SUPPORTING STATEMENT A

Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products (OMB Control Number 0910-0572)

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration's (FDA's) final rule entitled "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" (the final rule), which published on January 24, 2006 (71 FR 3922), and was effective on June 30, 2006, amended FDA's regulations governing the format and content of labeling for human prescription drug and biological products to require that the labeling of new and recently approved products contain highlights of prescribing information, a table of contents for prescribing information, reordering of certain sections, minor content changes, and minimum graphical requirements. These revisions were intended to make it easier for health care practitioners to access, read, and use information in prescription drug labeling, to enhance the safe and effective use of prescription drug products, and reduce the number of adverse reactions resulting from medication errors due to misunderstood or incorrectly applied drug information.

Section 201.56 (21 CFR 201.56) requires that prescription drug labeling contain certain information in the format specified in either § 201.57 (21 CFR 201.57) or § 201.80 (21 CFR 201.80), depending on when the drug was approved for marketing. Section 201.56(a) sets forth general labeling requirements applicable to all prescription drugs.

Section 201.57(a) requires that prescription drug labeling for new and more recently approved prescription drug products include “Highlights of Prescribing Information.” Highlights provides a concise extract of the most important information required under § 201.57(c) (the Full Prescribing Information (FPI)), as well as certain additional information important to prescribers. Section 201.57(b) requires a table of contents to prescribing information, entitled “Full Prescribing Information: Contents,” consisting of a list of each heading and subheading along with its identifying number to facilitate health care practitioners' use of labeling information. Section 201.57(c) specifies the contents of the FPI. Section 201.57(d) mandates the minimum specifications for the format of prescription drug labeling and establishes minimum requirements for key graphic elements such as bold type, bullet points, type size, and spacing.

2. Purpose and Use of the Information Collection

The regulations are part of FDA’s strategic initiative to manage the risks of medical product use and reduce adverse events involving the products that it regulates. The regulations on the content and format of labeling will make it easier for health care practitioners to access, read, and use information in prescription drug labeling, thereby increasing the extent to which they rely on labeling to obtain information. The regulations reflect those that the Agency believes will enhance the safe and effective use of prescription drug products, and in turn, reduce the number of adverse reactions resulting from medication errors due to misunderstood or incorrectly applied drug information. The requirements are important to the success of other initiatives aimed at improving patient care and decreasing the likelihood of medication errors. For example,

the DailyMed, a collaboration between FDA and the National Libarary of Medicine will be an innovative means of disseminating up-to-date and comprehensive medication information electronically for use in information systems that support patient care. The DailyMed will make current information about FDA-regulated products readily available to physicians, other health care practitioners, and patients. In addition, prescription drug labeling in the new format may also be utilized with electronic prescribing systems under development.

3. Use of Improved Information Technology and Burden Reduction

As discussed in this document, the drug product labeling affected by these regulations are submitted to FDA for approval as part of a new drug application (NDA), an abbreviated new drug application (ANDA), a biologics license application (BLA), or a supplement to an application. FDA has undertaken many initiatives to improve information technology used to submit these applications to the Agency.

In the Federal Register of December 11, 2003, FDA issued a final rule amending FDA regulations governing the format in which certain labeling is required to be submitted for review with NDAs, certain BLAs, ANDAs, supplements, and annual reports. The final rule requires the electronic submission of the content of labeling (i.e., the content of the package insert or professional labeling, including all text, tables, and figures) in NDAs, certain BLAs, ANDAs, supplements, and annual reports electronically in a form that FDA can process, review, and archive.

The following guidances for industry have been developed to improve the use of information technology in the submission of marketing applications for human drugs and related reports:

- "Indexing Structured Product Labeling."
- "Providing Regulatory Submissions in Electronic Format - Content of Labeling."
- "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and related Submissions Using the eCTD Specifications."
- "Providing Regulatory Submissions in Electronic Format - General Considerations."
- "Providing Regulatory Submissions in Electronic Format – Postmarketing Individual Case Safety Reports."
- "Providing Regulatory Submissions in Electronic Format - Prescription Drug Advertising and Promotional Labeling."
- "Providing Regulatory Submissions in Electronic Format – Receipt Date."
- "SPL Standard for Content of Labeling Technical Qs and As."

These guidance documents and others are available on FDA's Web site at http://www.fda.gov/drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

4. Efforts to Identify Duplication and Use of Similar Information

The information collection required as a result of these regulations does not duplicate any other information collection.

5. Involvement of Small Businesses or Other Small Entities

Under the Regulatory Flexibility Act, FDA analyzes regulatory options that would minimize any significant impact on small entities. FDA also assists small businesses in complying with regulatory requirements. As discussed in the "Analysis of Impacts" section of the January 24, 2006, final rule, FDA concluded that these regulations would not have a significant impact on most small entities, as defined by the Regulatory Flexibility Act. However, it is possible that a few small firms may be significantly affected.

6. Consequences of Collecting Information Less Frequently

The part of a prescription drug product's approved labeling directed to health care practitioners is the primary mechanism through which FDA and drug manufacturers communicate essential, science-based prescribing information to health care professionals. The primary purpose of prescription drug labeling is to provide practitioners with the essential information they need to prescribe the drug safely and effectively for the care of patients. This purpose would be hindered without the information collection requirements set forth in the regulations.

7. Special Circumstances Relating to the Guidelines in 5 CFR 1320.5

There is no inconsistency with the guidelines in 5 CFR 1320.5.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

As required under section 3506(c)(2)(B) of the Paperwork Reduction Act, FDA provided an opportunity for public comment on the information collection provisions of these regulations in the December 19, 2011, Federal Register (76 FR 78668). FDA received no comments on the information collection estimates.

9. Explanation of Any Payment or Gift to Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents under this rule.

10. Assurance of Confidentiality Provided to Respondents

Confidentiality of the information submitted under these regulations is protected under 21 CFR 314.430, 21 CFR 601, and 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under section 301(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(j)).

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

The PRA information collection analysis in the final rule (71 FR 3964-3967) (currently approved under OMB Control Number 0910-0572) estimated the reporting burden for a multi-year period. We are requesting that OMB extend approval for the

information in this collection, as described below, that will continue to be submitted to FDA during this multi-year period.

Annual Burden for Prescription Drug Labeling Design, Testing, and Submitting to FDA for new NDAs and BLAs (§§ 201.56 and 201.57) (Table 1)

New drug product applicants must: (1) Design and create prescription drug labeling containing Highlights, Contents, and FPI, (2) test the designed labeling (e.g., to ensure that the designed labeling fits into carton-enclosed products), and (3) submit it to FDA for approval. Based on the projected data estimated in the final rule, FDA estimates that it takes applicants approximately 3,349 hours to design, test, and submit prescription drug labeling to FDA as part of an NDA or a BLA under the revised regulations. Approximately 84 applicants submit approximately 105 new applications (NDAs and BLAs) to FDA per year, totaling 351,645 hours.

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

Table 1. – Estimated Reporting Burden For New Drug Applications

Category (21 CFR section)	Number of Respondents	Responses per Respondent	Annual Responses	Hours per Response	Total Hours
Annual Burden for Labeling Requirements in §§ 201.56 and 201.57	84	1.25	105	3,349	351,645
TOTAL:					**351,645**

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

13. Estimates of Total Annual Cost Burden to Respondents

FDA has estimated an average industry wage rate of $50.00 per hour for preparing and submitting the information collection requirements under the regulations. Using the averaged wage rate of $50.00 per hour, and multiplied times the annual burden hours estimated in the tables above, the total cost burden to respondents is $17,582,250 (351,645 hours x $50).

14. Annualized Cost to the Federal Government

Using the estimate of $50.00 per hour as the hourly wage for FDA reviewers to review labeling submissions under the proposal, and estimating that it takes an average of approximately 40 hours to review each of the estimated 105 submissions, the annualized cost to FDA as a result of this proposed rulemaking would be $210,000 (40 hours x 105 submissions x $50).

15. Explanation of Burden Changes or Adjustments

The January 24, 2006, final rule entitled "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" revised the content and format for prescription drug product labeling set forth in 21 CFR 201.56 and 57. This resulted in changes in burden from the information collection in the final rule are the result of reductions in the number of submissions that have occurred because 6 years have expired under the implementation plan. The implementation (See Table 5 of the final rule - specifies when applicants for already-approved drug products must implement the revised labeling) The plan provides a graduated time period by which all drug products approved before the effective date of the final rule must have revised labeling. Because all time periods have passed for implementing the revised labeling (except the June 30, 2013, date which comes early in the new extension period for 0910-0572), FDA only included for this extension request the burden for preparing and submitting the new prescription drug product labeling in drug product applications that FDA expects to receive annually during the upcoming three years.

Table 5 – Implementation Plan

Applications (NDAs, BLAs, and Efficacy Supplements) Required to Conform to New Labeling Requirements	Time by Which Conforming Labeling Must Be Submitted to the Agency for Approval
Applications submitted on or after June 30, 2006	Time of submission
Applications pending on June 30, 2006 and applications approved 0 to 1 year before June 30, 2006	June 30, 2009
Applications approved 1 to 2 years before June 30, 2006	June 30, 2010
Applications approved 2 to 3 years before June 30, 2006	June 30, 2011
Applications approved 3 to 4 years before June 30, 2006	June 30, 2012
Applications approved 4 to 5 years before June 30, 2006	Applications approved 4 to 5 years before June 30, 2006
Applications approved more than 5 years before June 30, 2006	Voluntarily at any time

16. Plans for Tabulation and Publication and Project Time Schedule

There are no publications.

17. Reason(s) Display of OMB Expiration Date Is Inappropriate

The Agency is not seeking to display the expiration date for OMB approval of the information collection.

18. Exception to the Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.