

OMB INFORMATION COLLECTION

FINAL RULE

PRESCRIPTION DRUG PRODUCT LABELING

MEDICATION GUIDE REQUIREMENTS

SUPPORTING STATEMENT

1. CIRCUMSTANCES REQUIRING INFORMATION COLLECTION

The Food and Drug Administration (FDA) is requesting approval from the Office of Management and Budget (OMB) for the reporting and recordkeeping requirements contained in the FDA final rule entitled “Prescription Drug Product Labeling; Medication Guide Requirements” (21 CFR Parts 201, 208,314, and 601). This final rule would require that 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 be dispensed with such information. These “Medication Guides” would inform patients about the most important information they should know about these products in order to use them safely and effectively. Included would be 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. FDA is taking this action to improve the public health by providing information necessary for patients to use certain medication safely and effectively.

The statutory authority is as follows: 21 U.S.C. 321 (n), 352 (a), 355 (d), 355 (e),355(j)(2)(A)(v), 355(j)(3)(G), 371(a), and 42 U.S.C.262 (Attachment).

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exemption from particular Medication Guide content or format requirements.

2. **HOW, BY WHOM, AND FOR WHAT PURPOSE INFORMATION USED**

This information collection would be available to the agency in order 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. **CONSIDERATION OF INFORMATION TECHNOLOGY**

The final rule 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.

In the mid-1980's , FDA began working with pharmaceutical sponsors to develop Computer-Assisted New Drug Applications (CANDA). CANDAs were designed to provide information (text, data, image) electronically to facilitate the review of applications. There efforts yielded valuable information but were limited because for each new drug review division sponsors tended to develop different hardware and software approaches. A reviewer might be confronted with an array of hardware, software, and review tools to conduct a review that differed between sponsors and applications. Also, CANDAs were never approved as a substitute for the archival copy, so firms were still required to submit copies.

One solution to limitations of CANDAs was an approach whereby staff responsible for a particular review discipline (e.g., chemistry, clinical) worked directly with pharmaceutical sponsors to develop a consistent approach that would be applicable to all sponsors and to all review divisions. Focus on this approach has evolved into the Electronic Regulatory Submission

and Review (ERSR) Program. This new initiative is intended to ensure both the electronic availability of information and the means to manipulate this information electronically to yield a review.

ERSR has been made possible by other developments. The harmonization of FDA Form 356h has ensured that NDA's, ANDAs' and Biological License Applications would contain comparable information in the same sections of the submission. The promulgation of the "Electronic Records; Electronic Signatures" final rule allowed FDA to accept electronic submissions without an accompanying paper archival copy because electronic records are equivalent to paper records and electronic signatures are equivalent to hand-written signatures provided the requirements of 21 CFR Part 11 are met and the document has been identified in the agency's public docket as being acceptable for filing. The Guidance for Industry on "Archiving Submissions in Electronic Format - NDAs" provides for the receipt and archival of electronic report forms and tabulations. Another Guidance for Industry entitled "Providing Regulatory Submissions in Electronic Format - NDAs" is currently under development.

ERSR is made up of a variety of projects that are in different stages of development and implementation. These projects are categorized into 3 areas: First, "Electronic Submissions" includes standards-related projects to define the format and content of regulatory submissions; written guidance for industry to follow in preparing electronic submissions; an Electronic Document Room project to accommodate the receipt, archive, and storage of electronic transmissions; an Electronic Gateway project to provide an agency-level central point for receipt of secure electronic transmissions and routing to the Centers; and scientific databases that include structured databases, reference guides, and analytical tools used by reviewers. Second, "Corporate Databases, Document bases and Applications" includes projects under the Electronic Document Management System and the Management Information System. Third, other electronic initiatives including technical infrastructure, technical support, and training.

ERSR will impact the underlying business processes related to regulatory submissions and

reviews. Document rooms will handle electronic media rather than paper copies. Reviewers will review submissions online and generate their review documents online. Reviewers will conduct data analysis using structured databases, which combine data extracted from the submission under review as well as historical data from earlier submissions. Industry sponsors and manufacturers will experience reduced paper costs and manpower to compile paper submissions and better access to application status information through electronic mail.

**4. IDENTIFICATION OF DUPLICATION AND SIMILAR INFORMATION
ALREADY AVAILABLE**

The reporting required by this proposed rule is not currently required by FDA and would not duplicate any other information collection. This reporting is the only practical means available for FDA to certify that Medication Guides include all the elements necessary for the patient to be adequately informed about prescription drug products.

5. SMALL BUSINESSES

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 less reporting responsibilities under this proposed regulation.

**6. CONSEQUENCES OF LESS FREQUENT INFORMATION COLLECTION AND
TECHNICAL OR LEGAL OBSTACLES.**

The frequency of this reporting requirement would be determined by the applicant's number of marketed prescription drug products subject to a Medication guide. Because most products will require a Medication Guide upon initial approval of the product, the same procedures used to

approve a product's professional labeling will be used to approve the product's Medication Guide.

7. SPECIAL CIRCUMSTANCES

The circumstances under which draft Medication Guides would be submitted for approval to FDA are specified in the Medication Guide regulations, in section 208.1. Submission requirements for all new drug applications (NDA's), abbreviated new drug applications (ANDA's), and biological product applications are will defined in sections 314.50, 314.70, 314.94, 601.2 and 601.12.

Although they include the submission of more than an original and two copies of labeling, these regulations have been adhered to consistently by the pharmaceutical industry. As noted above, the frequency of this reporting requirement would be determined by how many prescription drug products the applicant has that are determined to be subject to a Medication Guide. Because most products will require a Medication Guide upon initial approval of the product, the same procedures used to approve a product's professional labeling will be used to approve the product's Medication guide. This, together with the time frame goals of the Prescription Drug User Fee Act (PDUFA), will determine exactly when the reporting requirement is triggered. The final rule will not require reporting to be required on a regular basis (e.g., weekly, quarterly, semi-annually or annually).

8. OUTSIDE CONSULTATION

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. During the past fifteen years, as explained in the preamble to the proposed rule, FDA has met with numerous organizations and has reviewed and

conducted extensive research concerning patient use of prescription drug product information. In February, 1996, FDA held a 2-day (2/14-2/15) public workshop concerning the proposed rule that included this requirement, thus publicly consulting with numerous individuals concerning the issues raised by this final rule.

9. PAYMENT TO RESPONDENTS

There is no payment to respondents.

10. CONFIDENTIALITY OF INFORMATION

This proposed reporting burden has no confidentiality implications.

11. SENSITIVE QUESTIONS

This proposed reporting burden does not involve any sensitive questions.

12. BURDEN HOURS AND EXPLANATION

ESTIMATED REPORTING BURDEN

21 CFR Section	No. Of Respondents	No. Of Responses per Respondent	Total Annual Responses	Hours Per Response	Total Hours
208.20	8	1	8	242	1,936
314.70(b)(3)(ii) or 601.12(f)	2	1	2	24	48
208.24(e)	60,574	2.5	150,000	.0014	212
208.26(a)	1	1	1	4	4
Total					2,200

The estimates in the chart were determined as follows:

Annual number of responses--FDA estimates that, on average, no more than five to ten products annually would be classified as “serious and significant” and thus require Medication Guides. FDA believes that four of these products would be in the new approval process at the time this determination is made. One already-marketed product would require a Medication Guide, with two “supplementary” Medication Guides needed for products in the same narrow therapeutic class, and one Medication Guide needed for a generic product in this class. FDA’s initial preliminary regulatory impact analysis, Section XII of the preamble to the proposed rule, 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 (NME’s) or NDA’s. Based on an average annual professional labor cost of \$70,000, the cost of developing each model Medication Guide would be approximately \$11,666.

Using these assumptions, 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.

Therefore, using the average annual number of Medication Guides that FDA anticipates will be submitted for each category (see “annual number of responses” in the chart below), the annualized cost to applicants to develop the Medication Guides required by this proposed regulation would be approximately \$69,000.

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.

Finally, 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, over the next 3 years, assuming that 5 Medication Guides are required annually, an average of 10 Medication Guides annually would be available for prescribing and dispensing. Assuming a base of approximately 100,000 prescriptions dispensed for each of these products annually, and subtracting from this base the approximately 50 percent of products with Medication Guides that are dispensed in unit-of-use packages, results in a total of 500,000 prescriptions annually for products that pose a "serious and significant public health concern." Based on data collected in 1996, the agency estimates that at least 70 percent of patients are already receiving some kind of patient medication information voluntarily provided by pharmacists when they dispense prescriptions. Therefore, this final rule would represent an incremental burden, in terms of third party reporting, for only 30 percent, or about 150,000 of these prescriptions. Given 60,574 pharmacies, including chains, independents, and food/drug combinations, this represents an average of 2.5 prescriptions per store, per year. Because FDA estimates that, on average, it would take a pharmacist approximately 5 seconds (.0014hour) to provide a Medication Guide to a patient, the overall annual third party reporting burden for this final rule is approximately 212 hours. FDA has estimated that the average annual incremental cost of providing these Medication Guides over the first 3 years of implementation of the rule would be about \$19,800.

13. ANNUAL COST TO RESPONDENTS

FDA believes that there will not be significant annual cost to respondents to this requirement beyond those already specified in item 12 above that would be above and beyond costs incurred under the current system of voluntary-produced patient labeling for certain products.

14. ANNUAL COST TO 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 FTE's will be needed, nor should there be additional burdens on reviewers.

15. EXPLANATION OF CHANGE IN ITEMS 13 AND 14

There are no current similar requirements

16. STATISTICAL REPORTING

This reporting requirement does not employ statistical methods.

17. EXPIRATION DATE ON FORM

The required reporting forms accurately reflect the OMB approval number.

18. EXCEPTION TO CERTIFICATION STATEMENT

We are not seeking any exceptions to the certification statement listed in Item 19, "Certification for Paperwork Reduction Act Submission," of OMB Form 83-I.