
Guidance for Industry

Providing Regulatory Submissions in Electronic Format — Content of Labeling

DRAFT GUIDANCE

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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should be submitted within 60 days of publication of the *Federal Register* notice announcing the availability of the draft guidance.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*.

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**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**

Guidance for Industry

Providing Regulatory Submissions in Electronic Format — Content of Labeling

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Center for Biologics Evaluation and Research (CBER)**

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8 This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current
9 thinking on this topic. It does not create or confer any rights for or on any person and does not operate to
10 bind FDA or the public. You can use an alternative approach if it satisfies the requirements of the
11 applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff
12 responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the
13 appropriate number listed on the title page of this guidance.
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18 **I. INTRODUCTION**
19

20 This is one in a series of guidance documents intended to assist applicants making regulatory
21 submissions to the FDA in electronic format. Agency guidance documents on electronic
22 submissions will be updated regularly to reflect the evolving nature of the technology and the
23 experience of those using this technology.
24

25 This guidance discusses issues related to the submission of the content of labeling in electronic
26 format for marketing applications for human drug and biologic products, including new drug
27 applications (NDAs), abbreviated new drug applications (ANDAs), and biological license
28 applications (BLAs), except BLAs for Licensed Bloodborne Pathogen Tests for Blood and Blood
29 Components for Transfusion. The *content of labeling* is the labeling required under 21 CFR
30 201.100(d)(3) including all text, tables, and figures (commonly referred to as the package insert
31 or professional labeling). This guidance applies to the content of labeling provided with original
32 submissions, supplements, and annual reports. Copies of the formatted label and labeling and
33 specimens of enclosures required elsewhere in the regulations (e.g., 21 CFR 314.50(e)(2)(ii))
34 must still be submitted either electronically in PDF or on paper.
35

36 For a list of guidances that are under development on electronic submissions, see the guidance
37 *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>.

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

40
41 FDA's guidance documents, including this guidance, do not establish legally enforceable
42 responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should
43 be viewed only as recommendations, unless specific regulatory or statutory requirements are
44 cited. The use of the word *should* in Agency guidances means that something is suggested or
45 recommended, but not required.

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48 **II. BACKGROUND**

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50 **A. The Electronic Labeling Rule**

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52 In December 11, 2003, FDA published a final regulation (the electronic labeling rule) requiring
53 the submission of the content of labeling in electronic format for marketing applications (68 FR
54 69009). The requirements of the electronic labeling rule can be found in § 314.50(l) for NDAs, §
55 314.94(d) for ANDAs, § 601.14(b) for BLAs, and § 314.81(b) for annual reports to marketing
56 applications. The effective date of the rule is June 8, 2004. The regulations specify that the
57 content of labeling must be submitted electronically in a form that FDA can process, review, and
58 archive. The regulations also state that FDA will periodically issue guidance on how to provide
59 the electronic submission. This guidance provides information on how to submit the content of
60 labeling in electronic format.

61

62 **B. New Technology for Processing Labeling 63 and Labeling Changes**

64

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

74

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

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

- 86
- 87 • SPL allows the exchange of information between computer systems (for example, to
88 support the patient safety initiatives) in a way that cannot be accomplished with PDF.
 - 89 • The exchange of labeling changes with SPL can be easier and more efficient for both
90 FDA and manufacturers when compared with PDF. For example, with SPL, only those
91 sections or data elements of the labeling that are changed would need to be submitted
92 rather than the complete labeling.
 - 93 • SPL allows the comparison of text and specific data elements.
 - 94 • SPL can also be used to exchange information needed for other submissions, such as drug
95 listing, thus eliminating redundant data collection and improving efficiency.
- 96

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

105

106

107 **III. GENERAL ISSUES**

108

109 This guidance applies to the content of labeling required for any marketing application (ANDAs,
110 BLAs, NDAs) submission required to be submitted in electronic format under §§ 314.50(l)
111 314.81(b), 314.94(d), and 601.14(b).

112

113

113 **A. File Formats for Providing Content of Labeling**

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

116

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

119

120 For information on how to submit the content of labeling using PDF based on the Adobe
121 Systems Incorporated specifications, see the current Agency guidance on providing regulatory
122 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

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123 **B. Creating the Content of Labeling File**

124
125 See the HL7 published specifications for Structured Product Labeling (SPL) for details on how
126 to create the content of labeling file. The SPL specifications are available on the Internet at
127 http://hl7.org/lib_admin/docs.cfm?dir=library\committees\clinicaltrials&comm=rcrim. For
128 submission of labeling changes, you should only submit the labeling sections or data elements
129 that have changed.

130 131 **C. Sending the Submissions**

132
133 If you are providing the content of labeling as part of an electronic submission, you should
134 follow the appropriate Agency guidance document for sending in the submission. If you are
135 providing the content of labeling with a paper submission, see current Agency guidance on
136 providing regulatory submissions in electronic format.⁴ All submissions must be sent to the
137 appropriate central document room facilities as required under 21 CFR part 11. Electronic
138 documents that are sent directly to division document rooms or to reviewers bypass the controls
139 established for the receipt and archiving of documents and, therefore, are not considered valid
140 documents for review.

141 142 **D. Technical Problems or Questions**

143
144 If you have any questions on technical issues related to providing the content of labeling in
145 submissions according to the recommendations in this guidance, contact the appropriate
146 electronic submission coordinator at esub@cderr.fda.gov or esubprep@cber.fda.gov. Specific
147 questions pertaining to content should be directed to the appropriate review division or office.

148 149 150 **IV. ORGANIZING THE MAIN SUBMISSION FOLDER**

151
152 The content of labeling SPL file should be placed in a single folder titled *SPL*.

153
154 If the content of labeling in SPL is provided with an electronic submission, you should place the
155 file in the appropriate folders. For additional information on organizing the submission folder in
156 an electronic submission, see current Agency guidance on providing regulatory submissions in
157 electronic format.⁵

158

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.