

“*Serious adverse drug experience* is an adverse event that is fatal, or life-threatening, or requires professional intervention, or causes an abortion, or stillbirth, or infertility, or congenital anomaly, or prolonged or permanent disability, or disfigurement.”

E. Definition of Unexpected Adverse Drug Experience (§ 514.3)

(Comment 9) One comment suggested that FDA change the definition of “Unexpected drug experience” from “an adverse event that is not listed in the current labeling for the new animal drug,” to “an adverse event that is not listed in the current labeling for the new animal drug or reported in its Freedom of Information Summary(ies).” The comment highlighted the inclusion of the NADA file in the current rule’s definition of “unexpected drug experience” and that those incidences referenced in the NADA file may not be captured on the label. Therefore, there is concern that this change from the current § 510.300(b)(2)(i) will increase the number of reports to the NADA file. There is also a concern that this would increase FDA’s workload for labeling changes, especially for Type A medicated articles and OTC products. The comment maintained that it is inappropriate for FDA to exclude the NADA file, and include only the current label, from the definition since the freedom of information summary of the NADA file is publicly available. The comment further stated that it is inappropriate since the applicant is the primary source of the ADE and is responsible for determining if the report is unexpected.

We disagree with the comment. Although the freedom of information summary is a publicly available document, it is neither a practical substitute for a label, nor is it widely distributed and available with the label.

(Comment 10) One comment posed a scenario where an ADE is commonly recognized and not on the current label. It suggested that since the ADE is commonly recognized, it should be expected by FDA. The comment asked for the agency’s expectation/position on this scenario.

FDA requires that recognized ADEs be on the label. It is the position of the Center for Veterinary Medicine (CVM) that any serious, unexpected ADE be reported under § 514.80(b)(2).

F. Applicability of Records and Reports Concerning Experience With Approved New Animal Drugs (§ 514.80(a)(1))

(Comment 11) One comment objected to the requirement of “separate” filing systems in the sentence “Each applicant

and nonapplicant must establish and maintain indexed, separate, and * * *

The comment stated that this is a new requirement not present in the proposed rule for records and reports and it is not in § 514.300(a). Further, the comment argued that it is the applicant’s decision to determine whether files are stored separately or as part of another filing system. The comment requested an explanation for this change, and proposed that the word “separate” be deleted.

It was not FDA’s intention to make the determination as to whether files are stored separately or as part of another filing system. During FDA’s review of comments on the proposed rule for records and reports concerning duplicate reporting, it was determined that the proposed § 514.82 (nonapplicant) information should be combined with proposed § 514.80 (applicant) information. The use of the word “separate” in this sentence was FDA’s attempt to combine the information from proposed § 514.82 with § 514.80. Unfortunately, the combined verbiage has led to this unintended reading by the commenter. Also, it was not FDA’s intention that nonapplicants “establish and maintain indexed, separate, and complete files containing full records of all information * * * of a new animal drug * * *

It is the intention of FDA that nonapplicants “establish and maintain indexed, separate, and * * *

of only the information that they receive or otherwise obtain. Therefore, FDA has separated requirements for applicants from requirements for nonapplicants in order to clarify the meaning.

(Comment 12) One comment proposed that the clause “* * * that has not been previously submitted as part of the NADA or ANADA” be changed to “* * * that has not been previously submitted as part of an investigational new animal drug (INAD) file, the NADA or ANADA.” The comment expressed concern that the studies/information submitted to the INAD would be excluded from the exemption of being “previously submitted” until the sponsor incorporated the information by reference into the NADA/ANADA file.

FDA believes that changing the regulation to include INADs is outside the scope of this regulation. The scope of records and reports is for experiences with approved new animal drugs, not investigational uses. The consequences of adding INADs to this regulation would be that applicants of INADs would have to submit the information and data under § 514.80. Therefore, FDA

will not change the regulation to include INADs.

The following is the change to (§ 514.80(a)(1)):

(a) *Applicability.* (1) Each applicant must establish and maintain indexed and complete files containing full records of all information pertinent to safety or effectiveness of a new animal drug that has not been previously submitted as part of the NADA or ANADA. Such records must include information from domestic as well as foreign sources.

Each nonapplicant must establish and maintain indexed and complete files containing full records of all information pertinent to safety or effectiveness of a new animal drug that is received or otherwise obtained by the nonapplicant. Such records must include information from domestic as well as foreign sources.

G. Three-Day NADA/ANADA Field Alert Report (§ 514.80(b)(1))

(Comment 13) One comment asked what district office should be notified for 3-day NADA/ANADA field alert reports for U.S.-approved products that are manufactured outside of the United States.

Applicants should contact their FDA district office to determine the procedure for reporting 3-day alerts.

H. Fifteen-Day NADA/ANADA Alert Report (§ 514.80(b)(2))

(Comment 14) One comment opposed the use of the terminology “regardless of source of the information” in the reporting requirement for 15-day NADA/ANADA alert reports. The comment stated that “regardless of source” is overly broad. According to the comment, an ADE found by an employee of the company while browsing a chat room on the Internet would have to be reported to FDA. The comment also expressed concern that serious adverse events outside the United States be reported to FDA within 15 days.

The phrase “regardless of source” was added to emphasize that the agency wanted all reports of ADEs. A legitimate source is an identifiable reporter, an identifiable product, and one or more ADEs in animals or humans, regardless of whether the source is the Internet. If the event is a serious, unexpected adverse drug event then it must be reported in a 15-day NADA/ANADA alert report. All domestic and foreign ADEs for the U.S.-approved application should be submitted under § 514.80(b)(2) or (b)(4)(iv).

(Comment 15) One comment requested that FDA elaborate on the requirement of submission of reports of ADEs from foreign sources as it relates to § 514.80(a)(2). The comment stated that this requirement is not consistent