SUPPORTING STATEMENT

Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format – 0910-0530

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting that OMB extend approval under the Paperwork Reduction Act (44 USC 3501-3520) for the information collection resulting from the requirement that the content of labeling for prescription drug products be submitted to FDA electronically in a form that FDA can process, review, and archive. This requirement was set forth in the final rule entitled "Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format" (December 11, 2003; 68 FR 69009), which amended FDA regulations governing the format in which certain labeling is required to be submitted for FDA review with new drug applications (NDAs) (21 CFR 314.50(l)(1)(i)), including supplemental NDAs, abbreviated new drug applications (ANDAs) (21 CFR 314.94(d)(1)(ii)), including supplemental ANDAs, and annual reports (21 CFR 314.81(b)(2)(iii)(b)) (the final rule also applied to certain BLAs, but the information collection for these requirements is not part of this OMB approval request).

2. Purpose and Use of Information Collection

Each year FDA conducts a word-for-word comparison as part of the review process for more than 1,000 proposed labeling changes for approved NDAs and BLAs, and more than 2,600 proposed original and supplemental labeling changes for ANDAs. Because reviewers currently conduct these comparisons manually using two paper copies of the labeling, the process is slow and subject to error. Requiring the electronic submission of labeling for NDAs, certain BLAs, ANDAs, supplements, and annual reports greatly enhances the accuracy and speed of labeling review. This results in increased protection of the public health because electronic review and comparison of labeling files provides a higher degree of certainty that all sections of prescription drug labeling are correct.

3. Use of Improved Information Technology and Burden Reduction

In May 2009, FDA issued a guidance for industry entitled "Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Listing." The guidance describes how to electronically create and submit SPL files using defined code sets and codes for establishment registration and drug listing information, including labeling. This guidance currently covers FDA's preferred process for submitting the content of labeling in electronic format. In addition, FDA has issued other guidances on electronic submissions at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm064994.htm.

4. Efforts to Identify Duplicationand Use of Similar Information

The requirement to submit the content of labeling electronically is in addition to existing requirements that copies of the label and labeling and specimens of enclosures be submitted. However, requiring the electronic submission of the content of labeling greatly enhances the accuracy and speed of labeling review by FDA. This results in increased protection of the public health because electronic review and comparison of labeling files provides a higher degree of certainty that all sections of prescription drug labeling are correct.

5. Impact on Small Businesses or Other Small Entities

Although new drug development is typically an activity completed by large multinational drug firms, the information collection requested under the guidance applies to small as well as large companies. Under the Regulatory Flexibility Act, FDA regularly analyzes regulatory options that would minimize any significant impact on small entities. FDA also assists small businesses in complying with regulatory requirements.

6. Consequences of Collecting the Information Less Frequently

The content of labeling is required to be submitted electronically for review with NDAs, certain BLAs, ANDAs, supplements, and annual reports. FDA's review of

labeling is an integral part of its approval of marketing application for drugs and biologics. The labeling must be consistent with the approved conditions for marketing.

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

There is no inconsistency resulting from this final rule.

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

When we last requested that OMB extend approval for this information collection (see the Federal Register of March 29, 2006 (71 FR 15752)), we received several comments. Generally, the comments said that, unlike FDA's December 11, 2003, final rule, the agency has now identified Extensible Markup Language (XML) as the required file format for Structured Product Label documents (SPL), and that the burden hours and costs that were calculated in the final rule were based on the submission of the content of labeling in PDF. The comments said that the burden estimate in March 29, 2006, Federal Register notice does not take into account the amount of time required to obtain, install, and update the program required to create the electronic files in the new format, and that SPL is a relatively new format requiring an initial investment in software, training, and process change that cannot simply be converted from the Word or PDF version of labeling. The comments said that the process for creating the SPL labeling includes significant effort in mapping, coding, recreation of the file, and quality control.

In the December 13, 2006, Federal Register (71 FR 74924), we said that we will respond to the comments as soon as we have gathered sufficient information to address the costs specified in the comments, and that the public will have an opportunity to comment on the response at that time. The burden hours and costs associated with

making these submissions using the SPL standard are discussed under sections 12 and 13 below.

We published the 60-day notice for this extension request in the Federal Register of November 6, 2009 (74 FR 57491) and we received no comments.

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 guidance.

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 310(j) of the Act.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Hour Burden and Costs

Copies of product labeling have been required to be submitted to FDA for review in NDAs, certain BLAs, ANDAs, certain supplements, and annual reports under §§ 314.50, 314.70, 314.81, 314.94, 314.97, 314.98, 601.2, and 601.12. Under these regulations, copies of labeling may be submitted electronically or on paper. The final rule added the requirement to submit the content of labeling in electronic format to simplify the drug labeling review process and speed up the approval of labeling changes. The reporting burden for submitting labeling under §§ 314.50, 314.70, 314.81, 314.94, 314.97, and 314.98 has been estimated by FDA and the collection of information has

been approved by OMB under OMB control number 0910-0001. The reporting burden associated with current §§ 601.2 and 601.12 has also been estimated and this collection of information has been approved by OMB under OMB control number 0910-0338. We are not re-estimating these approved burdens in this action. Only the additional re-occurring reporting burdens associated with the electronic submission of the content of labeling in the final rule are estimated in this action.

We estimate that it should take applicants approximately 1.25 hours to convert the content of labeling from Word or PDF to SPL format. The main task involved in this conversion is copying the content from one document (Word or PDF) to another (SPL). Over the past few years, several enhancements have been made to SPL authoring software which significantly reduces the burden and time needed to generate well-formed SPL documents. SPL authors may now copy a paragraph from a Word or PDF document and paste the text into the appropriate section of an SPL document. In those cases where an SPL author needs to create a table, the table text may be copied from the Word or PDF document and pasted into each table cell in the SPL document, eliminating the need to retype any information. Enhancements have also been made to the software for conversion vendors. Conversion software vendors have designed tools which will import the Word version of the content of labeling and, within minutes, automatically generate the SPL document (a few formatting edits may have to be made).

Based on the number of content of labeling submissions received during 2006, 2007, and 2008, we estimate that approximately 5,000 content of labeling submissions are made annually with original NDAs, ANDAs, supplemental NDAs and ANDAs, and annual reports by approximately 450 applicants. Therefore, the total annual hours to

convert the content of labeling from Word or PDF to SPL format would be approximately 6,250 hours.

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

Content of labeling submissions in NDAs, ANDAs, supplemental NDAs and ANDAs, and annual reports	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
	450	11.11	5,000	1.25	6,250

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

Costs –

FDA has estimated an average industry wage rate of $75.00 per hour for preparing and submitting the information collection requirements under OMB Control Number 0910-0001. Using the averaged wage rate of $75.00 per hour, and multiplied times the total hour burden estimated above, the total cost burden to respondents is $ 468,750.

13. Estimates of Other Total Annual Cost Burden to Respondents and Recordkeepers

We continue to conclude that there are no capital costs or operating and maintenance costs associated with this collection of information. In May 2009, FDA issued a guidance for industry entitled "Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Listing." The guidance describes how to electronically create and submit SPL files using defined code sets and codes for establishment registration and drug listing information, including labeling. The information collection resulting from this guidance, discussed in the Federal Register of January 8, 2009 (74 FR 816), has been approved by OMB under Control Number 0910-0045. As discussed in the January 8, 2009, Federal Register notice, to create an SPL file and submit it to FDA, a registrant would need the following tools: A computer, appropriate software, access to the Internet, knowledge of terminology and standards, and access to FDA's electronic submission gateway (ESG). Registrants (and most

individuals) have computers and Internet access available for their use. If a business does not have an available computer or access to the Internet, free use of computers and the Internet are usually available at public facilities, e.g., a community library. In addition, there should be no additional costs associated with obtaining the appropriate software. In 2008, FDA collaborated with GlobalSubmit to make available free SPL authoring software that SPL authors may utilize to create new SPL documents or edit previous versions. (Information on obtaining this software is explained in section IV.A of the guidance "Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Listing.") In addition to the software, FDA also provides technical assistance and other resources, code sets and codes, and data standards regarding SPL files.

After the SPL file is created, the registrant would upload the file through the ESG, as explained in the January 8, 2009, Federal Register notice. A digital certificate is needed to use the ESG. The digital certificate binds together the owner's name and a pair of electronic keys (a public key and a private key) that can be used to encrypt and sign documents. A fee of up to $20.00 is charged for the digital certificate and the registrant may need to renew the certificate not less than annually. We are not calculating this fee as a cost for this extension because all applicants who submit content of labeling are also subject to the drug establishment registration and listing requirements and would have already acquired the digital certificate as a result of the May 2009 guidance on drug establishment registration and listing.

14. Annualized Cost Burden to the Federal Government

There are no significant additional FDA reviewer costs resulting from this requirement because the labeling is submitted as part of already required submissions related to the application approval process, as approved under OMB Control Numbers 0910-0001, 0910-0338, and 0910-0572.

15. Explanation for Program Changes or Adjustments

The changes in burden are the result of a re-calculation based on the guidance for industry entitled “Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Listing.”

16. Plans for Tabulation and Publication and Project Time Schedule

There are no publications.

17. Reasons 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 Certification for PRA Submissions

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