

for word-for-word comparisons of files. As for any direct communication between applicants and FDA requiring the editing of specific content of labeling, the guidance notes the utility of also submitting labeling in word processing format to facilitate this editing process. In addition, we are looking into new technologies to improve the methods for exchanging and reviewing labeling changes.

#### *E. Providing Labeling to FDA in Electronic Format*

(Comment 16) Two comments requested clarification on how to provide labeling with annual reports. They state that some of the confusion with the annual report labeling is because of the lack of a published guidance document on the submission of annual reports in electronic format. The comments also asked if the hard copy information submitted with annual reports containing electronic labeling (distribution, chemistry, manufacturing and controls, preclinical/clinical) should be submitted to the respective reviewing divisions, the central document room, or both.

(Response) As explained previously, the agency has issued guidance for the electronic submission of NDAs, ANDAs, and BLAs. Although there is no published guidance specifically on providing labeling with annual reports, submission of that labeling is covered by these other agency guidance documents on electronic submissions. Therefore, the content of labeling submitted with annual reports would be prepared and submitted electronically as described in the following FDA guidance documents: (1) "Providing Regulatory Submissions in Electronic Format—General Considerations," (2) "Providing Regulatory Submissions in Electronic Format—NDAs," and (3) "Providing Regulatory Submission in Electronic Format—ANDAs" (see section I for a description of these guidance documents).

It should be noted that this final rule only applies to the electronic submission of the content of labeling. It does not address the electronic submission of annual reports generally or any other part of an application. To the extent that the commenters asked for more detailed information about annual report submissions, applicants should continue following the regulations and guidance documents pertaining to those submissions.

(Comment 17) One comment requested harmonization of all elements of annual reports for NDAs, ANDAs, and BLAs.

(Response) As noted previously, the content of the annual report, other than labeling, is not affected by this regulation. However, the labeling submitted with an annual report will be prepared and submitted electronically in the same fashion as described for other electronic labeling submissions in an application (i.e., original labeling submissions in an NDA, ANDA, or BLA).

(Comment 18) One comment requested that Form FDA 2567 not be required with each labeling component submitted to a BLA because CDER does not require that such a form accompany labeling.

(Response) The agency agrees that Form FDA 2567 is not required when submitting BLA labeling electronically using form 356h (Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use). The form should only be used for human blood and blood components (The human blood and blood components circular is not covered by this rule. See comment 6 in section III of this document.)

(Comment 19) Generally, the comments supported our flexible approach regarding the acceptable content of labeling file format. The comments recognized that a flexible approach would enable the industry and FDA to take advantage of future improvements in computer technology and software design. They also agreed with the proposal to describe the method for submitting the content of labeling in guidance, but requested that FDA guidance accompany the final rule. Some comments, however, made suggestions for the use of specific technologies. In addition, we were requested to limit changes to the file format or software specifications.

(Response) Currently, guidance on the submission of labeling is included in the guidance for industry series "Providing Regulatory Submissions in Electronic Format" (see section I of this document). We understand that changes to the file format or software can lead to costly changes in the information technology systems used by industry. For this reason, we plan to limit future changes to those that can lead to increased benefits for both the agency and industry. As mentioned in section II of this final rule, the agency will not switch to new format or software until it is widely available.

(Comment 20) One comment asked that we identify the software used for working on an applicant's labeling (e.g., to compare texts) and whether the software is commercially available or proprietary.

(Response) Currently, the reviewers use Adobe Acrobat and Microsoft Word for reviewing labeling. Both are commercially available. As new technology is developed and we change the software used in reviews, we will make this information available to the public.

#### *F. Part 11 Requirements for Electronic Submissions*

(Comment 21) We received a number of comments related to the proposed exemption of the submission of electronic labeling from specific controls under §§ 11.10 and 11.30. Most of the comments were positive and supported the rationale for the exemptions. One comment, however, raised concerns about the effect of the proposed exemptions from part 11 requirements on the integrity of part 11 generally.

(Response) We have recently articulated our current thinking on part 11 in the draft guidance document entitled "Part 11, Electronic Records; Electronic Signatures—Scope and Application" (part 11 draft guidance) issued in the **Federal Register** of February 25, 2003 (68 FR 8775). Among other things, this part 11 draft guidance announces the agency's intent to exercise enforcement discretion in the manner specified in the draft guidance with respect to the specific part 11 requirements of validation (§ 11.10 (a)), copies of records (§ 11.10(b)), record retention, audit trails (§ 11.10(e) and (k)(2)), and any corresponding requirements in § 11.30. This final rule exempts the electronic submission of labeling content from the requirements of § 11.10(a), (c) through (h), and (k), and the corresponding requirements of § 11.30.

We recognize that there are some differences with respect to the exemptions from part 11 requirements provided in this final rule (i.e., § 11.10(a), (c) through (h), and (k), and the corresponding requirements of § 11.30), and the part 11 requirements set forth in the part 11 draft guidance for which the agency intends to exercise enforcement discretion (i.e., § 11.10(a) through (c), (e), and (k)(2), and any other corresponding requirements in 11.30)). Although the final rule does not provide an exemption from § 11.10(b), the part 11 draft guidance announces that we intend to exercise enforcement discretion with respect to that section in the manner described in the draft guidance.

The exemptions in the final rule and the part 11 requirements for which we intend to exercise enforcement discretion, as described in the part 11