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VICE PRESIDENT
SCIENCE POLICY AND TECHNICAL AFFAIRS



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April 26, 2002

Dockets Management Branch (MFA-305)
Food and Drug Administration
5630 Fishers Lane Rm. 1061
Rockville, MD 20852

Re: Docket No. 02N-0012 - Agency Information Collection Activities; Proposed Collection;
Comment Request; Postmarketing Adverse Drug Experience Reporting

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents America's leading research-based pharmaceutical and biotechnology companies. PhRMA members discover, develop, and produce most of the prescription medicines used in the United States and a substantial portion of the medicines used abroad. PhRMA has a long-standing and vital interest in post-marketing adverse event collection, reporting, and recordkeeping.

As world leaders in the discovery research, development, and production of innovative life-saving medicines, PhRMA member firms are actively involved, on a daily basis, in the collection, review, follow-up, and reporting of adverse events. For this reason, we appreciate the opportunity to provide comments on the reporting and recordkeeping requirements for post-marketing adverse drug experiences (21 CFR 310.305 and 21 CFR 314.80). Comments are formatted in accordance with the questions posed in the February 25, 2002 Federal Register notice.

1. Is the proposed collection of information necessary for the proper performance of FDA's functions, including whether the information will have practical value?
 - We would agree that the collection of adverse event information, both expedited and Periodic Reports, is necessary and has practical value in monitoring the safety of marketed products.
 - Some enhancements could be made to further improve the efficiency of this information collection; see responses to items 3 and 4 below.

2. Are FDA's estimates of the burden of the proposed collection of information, including the validity of the methodology and assumptions used, accurate?
 - It is not clear what methodology and assumptions were used by FDA to calculate either the annual reporting burden or the annual record-keeping burden of the proposed collection of information.
 - It would seem that the FDA's estimate of the burden reflects only the FDA's effort and not that of the respondents.
 - The annual number of responses (number of Periodic Reports prepared) per respondent is significantly underestimated. PhRMA member companies submit in excess of 400 Periodic Reports (annual and quarterly reports) every year.

02N-0012

Pharmaceutical Research and Manufacturers of America

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- Likewise, the hours per response for preparing Periodic Reports under 314.80(c)(2) are also grossly underestimated. On average, the preparation, quality control, and duplication of the NDA Periodic Reports take from 16 to 40 hours each.
- All adverse drug experience reports, including non-15-Day Alert Reports, need to be taken into account when calculating the burden, as all need to be reviewed, assessed, and processed for determination of "expedited" status and for inclusion in the Periodic Safety Update Reports (PSUR).

As an example, one member company received approximately 49,000 initial adverse drug experience reports in association with their marketed prescription products from worldwide sources in 2001, approximately 4800 of which qualified as 15-Day Alert Reports; this included both initial and follow-up reports. A second company received approximately 20,000 initial adverse event reports from worldwide sources in 2001, approximately 2,000 of which qualified as 15-Day Alert Reports; this included both initial and follow-up reports.

- With regard to the estimated annual recordkeeping burden, we question the statement that there are no capital, operating, or maintenance costs associated with maintaining records of adverse experience reports for ten years. Respondents must maintain facilities to store what amounts to tons of paper records in addition to back-up records on other media (scanned optical images, microfilm, etc.). Costs for storage and retrieval vary widely, depending on the volume of records, rental fees, transportation costs, and retrieval fees, but can be substantial (e.g., thousands of dollars per year).

3. Ways to enhance the quality, utility, and clarity of the information to be collected:

- It is important for FDA to move quickly to change their Periodic Reporting requirements to be consistent with the ICH Guidelines for Periodic Safety Update Reports. This will enable companies to submit the same report to all regulatory authorities globally, and will decrease the burden involved with preparing Periodic Reports specifically for FDA. Additionally, for those companies who have received a waiver from the agency to submit Periodic Reports in the PSUR format, this would decrease the burden of adding US-specific appendices to the reports.
- Periodic Safety Update Reports to FDA should not routinely include any information in addition to that included in the ICH Guidelines for Periodic Safety Update Reports. Specifically, FDA should not require full copies in either paper or electronic form of cases that were not subject to expedited reporting (i.e., that are not serious/expected and non-serious adverse events). If a potential signal arises about a specific product, FDA has the authority and opportunity to request all available information associated with any individual case(s).
- There should be more collaboration between FDA and respondents when FDA identifies a potential signal; for example, case reports should be shared and mutually discussed.

4. Ways to minimized the burden of the collection of information on the respondents:
- a. We are supportive of alternative methods to submit 15-Day Alert Reports (e.g., facsimile, electronic transmission).
 - b. Cost savings could be realized by both FDA and respondents by eliminating the requirement for submitting original literature articles as attachments to 15-Day Alert Reports. Articles would always be available to FDA on request. Elimination of this requirement would allow reports from the literature to be submitted electronically using the E2B format.
 - c. Cost savings could also be realized by eliminating the requirement to collect non-serious labeled events. Costs associated with collecting information that has little, if any, value has a substantial financial impact on both companies and the agency. Elimination of this requirement would free up valuable resources to focus attention on the more serious, unexpected cases.
 - d. The ability to transmit Periodic Report FDA 3500A forms electronically (via diskette and in the future using ICH E2B format) will decrease the processing time for these reports by eliminating pagination and physical handling. It is our understanding that FDA will require respondents (including those companies involved in the initial pilot program) to submit both paper and electronic copies of Periodic Report FDA 3500A forms for an undetermined period of time, effectively eliminating the potential timesavings. This period of duplicate reporting should be kept to the minimum period necessary for FDA to verify that the data in the electronic submission was loaded correctly into the FDA's AERS database. PhRMA urges FDA to consider and adopt the proposals of the CIOMS V Working Group regarding these matters.
 - e. We are supportive of Agency efforts to consider provisions for alternate methods of data storage other than through hard copy paper records. PhRMA member companies would like the option to choose and maintain methods for storage and retrieval of records according to the individual company's needs. Storing scanned optical images of records instead of paper copies would considerably decrease the need for large file rooms and extensive off-site storage facilities, and the costs associated with maintaining these facilities.

Thank you for the opportunity to comment on this important matter.

Sincerely,



Alice E. Till, Ph.D.