

Supporting Statement

Reporting Requirements

PRESCRIPTION DRUG PRODUCT LABELING
MEDICATION GUIDE REQUIREMENTS
OMB Control No. 0910-0393

A. Justification

1. Circumstances of Information Collection

Food and Drug Administration (FDA) regulations require the distribution of patient labeling, called Medication Guides, for certain prescription human drug and biological products used primarily on an outpatient basis that pose a serious and significant public health concern requiring distribution of FDA-approved patient medication information. These Medication Guides inform patients about the most important information they should know about these products in order to use them safely and effectively. Included are information such as the drug=s approved uses, contraindications, adverse drug reactions, and cautions for specific populations, with a focus on why the particular product requires a Medication Guide. These regulations are intended to improve the public health by providing information necessary for patients to use certain medication safely and effectively.

The regulations contain the following reporting requirements that are subject to the PRA. The estimates for the burden hours imposed by these regulations are listed below:

21 CFR 208.20 -- Applicants must submit draft Medication Guides for FDA approval according to the prescribed content and format.

21 CFR 314.70(b)(3)(ii) and 21 CFR 601.12(f) -- Application holders must submit changes to Medication Guides to FDA for prior approval as supplements to their applications.

21 CFR 208.24(e) -- Each authorized dispenser of a prescription drug product for which a Medication Guide is required, when dispensing the product to a patient or to a patient=s agent, must provide a Medication Guide directly to each patient unless an exemption applies under 21 CFR 208.26.

21 CFR 208.26 (a) -- Requests may be submitted for exemption or deferral from particular Medication Guide content or format requirements.

2. Purpose and Use of Information

This information collection enables the agency to determine whether the labeling for certain prescription drug products that FDA has designated as posing a serious and significant public health concern requiring distribution of FDA-approved patient medication information include Medication Guides which are acceptable to FDA.

3. Use of Improved Information Technology

The regulation requires applicants to submit Medication Guides to FDA for prior approval as supplements to their applications. As explained below, procedures and mechanisms are in place for this submission to be made electronically.

Electronic Regulatory Submissions for Archive. The Food and Drug Administration Modernization Act of 1997 (FDAMA) and the Prescription Drug User Fee Act (PDUFA) II reauthorization mandate that the agency develop and update its information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of investigational new drug applications and new drug applications, as defined in PDUFA, and related submissions. Moving an information-intensive activity, such as drug regulatory review, from a paper-based to an electronic environment will provide a number of benefits. This is true simply from the perspective of generating, handling, and storing the huge volumes of paper commonly associated with applications.

In general, these paper applications (often containing hundreds of volumes) are submitted with several copies, a process that can take several days longer than preparation of a corresponding electronic submission, which the agency can easily reproduce. Preparation of applications in electronic format results in direct cost savings related to materials, supplies, and paper handling logistics (i.e., labor, facilities). However, this is expected to be only a small portion of the potential savings. The most substantial burden reduction may not be in information recording, reporting, and record-keeping, but in the flexibility, efficiency, speed, and ease of filing required information that will result in cost savings to regulated industry, as well as FDA.

In September 1997, FDA published the Guidance for Industry on Archiving Submissions in Electronic Format X NDAs. This guidance provided for the receipt and archive of electronic Case Report Forms (CRF) and Case Report Tabulations (CRT) without an accompanying paper copy. In FY 1998, FDA established an Electronic Document Room (EDR) to manage the receipt and handling

of all electronic submissions. In January 1999, FDA published the Guidance for Industry on AProviding Regulatory Submissions in Electronic Format X NDAs≅. This guidance document covers the full NDA and is not limited to CRTs and CRFs.

FDA has received 264 NDAs with electronic components since January 1999. Of these 89 were new submissions. In the same period the agency has also received 273 supplements with electronic components of which 170 were new supplements. As of the end of August 2000, the agency's EDR was comprised of three groups of NDAs: those that consisted of items 11 and/or 12 only (109 or 42.4%); those that consisted of various items with or without items 11 and 12 (105 or 40.9%); and those consisting of nearly all 19 possible NDA data items (43 or 16.7%). A total of 197 (76.7%) of NDAs with electronic components had items 11 and/or 12 submitted in an electronic format.

Secure E-Mail. During a drug's development cycle, communications between agency review divisions and the company developing the drug is sensitive and proprietary. Prior to using secure E-mail, agency methods of Asecure≅ communication included U.S. mail, courier, telephone, and facsimile. These methods, some of which are not entirely secure, can be inefficient or time consuming, and can significantly contribute to the overall length of time involved in the drug review process. The widespread use of E-mail across the Internet offers a more efficient and scaleable means of information exchange. However, security risks of communicating over the Internet are well known. The information technology industry is answering security concerns by developing new standards of cryptographic techniques, E-mail formats, authentication algorithms, and other related aspects of secure communications. In 1998, the agency conducted a formal requirements study for secure E-mail which led to the selection of Worldtalk Corporation's WorldSecure Server as the base pilot platform. The agency completed a pilot, the final system design and implemented the production system in October 1999. The system is used across the Center for Drug Evaluation and Research to communicate with over 15 companies and more than 150 individuals in those companies. The system also provides virus scanning and extensive E-mail filtering capabilities.

ICH M2. The International Conference on Harmonisation (ICH) of Technical Requirements for the Registration of Pharmaceuticals for Human Use was formed to minimize waste in the discovery, development, regulation, manufacture, marketing, and use of human therapeutic products worldwide. The regulatory authorities of Europe, Japan, and the United States joined with their respective pharmaceutical trade associations in an agreement to take action

on harmonization by participating in the ICH.

The ICH Multi-disciplinary Group 2 (M2) Expert Working Group (EWG) was established to determine electronic standards and provide solutions to facilitate international electronic communication in the three ICR regions. The first effort of the M2 EWG was to establish a series of recommendations that would form the basis for standardized electronic communication in each of the three regions. These recommendations included physical media formats, secure communications, and structured data formats. Building on these standards, the EWG completed a detailed specification for the secure, electronic transmission of individual case safety reports (adverse event reports). The specification is being used to format and transmit electronic adverse event reports directly from a company's database to the FDA Adverse Event Reporting System (AERS).

The production of a specification for an electronic common technical document (CTD) was the next major effort assigned to the M2 EWG. The ICH Steering committee agreed in March 1999 that this effort should be undertaken by the M2 EWG in cooperation with the subject matter expert working groups for each section of the CTD. The CTD working groups are charged with harmonizing the format and content of the application documents for new product applications. The resulting ICH guidances, when implemented, will change the content and format of NDA submissions to the FDA. The M2 EWG is working with the CTD Step 2 documents to define the functionality to be included in the electronic submission for CTD submissions.

4. Efforts to Identify Duplication

The reporting required as a result of this information collection is not currently required by FDA and would not duplicate any other information collection.

5. Involvement of Small Entities

The reporting would apply equally to all applicants and dispensers whether large or small. However, because the number of products requiring Medication Guides overall will be relatively small, the smaller applicants would arguably sponsor many fewer drug products requiring Medication Guides and would, therefore, have fewer reporting responsibilities.

6. Consequences If Information Collected Less Frequently

The frequency of this reporting requirement would be determined by the applicant's number of marketed prescription drug products subject to a Medication Guide.

7. Consistencies with Guidelines in 5 CFR 1320.5(d)(2)

There is no inconsistency.

8. Consultations Outside the Agency

In the **Federal Register** of September 25, 2001 (66 FR 49024), FDA published a request for comments on the proposed collection of information. FDA received one comment. The comment stated that clarification is needed as to whether Medication Guides would be needed for medical devices that have a prescription drug either as a coating or incorporated into the material of the device, or as a component in a kit. The comment said that some of these types of products may be considered combination products.

FDA requested comments on the information collection burden estimates described in the notice. Because the comment does not pertain to the burden estimates, FDA has forwarded the comment to Docket Number 93N-0371, "Prescription Drug Product Labeling; Medication Guide Requirements." FDA appreciates the comment and will consider it as part of its Medication guide program.

FDA has determined that patients want Medication Guides and would benefit from them. However, FDA will not require such Medication Guides for all products, but only those that the agency determines pose a serious and significant public health concern requiring distribution of FDA-approved patient medication information. These Medication Guides will increase patients' knowledge about such prescription drugs, would enhance patient compliance with prescribed drug regimes, and would decrease inappropriate drug use, which is deemed to be especially problematic for these selected products. As explained in the proposed and final rules, FDA has met with numerous organizations and has reviewed and conducted extensive research concerning patient use of prescription drug product information.

9. Remuneration of Respondents

There is no payment to respondents.

10. Assurance of Confidentiality

This reporting burden has no confidentiality implications.

11. Questions of a Sensitive Nature

This reporting burden does not involve any sensitive questions.

12. Estimates of Annualized Hour Burden

Estimated Annual Reporting Burden

<u>21 CFR Section</u>	<u>Number of Respondents</u>	<u>Number of Responses Per Respondent</u>	<u>Total Annual Responses</u>	<u>Hours Per Response</u>	<u>Total Hours</u>
208.20	8	1	8	242	1,936
314.70(b)(3)(ii) 601.12(f)	3	1	3	24	72
208.24(e)	55,000	8.3	456,500	.0014	639
208.26(a)	1	1	1	4	4
TOTAL					2,651

13. Estimates of Annualized Cost Burden to Respondents

FDA estimates that, on average, approximately 8 products annually would be classified as A serious and significant and thus require Medication Guides. FDA's regulatory impact analysis estimated that applicants would require approximately 2 months of full-time effort (320 hours) to develop (i.e., develop for submission to FDA for review and approval) each model Medication Guide for new molecular entities (NMEs) or NDAs. Based on an average annual professional labor cost of \$70,000, the cost of developing each model Medication Guide would be approximately \$11,666.

FDA also estimated that the cost of developing each Medication Guide to supplement existing applications would be approximately \$5000, and the cost for each generic drug Medication Guide would be approximately \$500. In addition, FDA

estimates that the sponsor of one of the new or supplementary applications will request an exemption from at least some of the Medication Guide format or content requirements. FDA estimates that this will entail approximately 4 hours of work, or about \$200.

In addition, FDA estimates that two existing Medication Guides annually might require minor change under section 314.70(b)(3)(ii) or section 601.12(f), necessitating 3 days (24 hours) of full-time effort, for a total of \$1,200.

Under section 201.24(e), authorized dispensers are required to provide a Medication Guide directly to the patient (or the patient's agent) upon dispensing a product for which a Medication Guide is required. Thus, the final rule imposes a third-party reporting burden on authorized dispensers, who, for the most part, will be pharmacists. FDA estimates that, on average, it would take a pharmacist approximately 5 seconds (.0014hour) to provide a Medication Guide to a patient.

14. Estimates of Annualized Cost Burden to the Government

FDA and industry sponsors currently work to ensure the development and distribution of patient labeling on a product-by-product basis. Because FDA does not believe that the overall amount of this information will be increased by this rule, there should be no additional costs to the Federal Government. In fact, because this rule will provide greater clarity about what products will require Medication Guides, and what the format and content requirements will be, the costs to the Federal Government of ensuring that necessary patient labeling is produced are likely to decrease. No additional FTEs will be needed, nor should there be additional burdens on reviewers.

15. Changes in Burden

The change in burden is the result of new data on the number of submissions.

16. Time Schedule, Publication, and Analysis Plans

FDA does not intend to publish tabulated results of the information collection requirements that would be imposed by these requirements.

17. Displaying of OMB Approval Date

There are no forms associated with this collection.

18. Exception to the Certification Statement - Item 19

There are no exceptions to the certification statement
ACertification for Paperwork Reduction Act Submission.≡

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