporting other safety observations.

3.2.1. Minimum Criteria for Reporting

Lines 313-314
Current FDA guidance includes "fatal outcome" as one of the potential minimum criteria for reporting. It should be clarified whether "adverse reaction," as specified in ICH E2D, is intended to include "fatal outcome".

3.2.2. Time Clock Start Point

Line 322
To improve clarity, we suggest that the phrase *"day 0"* is highlighted.

4.1. Assessing Patient and Reporter Identifiability

Lines 343-345
The guidance describes *"age (or age category, e.g., adolescent, adult, elderly)...etc., as an automatic patient identifiable information."*

Comment:

Abbott believes age category as an identifier would lead to reporting a great number of patients without true identifiers because most articles in the literature describe the age range (such as 18 and above), therefore, most patients would be potentially reportable from each article, causing tremendous increase in number of reports.

Lines 346-349
It is stated in the guidance *"All parties supplying case information (or approached for case information) are subject to the notion of identifiability: ..."*

Comment:

The meaning of this sentence is unclear. To improve clarity, we suggest that the first part of the sentence be rephrased as follows:

"All parties supplying case information (or approached for case information) must be identifiable..."

Lines 351-355
The guidance states *"In the absence of qualifying descriptors, a report referring to a definite number of patients should not be regarded as a case until the minimum four criteria for case reporting are met. For example, 'Two patients experienced...' or 'a few patients experienced' should be followed up for patient-identifiable information before regulatory reporting."*

Comment:

This statement suggests that reports specifying, for example, "Two patients" or "a few patients" should not be reported, as they do not meet the minimum criteria for reporting (no identifiable patient). This is contrary to current experience regarding FDA expectation for these types of reports. Clarification of whether such cases are or are not reportable should be provided.