

Supporting Statement

OTC Human Drugs; for Labeling Requirements

OMB Control Number 0910-0340

Docket Number 2004N-0534

A. **Justification**

1. **Circumstances Necessitating Information Collection.**

The Food and Drug Administration (FDA) amended its regulations governing labeling requirements for human drug products to establish a standardized format for the labeling of all over-the-counter (OTC) drug products. The rule, issued on March 17, 1999 (64 FR 13254), added new section 201.66 to 21 CFR. The rule requires that the outside container or wrapper of the retail package (or the immediate container label if there is no outside container or wrapper) of all OTC drug products include uniform headings and subheadings, presented in a standardized order, with minimum standards for type size and other graphical features. FDA issued these requirements because it had determined that the design and format of labeling information varies considerably among OTC drug products and consumers may have difficulty reading and understanding the information presented on OTC drug product labeling. The rule is intended to enable consumers to better read and understand OTC drug product labeling and to apply this information to the safe and effective use of OTC drug products.

FDA's legal authority to modify and simplify the manner in which certain information is presented in OTC drug product labeling derives from sections 201, 502, 505, 507, and 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 352, 355, 357, and 371). Regulating the order, appearance, and format of OTC drug product labeling is consistent with FDA's authority to ensure that drug labeling conveys all material information to consumers (21 U.S.C. 321(n) and 352 (a)), and that labeling communicates this information in a manner that is likely to be read and understood by the ordinary individual under customary conditions of purchase and use (21 U.S.C. 352(c)). Regulating the content of OTC drug product labeling is consistent with FDA's authority to ensure that the products are safe and effective for use (21 U.S.C. 321(n), 321(p), 352, 355, and 357).

The labeling statements required under this rule are not subject to review by the Office of

Management and Budget because they are originally supplied by the Federal Government to the recipient for the purpose of disclosure to the public (5 CFR 1320.3(c)(2)) and therefore do not constitute a collection of information under the Paperwork Reduction Act of 1995 (44 U.S.C. 3510 et seq.).

Section 201.66 requires all OTC drug product manufacturers to format labeling as set forth in subsections (c) and (d). FDA has learned from the industry that OTC drug product manufacturers routinely redesign the labeling of OTC drug products as part of their usual and customary business practice. This rule provides varied time frames for implementing the OTC labeling requirements. Therefore, the majority of respondents have been able to format OTC drug product labeling in accordance with § 201.66 as part of their routine redesign practice, creating no additional paperwork or economic burden. The rule, issued on March 17, 1999, had a 6-year final implementation date of May 16, 2005. Therefore, except for a small number of OTC sunscreen drug products that have temporarily been exempted from this date, all OTC drug products will need to be in compliance by May 16, 2005.

FDA initially estimated that, of the 39,310 stock keeping units (SKUs) (individual products, packages, and sizes) marketed under a final monograph when the OTC labeling requirements were issued on March 17, 1999, approximately 32 percent, or 12,573 products, may necessitate labeling format changes sooner than provided under their usual and customary practice of label redesign. FDA estimated that of the 400 respondents who produce OTC drug products, including the 12,573 products described above, each may be required to respond approximately 31.4 times to this rule outside of their usual and customary practice. Each response was estimated to take, on the average, 4 hours, for a total of 50,292 hours per year. This burden was expected to be a one-time burden.

Although the usual and customary practice of label redesign minimized the burden for the remaining 68 percent of SKUs, or 26,737 products, marketed at the time the OTC labeling requirements were issued on March 17, 1999, additional time may have been necessary for each company to make the format changes under this rule. FDA has estimated that of the 400

respondents who produce OTC drug products, each may be required to respond approximately 66.8 times to bring the 26,737 products into compliance with this rule. FDA estimated that for this group, each response would take an average of 2.5 hours for a total of 66,842 hours. This was expected to be a one-time burden. The chart reflects this group on the second line.

Section 201.66(c) and (d) required OTC drug product manufacturers with approved or pending new drug applications (NDAs) and abbreviated drug applications (ANDAs) to submit to FDA supplements and amendments regarding labeling changes pursuant to 21 CFR 314.60(a), 21 CFR 314.70, 21 CFR 314.97, and 21 CFR 314.96(a). In the proposed rule, FDA attributed this paperwork burden to these specific NDA and ANDA regulations. For the final rule, FDA redesignated the burden under 21 CFR 201.66(c) and (d). Under 21 CFR 314.70 (b)(33)(ii), application holders must submit revised labeling to FDA for prior approval as supplements to their approved applications. Under 21 CFR 314.60(a), applicants must submit revised labeling to FDA as an amendment to a pending application. Under 21 CFR 314.97, abbreviated application holders must submit revised labeling to FDA for prior approval as supplements to their approved applications (generic drugs). Under 21 CFR 314.96(a), applicants must submit revised labeling to FDA as an amendment to a pending abbreviated application (generic drugs).

Under 21 CFR 201.66 (e), respondents subject to this rule are required to submit requests in writing for exemptions and deferrals from the specific requirements of 21 CFR 201.66. Based on its experience with exemption and deferral requests under similar provisions, FDA estimates that approximately 16% of the total number of respondents, or 25 manufacturers, packers, or distributors, are likely to submit such requests on the average of one time per year. Such requests take an average of 24 hours each for a total of 2,400 hours annually.

Section 201.66 requires all OTC drug product manufacturers to format labeling as set forth in subsections (c) and (d). The estimated numbers in the chart below included the one-time general formatting burden for all respondents. The estimated number for subsections (c) and (d) also include the one-time burden of submitting supplements and amendments regarding labeling

changes to approved or pending new drug applications (NDAs) and abbreviated drug applications (ANDAs) under 21 CFR 314.60 (a), 21 CFR 314.70, 21 CFR 314.97, and 21 CFR 314.96(a). In the proposed rule, FDA designated the paperwork burden under these NDA and ANDA regulations. For the final rule, FDA redesignated the burden under 21 CFR 201.66(c) and (d).

Based on information and experience, FDA estimated that approximately 400 respondents would be subject to the provisions of 21 CFR 201.66(c) and (d). Of the 400 respondents, 350 or fewer were subject to one or more of the NDA and ANDA regulations requiring supplements or amendments for labeling changes. On the average, each respondent was expected to make one-time label formatting changes and submissions to NDAs and ANDAs approximately 3.6 times, with each response an average of 2 hours. This reporting burden, which was listed in the chart below, should have passed as virtually all OTC drug products marketed on March 17, 1999 under NDAs and ANDAs have already been relabeled in the new OTC drug labeling format.

2. How, By whom, and for What Purpose

The purpose of this rule was to establish a standardized format for the labeling of all OTC drug products so that the labeling will be clear, simple, and easier to read. Variability in the design, format, and placement of required OTC drug product labeling information may make it difficult for consumers to both find and read important information. In order for consumers to safely and effectively use OTC drug products, important labeling information must be readily accessible, readable, easily understood, noted, and acted upon. If information is not processed or is ignored due to factors affecting readability, such as small print size, it cannot provide the health benefits that would result from the safe and effective use of OTC drug products. Nevertheless, warnings, cautions, and contraindications, which are relatively technical, in the past have often been presented in small print. Moreover, the amount of information and the lack of uniform presentation of that information previously found on OTC drug product labels often

made it difficult to compare labels. The variability of such information may lead to market inefficiencies that include suboptimal purchases, inappropriate price-quality relationships, and competitive inefficiencies. FDA has determined that standardized labeling format, minimum print size, and consistent text will enhance consumers' ability to find and read relevant safety information. Potential benefits include easier product comparison, improved consumer decision making and self-treatment, and fewer adverse drug experiences.

3. Considerations of Information Technology

FDA allows pharmaceutical sponsors to submit Computer-Assisted New Drug Applications (CANDA). CANDAs provide information (text, data, image) electronically to facilitate FDA review of applications (including the submission of information required under this rule, such as labeling supplements and amendments). CANDAs enable FDA and pharmaceutical sponsors to have electronic dialogue on labeling design and revisions required by the rule. Focus on this approach has evolved into FDA's Electronic Regulatory Submission and Review (ERSR) Program. This initiative helps to ensure both the electronic availability of information and the means to manipulate this information electronically to yield a review.

4. Identification of Duplication

The reporting resulting from this rule only applies to the labeling of OTC drugs subject to an approved application. This reporting requirement is the only practical way for FDA to ensure that the product labeling complies with the new format and content requirements. The reporting is consistent with existing reporting requirements for products subject to an approved application and does not duplicate any other information collection.

5. Small Businesses

FDA is requiring affected entities to change the information panel for affected OTC drug

products. Among the steps FDA has taken to minimize the impact on small entities is (this is discussed in more detail in the final rule under part VIII Analysis of Impacts): (1) To provide enough time for implementation to enable entities to use up existing label stock, (2) to provide sufficient time to coordinate a substantial proportion of the label changes with routine industry-initiated labeling changes, (3) to provide a mechanism for applying for an exemption or a deferral (when the requirements are judged inapplicable, impracticable, or unnecessary), and (4) to provide additional time to comply for individual OTC drug products having sales of less than a smaller dollar figure. While this last provision to extend the compliance time provides flexibility for a substantial number of individual OTC drug products, the impact on overall retail sales is negligible. FDA has also provided over 6 years from the date of the final rule (from March 17, 1999 until May 16, 2005) for the required labeling changes to be implemented. FDA believes that the above actions provide substantial flexibility and reductions in cost for small entities.

6. Consequences of Less Frequent Information Collection and Technical or Legal Obstacles

FDA would be unable to determine, before an OTC drug product is available to consumers, whether the labeling complies with the revised format and content requirements.

7. Inconsistencies with 5 CFR 1320.6 or Special Circumstances

Data collection for applications is consistent with all the requirements of section 1320.6.

8. Consultations with outside Sources

In the Federal Register, of January 4, 2005 (70 FR 362), the agency requested comments on the proposed collection of information. There were no comments received.

Prior to and after issuance of the final rule, many consumers expressed concern to FDA

about the legibility and understandability of OTC drug product labeling. Many individuals, especially the elderly, mentioned small print size, print style, and lack of color contrast. Consumers stated that poor labeling legibility may cause them to select an improper dose, which may result in adverse drug reactions. Consumers have also submitted comments to FDA about the print size of OTC drug product labeling in various OTC drug product rulemakings.

In response to these consumer comments and a citizen petition from a pharmacist group, FDA published two requests for public comments in the FEDERAL REGISTER that related to the legibility and understandability of OTC drug product labeling. In addition, in an effort to solicit more information and views on what specific aspects of OTC drug product labeling design would improve communication to consumers, FDA held a public hearing on September 29, 1995.

The hearing addressed consumer use, legibility and consumer comprehension of OTC drug product labeling, OTC drug product labeling design features, and behavioral issues. At the public hearing, 22 parties (including representatives from Government agencies, universities, industry associations, consumer associations, and corporations) made presentations.

In February 1996, FDA conducted a focus group study to investigate consumers' perceptions of risks and benefits of prescription and OTC drugs. The study looked specifically at how consumers react to different wording, claims, and statements (including the format and order of the information) contained in prescription and OTC drug product labeling. Participants confirmed that it would be beneficial to emphasize side effects and warnings, either by using bullets, bold type, block lettering, or larger type. Although there was no consensus about the best placement order for the information, the participants agreed that simple directions would be beneficial and labeling information should be in plain English so they could better understand what the ingredients were and how the drug works. Participants stated that this increased knowledge would help to alleviate their concerns of any health risk from taking the drug.

FDA published a proposed rule on February 27, 1997, setting forth for public comment the new proposed labeling requirements that are the subject of this supporting statement. FDA also requested comment on two labeling studies discussed in the proposal and provided over 7 months for comment. The final rule discussed the more than 1,800 comments received.

9. Payments or gifts to Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents under these labeling requirements.

10. Confidentiality of Information

The reporting requirements have no confidentiality implications.

11. Sensitive Questions

There are no questions of a sensitive nature.

12. Total Hour Burden to Respondents

Section 201.66 requires all OTC drug product manufacturers to format labeling as set forth in subsections (c) and (d). FDA has learned from the industry that OTC drug product manufacturers routinely redesign the labeling of OTC drug products as part of their usual and customary business practice. This rule provides varied time frames for implementing the OTC drug product labeling requirements. Therefore, the majority of respondents could format OTC drug product labeling in accordance with § 201.66 as part of their routine redesign practice, creating no additional paperwork or economic burden. FDA previously estimated that 12,573 out of 39,310 SKUs (32%) marketed under a final monograph were affected by the March 17, 1999 OTC drug product labeling final rule and may have to implement labeling format changes sooner than provided under their usual and customary practice of label redesign. FDA estimated

that of 400 respondents who produce OTC drug products, including the 12,573 products described above, each may have to respond approximately 31.4 times to this rule outside of their usual and customary practice. Each response was estimated to take, on the average, 4 hours, for a total of 50,292 hours per year. This burden was expected to be a one-time burden.

FDA estimated that the usual and customary practice of label design would minimize the burden for the remaining 68% of SKUs (26,737 products) marketed when the final rule issued. FDA also determined that additional time may be necessary for each company to make the format changes under this rule. FDA estimated that of the 400 respondents who produce OTC drug products, each may be required to respond approximately 66.8 times to bring the 26,737 products into compliance with this rule. FDA estimated that for this group, each response would take an average of 2.5 hours for a total of 66,842 hours. This was expected to be a one-time burden. The chart reflects this group on the second line.

Section 201.66(c) and (d) also require OTC drug product manufacturers with approved or pending new drug applications (NDAs and abbreviated drug applications (ANDAs)) to submit to FDA supplements and amendments regarding labeling changes pursuant to 21 CFR 314.60(a), 21 CFR 314.70, 21 CFR 314.97, and 21 CFR 314.96(a). Based on its records and experience, FDA estimated that approximately 61 respondents had NDAs and ANDAs to which supplements and amendments would be required. FDA estimated that approximately 522 applications (350 NDAs and 172 ANDAs) would require supplements or amendments regarding labeling changes under 201.66(c) and (d), an average of 8.5 submissions per respondent. Based on information and experience, FDA estimated that each submission would take an average of 2 hours to prepare, for a total of 1,040 hours annually. This burden was also expected to be a one-time burden.

Under 21 CFR 201.66(e), respondents subject to this rule could submit requests in writing for exemptions and deferrals from the specific requirements of 21 CFR 201.66. Based on its experience with exemption and deferral requests under similar provisions, FDA estimated

that approximately 16% of the total number of respondents, or 25 manufacturers, packers, or distributors, were likely to submit such requests on the average of one time per year. FDA estimated that these requests may average 24 hours each, for a total of 2,400 hours annually.

Since March 17, 1999, FDA has published six additional major final rules on OTC drug monographs and several minor amendments to existing final monographs. The effective date for relabeling OTC drug products in the new format occurred by the end of 2004, except for OTC sunscreen drug products (for which implementation of the new labeling requirements has been stayed indefinitely while FDA amends the monograph for these products) and a small number of other OTC drug products with annual sales less than \$25,000. Based on information in the six final rules issued since 1999, FDA estimates that 11,250 additional SKUs (out of the original 26,737 that needed to be relabeled in the new format) have already been affected by the final rule. Thus, 15,487 SKUs remain to be affected by the OTC drug product labeling final rule, minus approximately 2,000 OTC sunscreen drug product SKUs. All of these except the sunscreen drug products will need to have the new labeling format by May 16, 2005, for products initially introduced or initially delivered for introduction into interstate commerce after that date. As the number of products remaining to be affected by the OTC drug products labeling final rule is close to the number of products that were affected at the time the final rule published on March 17, 1999, in this current supporting statement FDA is using the same numbers of respondents, annual frequency per response, and total annual responses it estimated in 1999.

TABLE 1.--Estimated Annual Reporting Burdeno

Estimated Annual Reporting Burden					
21 CFR Section	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours Per Response	Total ¹ Hours

Estimated Annual Reporting Burden					
201.66 ²	400	31.43	12,573	4	50,292
201.66	400	66.8	26,737	2.5	66,842
201.66 (c), (d) ²	61	8.5	522	2	1,044
201.66(e)	25	4	100	24	2,400
Total			39,932		120,578

oThere are no capital costs or operating and maintenance costs associated with this information collection.

5One-time burden.

13. Total Annual Cost Burden to Respondents

Based on an hourly industry cost of \$108 (wages plus overhead), the total cost burden to respondents would be \$5,803,488 (53,736 X \$108).

14. Annualized Cost to FDA

FDA estimates that it would take application reviewers approximately 30 minutes to review supplements and amendments and other revised OTC drug product labeling submissions (for products marketed under OTC drug monographs). Based on an hourly cost to FDA of \$108 (wages plus overhead), and based on a total of 13,487 submissions [15,487 minus 2,000], the total potential cost to FDA if labeling for all SKUs was reviewed would be \$ 1,456,596.

15. Explanation of in Item 13 and 14, Changes in Burden

The reporting burden for the OTC labeling final rule has changed from that in the proposal to show that the burden, which was originally attributed to regulations for the filing of supplements and amendments to new drug applications and abbreviated new drug application, is more appropriately attributed to 210.66 (c) and (d). The reporting burden in the final rule also includes separate entries for formatting and filing requests for exemptions and deferrals, which were inadvertently omitted in the proposed rule.

16. Publication of Information Collection Results/Statistical Reporting

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

17. Display of OMB Expiration Date on Form Approval Date

There are no forms associated with this collection.

18. Exceptions to ACertification Statement.

There are no exceptions to the certification statement identified in Item 19, Certification for Paperwork Reduction Act Submission, A of OMB Form 83-I.