Guidance for Industry

Providing Regulatory Submissions in Electronic Format — Content of Labeling

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication of the *Federal Register* notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions on the content of the draft document contact (CDER) Randy Levin, 301-594-5411 or (CBER) Robert Yetter, 301-827-0373.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

February 2004
Electronic Submissions

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Table of Contents

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This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This is one in a series of guidance documents intended to assist applicants making regulatory submissions to the FDA in electronic format. Agency guidance documents on electronic submissions will be updated regularly to reflect the evolving nature of the technology and the experience of those using this technology.

This guidance discusses issues related to the submission of the content of labeling in electronic format for marketing applications for human drug and biologic products, including new drug applications (NDAs), abbreviated new drug applications (ANDAs), and biological license applications (BLAs), except BLAs for Licensed Bloodborne Pathogen Tests for Blood and Blood Components for Transfusion. The *content of labeling* is the labeling required under 21 CFR 201.100(d)(3) including all text, tables, and figures (commonly referred to as the package insert or professional labeling). This guidance applies to the content of labeling provided with original submissions, supplements, and annual reports. Copies of the formatted label and labeling and specimens of enclosures required elsewhere in the regulations (e.g., 21 CFR 314.50(e)(2)(ii)) must still be submitted either electronically in PDF or on paper.

For a list of guidances that are under development on electronic submissions, see the guidance *Regulatory Submissions in Electronic Format — General Considerations*.[2] The general

[1] This guidance has been prepared by the Information Management Program in the Center for Drug Evaluation and Research (CDER).

[2] We update guidances periodically. To make sure you have the most recent version of a guidance, check the CDER guidance page at http://www.fda.gov/cder/guidance/index.htm.

considerations guidance also addresses issues (e.g., appropriate file formats, media, and submission procedures) that are common to all submission types.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. The Electronic Labeling Rule

In December 11, 2003, FDA published a final regulation (the electronic labeling rule) requiring the submission of the content of labeling in electronic format for marketing applications (68 FR 69009). The requirements of the electronic labeling rule can be found in § 314.50(l) for NDAs, § 314.94(d) for ANDAs, § 601.14(b) for BLAs, and § 314.81(b) for annual reports to marketing applications. The effective date of the rule is June 8, 2004. The regulations specify that the content of labeling must be submitted electronically in a form that FDA can process, review, and archive. The regulations also state that FDA will periodically issue guidance on how to provide the electronic submission. This guidance provides information on how to submit the content of labeling in electronic format.

B. New Technology for Processing Labeling and Labeling Changes

The regulations require that the content of labeling be submitted in a form that we can process, review, and archive. Since 1999, FDA has been receiving the electronic content of labeling in Portable Document Format (PDF), and this format has allowed us to process, review and archive the content of labeling. Recently, however, recommendations from the Institute of Medicine and the National Committee on Vital and Health Statistics and mandates in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Public Law 108-173) have created a new role for electronic labeling information. Electronically formatted content of labeling will be used to support health information management technologies such as electronic prescribing and the electronic health record (EHR).

We have determined that our current procedures using PDF are not adequate to support these initiatives. To meet the new mandates, the Agency is proposing to change the way it processes, reviews, and archives the content of labeling. The Agency is proposing to adopt a new technology for exchanging information between computer systems called Clinical Document Architecture (CDA). CDA was developed by Health Level Seven (HL7), an ANSI accredited standards development organization. CDA allows information to be exchanged in extensible markup language (XML) and is the standard being investigated for the EHR.

FDA, working with other interested parties in HL7, has adapted CDA for labeling in a proposed HL7 standard called Structured Product Labeling (SPL). When compared with PDF, SPL exhibits the following advantages.

- SPL allows the exchange of information between computer systems (for example, to support the patient safety initiatives) in a way that cannot be accomplished with PDF.
- The exchange of labeling changes with SPL can be easier and more efficient for both FDA and manufacturers when compared with PDF. For example, with SPL, only those sections or data elements of the labeling that are changed would need to be submitted rather than the complete labeling.
- SPL allows the comparison of text and specific data elements.
- SPL can also be used to exchange information needed for other submissions, such as drug listing, thus eliminating redundant data collection and improving efficiency.

The Agency is developing an automated system using SPL for processing and managing labeling and labeling changes. When this draft guidance is finalized, absent significant objections, FDA is likely to identify SPL in public docket number 92S-0251 as a format that we can use to process, review, and archive the content of labeling. During our transition to the automated system, the Agency would be able to accept the content of labeling in either PDF or SPL file format. After the automated system is implemented, PDF would no longer be a format that we can use to process, review, and archive the content of labeling. At this time, it is our goal to complete the transition to SPL format for content of labeling submissions by the end of 2004.

III. GENERAL ISSUES

This guidance applies to the content of labeling required for any marketing application (ANDAs, BLAs, NDAs) submission required to be submitted in electronic format under §§ 314.50(l) 314.81(b), 314.94(d), and 601.14(b).

A. File Formats for Providing Content of Labeling

The content of labeling can be provided in PDF or SPL file format.

This guidance describes how to submit the content of labeling using XML based on the HL7 SPL specifications.

For information on how to submit the content of labeling using PDF based on the Adobe Systems Incorporated specifications, see the current Agency guidance on providing regulatory submissions in electronic format.[3]

[3] See the guidances for industry entitled *Providing Regulatory Submissions in Electronic Format — NDAs* and *Providing Regulatory Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format — Biologics Marketing Applications*. To make sure you have the most recent version of a guidance, check

B. Creating the Content of Labeling File

See the HL7 published specifications for Structured Product Labeling (SPL) for details on how to create the content of labeling file. The SPL specifications are available on the Internet at http://hl7.org/lib_admin/docs.cfm?dir=library\committees\clinicaltrials&comm=rcrim. For submission of labeling changes, you should only submit the labeling sections or data elements that have changed.

C. Sending the Submissions

If you are providing the content of labeling as part of an electronic submission, you should follow the appropriate Agency guidance document for sending in the submission. If you are providing the content of labeling with a paper submission, see current Agency guidance on providing regulatory submissions in electronic format.[4] All submissions must be sent to the appropriate central document room facilities as required under 21 CFR part 11. Electronic documents that are sent directly to division document rooms or to reviewers bypass the controls established for the receipt and archiving of documents and, therefore, are not considered valid documents for review.

D. Technical Problems or Questions

If you have any questions on technical issues related to providing the content of labeling in submissions according to the recommendations in this guidance, contact the appropriate electronic submission coordinator at esub@cder.fda.gov or esubprep@cber.fda.gov. Specific questions pertaining to content should be directed to the appropriate review division or office.

IV. ORGANIZING THE MAIN SUBMISSION FOLDER

The content of labeling SPL file should be placed in a single folder titled *SPL*.

If the content of labeling in SPL is provided with an electronic submission, you should place the file in the appropriate folders. For additional information on organizing the submission folder in an electronic submission, see current Agency guidance on providing regulatory submissions in electronic format.[5]

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the CDER guidance page at http://www.fda.gov/cder/guidance/index.htm or the CBER guidance page at http://www.fda.gov/cber/guidelines.htm.

[4] See footnote 3.

[5] See footnote 3.