

DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration

[Docket No. 96N-0446]

**Agency Information Collection Activities; Submission for OMB Review;  
Postmarketing Reporting of Adverse Drug Experiences**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

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**SUMMARY:** The Food and Drug Administration (FDA) is announcing that the proposed collection of information listed below has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995 (the PRA).

**DATES:** Submit written comments on the collection of information by *(insert date 30 days after date of publication in the Federal Register)*.

**ADDRESSES:** Submit written comments on the collection of information to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Desk Officer for FDA.

**FOR FURTHER INFORMATION CONTACT:** Karen L. Nelson, Office of Information Resources Management (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1482.

**SUPPLEMENTARY INFORMATION:** In compliance with section 3507 of the PRA (44 U.S.C. 3507), FDA has submitted the following proposed collection of information to OMB for review and clearance.

**Postmarketing Reporting of Adverse Drug Experiences—21 CFR 310.305 and 314.80 (OMB Control Number 0910–0230—Reinstatement)**

Section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) requires applicants to submit data showing whether a drug is safe and effective. FDA is authorized to issue regulations requiring the recordkeeping and reporting necessary to enable it to evaluate the safety or effectiveness of a drug product, including whether the product is misbranded or adulterated under sections 501 and 502 of the act (21 U.S.C. 351 and 352). Under §§ 310.305 and 314.80 (21 CFR 310.305 and 314.80), FDA set forth reporting and recordkeeping requirements regarding adverse drug experiences.

All applicants who have received marketing approval of drug products are required to file Alert Reports with FDA regarding serious, unexpected adverse drug experiences, as well as followup reports on the adverse drug experiences when the applicant receives new information or as requested by FDA (§ 314.80(c)(1)). The Alert Reports include reports of all foreign or domestic adverse experiences, as well as reports obtained in scientific literature (§ 314.80(d)), and if there is a reasonable possibility that the drug caused the adverse experience, reports from postmarketing studies (§ 314.80(e)). Under § 314.80(c)(2), applicants must provide periodic reports of adverse drug experiences. Under § 314.80(i), applicants must keep for 10 years records of all adverse drug experience reports known to the applicant.

For marketed prescription drug products without approved new drug applications or abbreviated new drug applications, manufacturers, packers, and distributors are required to report to FDA serious, unexpected adverse drug experiences, as well as followup reports on the adverse drug experiences when the applicant receives new information or as requested by FDA (§ 310.305(c)(1) and (c)(2)). Under § 310.305(f), each manufacturer, packer, and distributor shall maintain for 10 years records of all adverse drug experiences required to be reported.

The primary purpose of FDA's adverse drug experience reporting system is to provide a signal for potentially serious safety problems with marketed drugs. Although premarket testing discloses

a general safety profile of a new drug's comparatively common adverse effects, the larger and more diverse patient populations exposed to the marketed drug provide, for the first time, the opportunity to collect information on rare, latent, and long-term effects. Signals are obtained from a variety of sources, including reports from patients, treating physicians, foreign regulatory agencies, and clinical investigators. Information derived from the adverse drug experience reporting system contributes directly to increased public health protection because the information enables FDA to make important changes to the product's labeling (such as adding a new warning) and, when necessary, to initiate removal of a drug from the market.

Respondents to this collection of information are manufacturers, packers, distributors, and applicants.

In the **Federal Register** of December 30, 1997 (62 FR 67874), the agency requested comments on the proposed collection of information. FDA received one comment. The comment questioned the accuracy of several of the information collection burden estimates, and suggested higher estimates for annual frequency per response and hours per response. In light of this comment, the agency reevaluated its estimates and is revising its previous estimate of the number of periodic reports prepared per respondent, from the 1.5 originally reported to 18. On review, FDA determined that this number reflects the average number of periodic reports it receives. A periodic report includes a narrative summary, individual case safety reports, and history of actions taken. In addition, the agency is revising the hours per response for preparing a periodic report under § 314.80(c)(2) from 5 to 28 hours. The comment suggested, and FDA agrees, that 28 hours more accurately reflects the amount of time required to prepare a response.

The comment also suggested ways to enhance the quality, utility, and clarity of the information to be collected and ways to minimize the burden of the collection of information on respondents.

FDA is in the process of revising its safety reporting and recordkeeping regulations and will consider these comments in developing its rulemaking. The respondent has had and will have an opportunity for comment on these rulemaking initiatives. In the **Federal Register** of October 27,

1994 (59 FR 54046), FDA published a proposed rule to amend its postmarketing expedited and periodic safety reporting requirements, as well as others, to implement international standards and to facilitate the reporting of adverse drug experiences. In the **Federal Register** of October 7, 1997 (62 FR 52237), FDA published a final rule amending its expedited safety reporting regulations to implement certain recommendations in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) E2A guidance on definitions and standards for expedited reporting (58 FR 37408, July 9, 1993). At this time, the agency is further considering recommendations in the ICH E2A guidance for additional amendments to its postmarketing expedited safety reporting regulations. With respect to the proposed amendments to the periodic adverse drug experience reporting requirements in the proposal of October 27, 1994, FDA has decided to repropose these amendments based on recommendations in the ICH E2C guidance on periodic safety update reports (62 FR 27470, May 19, 1997). In developing the reproposal, FDA will also consider comments submitted in response to the proposed rule of October 27, 1994, regarding periodic adverse experience reports. FDA is also considering rulemaking concerning the electronic submission of postmarketing expedited and periodic safety reports using standardized medical terminology, data elements, and electronic transmission standards recommended by the ICH.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN<sup>1</sup>

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
310.305(c)(5)	1	1	1	1	1
314.80(c)(1)(iii)	5	1	5	1	5
314.80(c)(2)	683	18	12,300	28	344,400
Total					344,406

<sup>1</sup> The reporting burden for §§ 310.305(c)(1), (c)(2), (c)(3), and 314.80(c)(1)(i) and (c)(1)(ii) was reported under OMB control number 0910-0291. There are no capital costs or operating and maintenance costs associated with this collection of information.

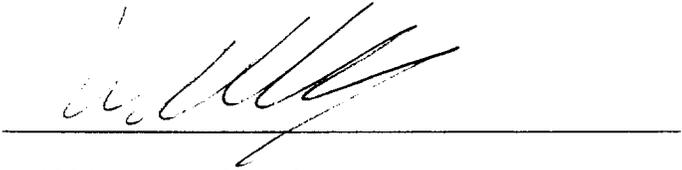
TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN<sup>1</sup>

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
310.305(f)	25	1	2	1	25
314.80(i)	683	1	683	1	683
Total					708

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

The numbers in Tables 1 and 2 of this document are accurate as of the time of publication. FDA is in the process of revising its safety reporting and recordkeeping regulations. These numbers may change when the revisions to those regulations are finalized.

Dated: January 22, 1999  
January 22, 1999



William K. Hubbard  
Associate Commissioner for Policy Coordination

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