

a proposed rule (the proposed rule for records and reports) to revise § 510.300 (21 CFR 510.300) and to redesignate it as § 514.80 (21 CFR 514.80). This regulation implements section 512(l) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360b(l)) which provides that, following approval of an NADA or ANADA, applicants must establish and maintain records and make reports to the agency as prescribed by regulation or order. We (FDA) proposed the revision in order to more clearly define the kinds of information to be maintained and submitted by the applicant and to revise the timing and content of certain reports to enhance the usefulness of the information.

After considering comments submitted in response to the proposed rule for records and reports, FDA adopted the rule in modified form in an interim final rule. The scope and coverage of the interim final rule differed in some respects from the proposed rule for records and reports. The proposed rule for records and reports covered NADAs, ANADAs, and medicated feed applications (MFAs). In contrast, the interim final rule covered only NADAs and ANADAs. The Animal Drug Availability Act of 1996 (ADAA) (21 U.S.C. 360b(a) and (m)) amended the statutory provisions in the act regarding medicated feeds and eliminated MFAs. Therefore, the interim final rule did not address MFAs. However, the interim final rule retained reporting requirements for adverse drug experiences (ADEs) with feeds incorporating approved Type A medicated articles.

While the proposed rule for records and reports proposed to remove 21 CFR 510.310, which addressed records and reports for new animal drugs approved before June 20, 1963, we issued a final rule that revoked this provision in response to the Administration's "Reinventing Government Initiative" (61 FR 37680, July 19, 1996). The proposed rule for records and reports followed a style and format similar to the human drug records and reports regulations in part 314 (21 CFR part 314). The interim final rule maintained a similar style and format, but removed many of the proposed records and reports requirements that are not necessary to monitor animal drugs.

In response to initial concerns over duplicate reporting, FDA had removed proposed § 514.82 from the interim final rule, which concerned records and reports from manufacturers, packers, labelers, and distributors other than the applicant. However, the agency did retain certain record and report requirements for nonapplicants (defined

in new § 514.3) (21 CFR 514.3)) and in § 514.80(b) of the interim final rule. Under § 514.80(b)(3), nonapplicants must submit reports of adverse events to applicants and, if they choose, also to FDA. FDA requires such reports under the authority of sections 501 and 701 of the act (21 U.S.C. 351 and 371) and section 512(l) of the act. Keeping track of such reports helps the agency assure that the new animal drug meets the requirements of the act as to safety as required by section 501. Additionally, section 512(l) requires applicants to report adverse events that the applicant has "received or otherwise obtained." In this instance, FDA is requiring that the applicant "receive" reports from other parties that are listed on the label by requiring that the nonapplicants give the reports to the applicants. For purposes of clarity, the agency also made some changes to the text and organization of the interim final rule.

On February 4, 2002, the interim final rule on ADE records and reports was published in the **Federal Register** with an effective date of August 5, 2002 (67 FR 5046). In the **Federal Register** of July 31, 2002 (67 FR 49568), the effective date of the interim final rule published at 67 FR 5046 was delayed indefinitely. We received and reviewed 33 comments on the interim final rule from 4 commenters. In response to those comments, the agency is withdrawing the interim final rule published February 4, 2002 (67 FR 5046) and issuing this final rule.

## II. Comments on the Interim Final Rule

The agency received four sets of comments on the interim final rule for records and reports, three from industry associations, and one from a pharmaceutical company. A discussion of the comments and our response follows. In the interest of clarity, the comments are addressed by relevant section of the rule, with general comments following.

### A. Definition of Adverse Drug Experience (§ 514.3)

(Comment 1) One comment suggested that the definition of "Adverse Drug Experience" be changed from "Failure of a new animal drug to produce its expected pharmacological or clinical effect (lack of effectiveness)" to "Unusual failure of a new animal drug to produce its expected pharmacological or clinical effect (lack of effectiveness)." The comment states that it is the unusual failure to respond to therapy that is of concern. The agency stated in comment 7 of the preamble to the interim final rule that failures to respond to therapy were expected. The

comment responded "that current product labeling does not usually address efficacy failures." According to the comment, a failure not listed on the label would be considered unexpected and thus must be a 15-day NADA/ANADA alert report.

FDA agrees with the comment and does not intend for all effectiveness failures to be defined as ADEs. To this end, FDA will clarify the definition by changing the phrase "expected pharmacological or clinical effect (lack of effectiveness)" to "expected pharmacological or clinical effect (lack of expected effectiveness)." FDA also will continue to work with applicants and provide advice to applicants in determining reportable events. For example, consider a drug that is expected to cure 80 percent of the animals treated, but cures 90 percent. While there is still a 10 percent failure rate, the success rate is above the expected rate of 80 percent; therefore, this is not a reportable ADE. However, if a drug is expected to cure 80 percent of the animals treated, but cures only 40 percent, which is a 60 percent failure rate and below the expected rate, a reportable ADE has occurred. This would be reported as a 15-day NADA/ANADA alert report since it is an unexpected ADE.

### B. Definition of Applicant (§ 514.3)

(Comment 2) One comment suggested that the definition of "Applicant" be changed from "Applicant is a person who owns a new animal drug application or ANADA" to "Applicant is a person who holds a new animal drug application or an ANADA." The comment explained that the actual owner of an application may be different from the sponsor of the application. It may be a parent company with the U.S. company being the sponsor. The comment agreed with the agency's statement in the preamble to the interim final rule that the term "applicant is limited to the holder of an approved application (NADA or ANADA) \* \* \*."

The agency will revise the definition of "applicant" in § 514.3 as follows:

"*Applicant* is a person or entity who owns or holds on behalf of the owner the approval for an NADA or an ANADA, and is responsible for compliance with applicable provisions of the act and regulations."