

(Response) The agency did not intend to restrict the voluntary submission of labeling in electronic format. Under part 11, an applicant may submit labeling in electronic format as long as the controls in part 11 are met and the labeling is listed in public docket number 92S-0251.⁷ Because the agency has listed labeling in conjunction with NDAs, BLAs, and ANDAs in public docket number 92S-0251, applicants may submit all labeling for an NDA, BLA, or ANDA in electronic format.

(Comment 10) Two comments suggested that the electronic submission of labeling submitted with annual reports under § 314.81 should be optional if the product's labeling has not been revised beyond editorial changes. The comments noted that the labeling revisions to older products are infrequent and often insubstantial in nature; therefore, the submission of annual report labeling is not justified by the objectives of this rule.

(Response) FDA disagrees that the electronic submission of labeling in the annual report is not justified by the objectives of the final rule. The labeling submitted with the annual report, aside from editorial corrections, can also include other changes related to the manufacturing of the product. As with other labeling changes, these changes must be reviewed and require the same degree of comparison with previous versions of labeling. In addition, the labeling changes described in the annual report must be included in FDA's database. Finally, it is important to note that in our economic analysis, we found that the one-time costs to convert the labeling in annual reports to electronic format would not be overly burdensome (see section VIII of this document). Accordingly, the electronic submission of labeling submitted with annual reports under § 314.81 is not optional.

C. Reviewer Support and Training

(Comment 11) Some comments expressed concern that reviewers will accept "special requests" to receive the labeling in paper format or other formats to bypass existing agency guidance on electronic submissions. These same comments emphasized the importance of training and support of reviewers and

staff in the use of electronic review and version comparison utilities.

(Response) FDA agrees that reviewers should not "bypass" our guidance documents. We train reviewers and managers on the details and provisions of guidance documents. When there are differences in opinion concerning the meaning of such provisions, it is best for the applicant and agency personnel to discuss those differences to ensure that everyone understands the relevant issues and the parties' respective positions. In addition, we will update our specific policy and procedure documents for reviewers to help enforce the common practice of reviewing documents electronically. The reviewers and staff will have sufficient training and support to fulfill their duties in reviewing the electronic version of the content of labeling.

(Comment 12) One comment pointed out that the Office of Generic Drugs (OGD) has limited experience with electronic labeling because it has only recently published guidance on providing an ANDA in electronic format.⁸ The comment recommended that OGD pilot a program with industry to accept and process electronic labeling before the effective date of this rule.

(Response) FDA does not believe a pilot program is necessary to prepare OGD reviewers for the implementation of this rule. OGD reviewers used the electronic label review technology for many years before the issuance of the guidance on electronic submissions of ANDAs⁹ and; therefore, have adequate experience in this area.

D. Requiring Electronic Submission

(Comment 13) The comments were overwhelmingly supportive of requiring the electronic submission of the content of labeling. The comments commend FDA's goal of using electronic labeling to facilitate labeling reviews. However, a few comments suggested that the agency use appropriate metrics for tracking the gains associated with the electronic submission of labeling.

(Response) The agency agrees with the comment, and notes that, as explained in section II.A of the proposed rule, there will be numerous benefits from the regulation, particularly through enhancing the accuracy and speed of the labeling review process. Nevertheless, it may be difficult to quantify precisely the improvements derived solely from receiving labeling in electronic format because we also plan

to improve our current business practice for processing and reviewing such labeling changes. To the extent possible, we plan to evaluate the success of all these changes and hope to make the results of our evaluations available to the public.

(Comment 14) A few comments suggested that the implementation of the rule would improve the availability of labeling to the public.

(Response) We believe that a number of changes are needed to improve the public's access to medication information. This rule is an important and necessary step toward that goal, because it will greatly enhance the accuracy and speed of labeling reviews. We are actively working with the pharmaceutical industry, other government agencies, and health care information suppliers to achieve success in this area. For example, we are currently working with several agencies, including the National Library of Medicine, on an initiative to promote patient safety through accessible medication information (DailyMed Initiative). The electronic submission of the content of labeling will allow the agency to provide the DailyMed system with labeling in a comprehensive, reliable, and structured format. The DailyMed can then use this information to make information on medications available to the public. Consumers, health professionals, and others may use this information in several ways, including to identify drug interactions, contraindications, and possible adverse reactions.

(Comment 15) Some comments suggested that the use of electronic labeling may lead to improvement in the communication between the agency and industry when the review division requests modifications for proposed labeling changes. Specifically, the comments referred to word processing software available for tracking changes and editing documents. In addition, the comments suggested that the use of a secure electronic mail exchange system between applicants and the agency during labeling negotiations could be beneficial.

(Response) We appreciate the suggestion and our guidance document entitled "Providing Regulatory Submissions in Electronic Format—NDAs," currently describes submission of the content of labeling in a word processing format in addition to PDF to support editing changes. As mentioned in the proposed rule, PDF is the only type of electronic file format that we have the ability to process, review, and archive because it is currently the most cost effective and best meets our needs

⁷ A recent draft guidance issued by the agency provides for the exercise of enforcement discretion with respect to the following part 11 requirements: Validation (§ 11.10(a) (21 CFR 11.10(a))); copies of records § 11.10(b)); record retention (§ 11.10(c)); audit trails (§ 11.10(e) and (k)(2)); and any corresponding requirements in § 11.30. See FDA guidance for industry entitled "Part 11, Electronic Records; Electronic Signatures—Scope and Application," available at www.fda.gov/cder/guidance.

⁸ See "Providing Regulatory Submission in Electronic Format—ANDAs" guidance (67 FR 43331, June 27, 2002).

⁹ Id.