

local office communications required by paragraph (b)(4) of this section; and all local office compliance, supervisory, and procedures manuals required by paragraph (e)(6) of this section.

(2) The capability of electronically displaying and immediately producing printed copies of the local office records described herein in a local office will be deemed to comply with the local office record maintenance requirements of this section. This capability shall not be deemed to supersede paragraph (f) of this section.

(3) With respect to a single-agent office of a member, broker or dealer, local office records may be aggregated with the records of one or more other such offices in a regional record depository if the following requirements are met:

(i) The regional record depository, which may be another office of the member, broker or dealer, is located within the same state as the single-agent office.

(ii) The records stored in the regional record depository can be easily disaggregated and accessed for the single-agent office to the same extent as if the single-agent office kept separate records in compliance with the local office record-keeping requirements of this section.

(m) When used in this section:

(1) The term *associated person* shall have the meaning set forth in § 240.17a-3(f)(1).

(2) The term *local office* shall have the meaning set forth in § 240.17a-3(f)(2).

(3) The term *principal* shall have the meaning set forth in § 240.17a-3(f)(3).

(4) The term *securities regulatory authority* shall have the meaning set forth in § 240.17a-3(f)(4).

Dated: October 22, 1996.

By the Commission.

Margaret H. McFarland,

Deputy Secretary.

Exhibit A

(Note: This Exhibit will not appear in the Code of Federal Regulations)

*Model State Regulation Governing Access to Records Required To Be Kept By Broker-Dealers (Prepared by NASAA)*

#### I. Required Books and Records.

Every broker-dealer registered in this State shall comply with the record-keeping requirements of 17 CFR 240.17a-3 (hereinafter "Rule 17a-3") and 17 CFR 240.17a-4 (hereinafter "Rule 17a-4"), promulgated under the Securities Exchange Act of 1934.

#### II. Access to Records.

##### (a) Duty to produce.

All records required to be maintained shall be kept within the possession and control of the broker-dealer, except as permitted in section (e) below with respect to a broker-

dealer that has ceased transacting business in securities or that has terminated its registration. All records within the possession or control of a broker-dealer shall be produced to [the Administrator] or [the Administrator's] designee upon request. Every broker-dealer shall ensure that each office makes available to [the Administrator] or [the Administrator's] designee all local office records required by Rules 17a-3 and 17a-4.

##### (b) Time in which to produce.

It is the responsibility of each broker-dealer to make all required records quickly and easily accessible. Whenever records are required to be produced by this rule, the time limits set forth in this subparagraph shall control. When requested records are present on the premises of a broker-dealer, including paper records in a local office and electronic records retrievable over a computer terminal, they shall be produced immediately. When requested records are not present on the premises, such as microfilm in a central storage location outside this State, they shall be produced no later than the third business day after the date of the request. For good cause shown in writing, such as the unusually large scope of a request requiring production of a large volume of records, [the Administrator] may extend the time period for production.

##### (c) Forms of record retention; duty to organize.

Every broker-dealer shall ensure that all records required to be maintained shall be organized and made available for examination in one of the forms specified in Rules 17a-3 and 17a-4. Such records shall be authentic, accurate, legible, complete, and current (where a record requires updating). They shall be organized in a systematic and easily recognized order, such as chronologically or alphabetically, and they shall be easily accessible and readily explained. Each broker-dealer shall without delay make available to [the Administrator] or [the Administrator's] designee an individual who is familiar with the records (or type of records) and qualified to explain them. In the case of any records that require equipment to allow review or copying, the broker-dealer shall immediately make available such equipment in working order to the office that has responsibility to maintain the records.

##### (d) Duty to cooperate.

Every broker-dealer and broker-dealer employee shall cooperate with efforts by the [the Administrator] or [the Administrator's] designee to review for compliance with this regulation. [The Administrator] or [the Administrator's] designee may conduct announced or unannounced examinations at any office within or outside this State to review the business activities of the broker-dealer. Every broker-dealer shall furnish access to all areas of its securities operations conducted on or off the premises and otherwise facilitate the examination. [The Administrator] or [the Administrator's] designee may further require that any records subject to examination by submitted [the Administrator's] agency to determine compliance with applicable laws and regulations.

##### (e) Miscellaneous records.

Every broker-dealer shall make available for examination all records in its possession or control that are in any way related to its business or that may lead to evidence pertaining to its business regardless of whether or not routine maintenance of such records is required by this regulation or Rules 17a-3 and 17a-4. Such records which are not in the immediate possession of the broker-dealer but which the broker-dealer has the ability to obtain must be obtained and produced [the Administrator] or [the Administrator's] designee on request, unless such records are equally available to [the Administrator].

##### (f) Privileged records.

If, in response to a request for records by [the Administrator] or [the Administrator's] designee during an examination or investigation, a broker-dealer refuses to produce any record on a claim of privilege, each such document must be identified in detail and the specific privilege identified as to each item. An assertion of privilege does not excuse a broker-dealer from maintaining records.

##### (g) Records retention time periods; control by other parties.

All records required by this rule shall be maintained for the time periods specified in the applicable provisions of Rules 17a-3 and 17a-4. Should a broker-dealer cease transacting business in securities to terminate its registration, the broker-dealer shall continue to maintain the records for the time period specified in Rules 17a-3 and 17a-4. Should a terminated broker-dealer have another party maintain control of the broker-dealer's records, notice shall include the reason for the arrangement and the name, address, and telephone number of the other party.

##### (h) Waiver of requirements.

[The Administrator] may, for good cause as determined in [the Administrator] discretion, waive any requirements in this regulation with respect to any requirements in this regulation with respect any broker-dealer or class of broker-dealers.

[FR Doc. 96-27611 Filed 10-25-96; 8:45 am]

BILLING CODE 8010-01-P

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### 21 CFR Parts 310, 314, and 600

[Docket No. 96N-0108]

### Postmarketing Expedited Adverse Experience Reporting for Human Drug and Licensed Biological Products; Increased Frequency Reports

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to

amend its postmarketing expedited adverse experience reporting regulations to revoke the requirement for increased frequency reports for human drug and licensed biological products as expedited reports. This action, which is part of the President's regulatory reinvention initiative, is based on FDA's determination that increased frequency reports, as currently required, have not contributed to timely identification of safety problems requiring regulatory action and are no longer necessary for FDA surveillance of postmarketing adverse experiences. This action would simplify and streamline postmarketing expedited reporting of adverse experiences for human drug and licensed biological products.

**DATES:** Written comments by January 13, 1997. The agency proposes that any final rule that may issue based on this proposal become effective 30 days after its date of publication in the Federal Register.

**ADDRESSES:** Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

**FOR FURTHER INFORMATION CONTACT:** Audrey A. Thomas, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-594-1049.

#### **SUPPLEMENTARY INFORMATION:**

##### **I. Introduction**

On March 4, 1995, President Clinton issued a memorandum titled "Regulatory Reinvention Initiative." This memorandum, part of the reform of the Federal regulatory system, directed heads of departments and agencies to undertake a page-by-page review of their existing regulations and to eliminate or modify those that are outdated or otherwise in need of reform. The President's directive was issued because private businesses, especially small ones, often face a profusion of overlapping and sometimes conflicting rules from Federal regulatory objectives.

As part of their review, agencies were charged to consider the following issues carefully: Is the regulation obsolete; could its intended goal be achieved in more efficient, less intrusive ways; are there private sector alternatives, such as market mechanisms, that can better achieve the public good envisioned by the regulations; could private business, setting its own standards and being subject to public accountability, do the job as well; and could the States or local governments do the job, making the Federal regulation unnecessary.

In response to the President's regulatory reinvention initiative, FDA conducted a comprehensive review of its existing regulations and identified regulations to eliminate or modify. Although this proposal was not a result of the initial review of regulations, FDA is continuing its efforts to carry out the President's program. The current proposal to revoke parts of its regulations in §§ 310.305, 314.80, and 600.80 (21 CFR 310.305, 314.80, and 600.80) that require postmarketing expedited increased frequency reports of adverse experiences for human drug and licensed biological products is part of the continuing effort.

##### **II. Background**

In the Federal Register of February 22, 1985 (50 FR 7452), FDA published revised regulations governing the approval for marketing of new drugs for human use, which included revisions to its adverse experience reporting requirements. Under § 314.80(c)(1)(ii), any applicant with an approved new drug application (NDA) is required to submit expedited increased frequency reports for any significant increase in frequency of an adverse experience that is both serious and expected. In the Federal Register of July 3, 1986 (51 FR 24476), FDA published regulations for adverse experience reporting for marketed prescription drugs without approved NDA's or abbreviated new drug applications (ANDA's). Under § 310.305(c)(4), any manufacturer, packer, or distributor of a marketed prescription drug without an approved NDA or ANDA is required to submit expedited increased frequency reports for any significant increase in frequency of an adverse experience that is both serious and expected. In the Federal Register of April 28, 1992 (57 FR 17950), FDA published regulations for ANDA's, including requirements for adverse experience reporting for drugs with approved ANDA's and abbreviated antibiotic drug applications (AADA's). Under § 314.98 (21 CFR 314.98), any applicant with an approved ANDA or AADA is required to comply with the requirements of § 314.80 regarding the reporting and recordkeeping of adverse experiences. In the Federal Register of October 27, 1994 (59 FR 54034), FDA finalized regulations for adverse experience reporting for licensed biological products. Under § 600.80(c)(1)(ii), manufacturers of licensed biological products are required to submit expedited increased frequency reports for any significant increase in frequency of an adverse experience that is both serious and expected.

Under §§ 310.305(c)(4), 314.80(c)(1)(ii) and (c)(1)(iii), and 600.80(c)(1)(ii) and (c)(1)(iii), applicants and manufacturers, packers, and distributors, including licensed manufacturers, are required to review periodically (at least as often as the periodic reporting cycle) the frequency of reports of adverse experiences that are both serious and expected and reports of therapeutic failure (lack of effect), regardless of source, and report any significant increase in frequency as soon as possible but in any case within 15 working days of determining that a significant increase in frequency exists. For drugs with an approved NDA or ANDA, or licensed biological products, the reporting interval is quarterly in the first 3 years of marketing and annually thereafter (§§ 314.80(c)(2) and 600.80(c)(2)), while for marketed prescription drugs without an approved NDA or ANDA, the reporting interval is annually (§ 310.305(c)(4)).

Operationally, an increased frequency exists if the adjusted reporting for the reporting interval is at least two times greater than the adjusted reporting for the comparison interval (previous reporting interval). Reporting is adjusted by the ratio of estimated drug use for the reporting interval to that of the comparison interval. If the number of reports received during the reporting interval is less than four, an increased frequency report is not required (see CDER's "Guideline for Postmarketing Reporting of Adverse Drug Experiences," March 1992 and/or CBER's "Guideline for Adverse Experience Reporting for Licensed Biological Products," October 1993).

These regulations are intended to ensure that applicants and manufacturers, packers, and distributors, including licensed manufacturers, identify increases in the incidence of serious, labeled adverse experiences that occur with changes in medical practice, such as using a drug or biological product in higher risk populations, at higher dosages, or concomitantly with other drugs or biological products causing interactions. FDA intended for these reports to detect increasing incidences of serious, labeled adverse experiences that were not anticipated from premarketing clinical trials and that would necessitate labeling changes or other regulatory actions.

FDA is proposing to amend its postmarketing expedited adverse experience reporting regulations by revoking the requirement for expedited increased frequency reports in §§ 310.305(c)(4), 314.80(c)(1)(ii), and 600.80(c)(1)(ii). This action would not

affect the requirement for expedited reporting of all serious, unexpected adverse experiences. Applicants and manufacturers, packers, and distributors, including licensed manufacturers, must continue to submit 15-day alert reports and followup reports for serious, unexpected events, as required under §§ 310.305(c), 314.80(c), 314.98, and 600.80(c). FDA is also proposing to revoke the definition of "increased frequency" in §§ 310.305(b)(5), 314.80(a), and 600.80(a). This term is defined as an increase in the rate of occurrence of a particular adverse drug (or biological product) experience, e.g., an increased number of reports of a particular adverse drug (or biological product) experience after appropriate adjustment for drug (or biological product) exposure.

In the Federal Register of October 27, 1994 (59 FR 54046), FDA proposed to amend, among other things, its regulations for periodic postmarketing reporting of adverse experiences for human drug and licensed biological products in §§ 314.80(c)(2) and 600.80(c)(2). FDA proposed to amend the requirements for the content of periodic adverse experience reports by adding a section for overall safety evaluation. This section would contain a critical analysis and full discussion of the safety information provided in the periodic report as it pertains to a number of matters, including increased frequencies of known toxicity. FDA based this proposed revision on recommendations developed by the World Health Organization's Council for International Organizations of Medical Sciences (CIOMS) Working Group II. Recently, the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) developed, based on the CIOMS II proposals, a draft guideline for periodic reporting entitled "Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs" (the ICH E2C guideline). The ICH E2C draft guideline, published in the Federal Register of April 5, 1996 (61 FR 15352), recommends that the overall safety evaluation section of periodic safety update reports highlight any new information on increased frequencies of known adverse drug reactions, including comments on whether it is believed that these data reflect a meaningful change in adverse drug reaction occurrences. Thus, under this guideline, regulatory authorities would be able to obtain reports of increased frequencies from periodic reports. FDA

plans to finalize its proposed amendments to the periodic postmarketing safety reporting regulations after consensus is reached by ICH on a final guideline on postmarketing periodic safety update reports.

### III. FDA's Experience With Increased Frequency Reports

FDA has found that increased frequency reports have rarely prompted regulatory action during the time that the agency has been receiving such reports. These reports have been of little value in identifying increased incidences of serious, labeled experiences.

From January 1, 1987, to May 31, 1995, FDA received approximately 1,800 increased frequency reports. Over this period, FDA identified only a small number of drug/biological product safety problems where increased frequency reports played a role in risk assessment that resulted in regulatory action, three examples of which are given below. For each of the examples, the safety problems may have been detected in other safety reports required by FDA such as periodic adverse experience reports, field alert reports, or annual reports.

One safety problem involved buprenorphine, a narcotic agonist-antagonist analgesic approved in 1985 and labeled at that time as causing less respiratory depression than morphine. In 1986, FDA received an increased frequency report for respiratory depression with buprenorphine, prompting careful monitoring. This resulted in labeling changes and warnings that buprenorphine may depress respiration in a manner equivalent to an equianalgesic dose of morphine.

A second safety problem involved an increased frequency report of neurotoxicity caused by a medication administration error when vincristine, an antineoplastic, was mistaken for methotrexate, another antineoplastic, and administered intrathecally. This resulted in the repackaging of vincristine to avoid confusion with methotrexate.

A third safety problem involved Orthoclone OKT3, a monoclonal antibody used as an immunosuppressant for treatment of acute allograft rejection in renal, cardiac, and hepatic transplant patients. In 1990, FDA received an increased frequency report for anaphylaxis and serum sickness associated with Orthoclone OKT3. Two of three anaphylaxis patients were undergoing second courses of therapy. This report

resulted in labeling amendments including the addition of a boxed warning on the risk of anaphylaxis after any dose and a boldface paragraph providing further details.

FDA has also received increased frequency reports for adverse experiences that were previously identified as potential problems in premarketing clinical trials. For example, based on FDA's review of NDA data on ketorolac, an analgesic, the agency was aware of its potential for causing upper gastrointestinal bleeding (UGIB) and renal failure when given at higher doses. Following approval in 1989, the sponsor was asked to conduct a postmarketing safety study. Meanwhile, in 1992, FDA received increased frequency reports for UGIB and renal failure. However, a causal relationship between these adverse experiences and ketorolac could not be established from the increased frequency reports because of uncertainties caused by the underlying illness, concomitant drug administration, and the indication (postsurgical analgesia) for which ketorolac was being used. Following a review of the postmarketing safety study, FDA required labeling changes to address the safety problems associated with ketorolac. Thus, the increased frequency reports did not contribute to the risk assessment that resulted in this regulatory action.

FDA has found that expedited postmarketing adverse experience reporting systems are best used to identify rare, unexpected adverse drug reactions such as aplastic anemia, hepatic necrosis, renal failure, or anaphylaxis that were not detected in preclinical studies or clinical trials during drug development. For such unexpected reactions, warnings can be added to the labeling without quantifying the incidence of the reaction. Warnings for expected adverse reactions (such as those obtained in increased frequency reports) are already in the labeling. In addition, risk information regarding incidence cannot generally be ascertained from an increased frequency report but requires controlled studies.

### IV. Limitations of Increased Frequency Reports

Increased frequency information is derived from incidence rates. An incidence rate is estimated by dividing the number of adverse experiences (numerator) by the number of persons exposed to a drug or biological product (denominator). For increased frequency reports, applicants and manufacturers, including licensed manufacturers,

compare incidence rates estimated for the reporting interval with rates estimated for the previous reporting interval.

FDA is aware of several factors that affect the accuracy of incidence rates. First, health care providers do not report all adverse experiences. The percentage of adverse experiences reported is unknown and varies unpredictably over time. Hence, the numerator cannot be reliably estimated. Second, the number of persons exposed to a drug or biological product during a reporting period is not precisely known; it is estimated from sales or production data. The lag time between production or sales by the manufacturer and consumption by patients can vary, thus adding further distortion to comparisons between reporting periods. Hence, the denominator is not always reliably estimated. Third, adverse experience reports may be used for calculating increased frequencies even though the suspect drug or biological product did not necessarily cause the adverse experience. Assessment of causality is frequently limited by incomplete data and uncertainty caused by the underlying illness, indication, or other drug exposures. Fourth, increased frequency calculations are based on the dates when adverse experience reports are received by the sponsor. If health care providers hold adverse experience reports and submit them all at one time, there can be a cluster of adverse experiences that fall into one reporting period creating a false-positive signal.

Thus, the reliability of increased frequency reports is limited because of the difficulty in accurately estimating incidence rates. FDA has concluded that these concerns make it difficult to rely on increased frequency reports as a tool for identifying important safety problems requiring labeling changes or other regulatory action.

#### V. Public Comments on Increased Frequency Report Requirements

In the October 27, 1994, proposed rule, FDA proposed to amend its regulations for expedited and periodic premarketing and postmarketing safety reporting of adverse experiences for human drug and biological products. The proposal included revisions to the postmarketing increased frequency report requirements under §§ 310.305, 314.80, and 600.80. FDA proposed to amend these requirements by altering the time period for submitting increased frequency reports from 15 working days to 15 calendar days, and by revising the reporting interval. Under proposed § 310.305, this interval would be increased from at least once a year to at

least twice a year, and, under proposed §§ 314.80 and 600.80, this interval would be revised from at least quarterly for the first 3 years of marketing and annually thereafter to at least twice a year. FDA did not receive any comments on these proposed increased frequency reporting revisions.

However, FDA received comments from 12 pharmaceutical companies and 1 individual regarding other aspects of the current increased frequency reporting requirements that were not within the scope of the October 27, 1994, proposal. FDA considered these comments in developing the current proposal.

Nine comments opposed the requirement for increased frequency reports. One comment stated that there is "common agreement" that increased frequency assessments have not provided information on significant safety risks to patients. Another comment stated that it was not aware of any important safety signal that had been identified by an increased frequency report. One comment stated that there is no benefit to be gained from increased frequency assessments, especially for drugs that are not the subject of an approved application. Another comment noted that applicants have available other mechanisms to identify and characterize changes in the nature and frequency of adverse experiences reported to them. Another comment noted that no provision exists for increased frequency calculations in the recommendations of either ICH or CIOMS. Three comments recommended that FDA revoke the requirement unless the agency can show that these reports have produced safety information not otherwise obtainable (for example, important labeling revisions or the initiation of other communication to enhance the safe and effective use of drugs).

One comment opposed increased frequency reports of therapeutic failure for over-the-counter (OTC) drugs subject to an approved application. The comment contended that such reports are generally not unexpected from consumers of OTC drugs and are unlikely to involve serious outcomes. The comment requested that FDA limit these reports to prescription drugs and to cases involving serious consequences. Another comment requested that FDA limit increased frequency reports of therapeutic failure to U.S. reports.

One comment requested clarification of the methodology for estimating increased frequency rates because the FDA guideline describing these methods is vague. The comment noted that the "Guideline for Postmarketing Reporting

of Adverse Drug Experiences" refers to the use of either an arithmetical or statistical method of analysis without specifying either method. The comment said that use of the arithmetic method can produce an increased frequency calculation that would not be replicated by the statistical method (and conversely for the statistical method), thus leading to conflicting interpretations of increased frequency. Another comment requested clarification of the sources of data to be used for increased frequency analyses because of confusion caused by §§ 314.80(d)(1) and 600.80(d)(1), which state that increased frequency reports required under §§ 314.80(c)(1)(ii) and 600.80(c)(1)(ii) apply only to reports found in scientific and medical journals, either as the result of a formal clinical trial or from epidemiological studies or analyses of experience in a monitored series of patients.

#### VI. Request for Comments

Interested persons may, on or before January 13, 1997, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

#### VII. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(8) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

#### VIII. Paperwork Reduction Act of 1995

This proposed rule does not require information collections and, thus, is not subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (Pub. L. 104-13).

#### IX. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96-354). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic,

environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the proposed rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because this proposed rule would simplify and streamline current requirements, the agency certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

#### X. Effective Date

FDA proposes that any final rule that may issue based on this proposal become effective 30 days after its date of publication in the Federal Register.

#### List of Subjects

##### 21 CFR Part 310

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

##### 21 CFR Part 314

Administrative practice and procedure, Confidential business information, Drugs, Reporting and recordkeeping requirements.

##### 21 CFR Part 600

Biologics, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 310, 314, and 600 be amended as follows:

#### PART 310—NEW DRUGS

1. The authority citation for 21 CFR part 310 continues to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 512–516, 520, 601(a), 701, 704, 705, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 360b–360f, 360j, 361(a), 371, 374, 375, 379e); secs. 215, 301, 302(a), 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 242(a), 262, 263b–263n).

2. Section 310.305 is amended by revising paragraph (a), by removing paragraph (b)(5), by removing paragraph

(c)(4), by redesignating paragraphs (c)(5) and (c)(6) as paragraphs (c)(4) and (c)(5), respectively, by revising the first sentence of newly redesignated paragraph (c)(4), and by revising paragraph (f)(1) to read as follows:

#### § 310.305 Records and reports concerning adverse drug experiences on marketed prescription drugs for human use without approved new drug applications.

(a) *Scope.* FDA is requiring manufacturers, packers, and distributors of marketed prescription drug products that are not the subject of an approved new drug or abbreviated new drug application to establish and maintain records and make reports to FDA of all serious, unexpected adverse drug experiences associated with the use of their drug products.

\* \* \* \* \*

(c) \* \* \*

(4) In order to avoid unnecessary duplication in the submission of, and followup to, reports required in this section, a packer's or distributor's obligations may be met by submission of all reports of serious adverse drug experiences to the manufacturer of the drug product. \* \* \*

\* \* \* \* \*

(f) *Recordkeeping.* (1) Each manufacturer, packer, and distributor shall maintain for a period of 10 years records of all adverse drug experiences required under this section to be reported, including raw data and any correspondence relating to the adverse drug experiences, and the records required to be maintained under paragraph (c)(4) of this section.

\* \* \* \* \*

#### PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG OR AN ANTIBIOTIC DRUG

3. The authority citation for 21 CFR part 314 continues to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 701, 704, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 371, 374, 379e).

4. Section 314.80 is amended by removing the definition for *Increased frequency* in paragraph (a), by removing paragraph (c)(1)(ii), by redesignating paragraphs (c)(1)(iii) and (c)(1)(iv) as paragraphs (c)(1)(ii) and (c)(1)(iii), respectively, by revising the first two sentences in the introductory text of newly redesignated paragraph (c)(1)(ii), by removing the last sentence in paragraph (d)(1), by revising paragraph (f)(1), and by revising the last sentence in paragraph (l) to read as follows:

#### § 314.80 Postmarketing reporting of adverse drug experiences.

\* \* \* \* \*

(c) \* \* \*

(1) \* \* \*

(ii) The requirements of paragraph (c)(1)(i) of this section, concerning the submission of 15-day alert reports, shall also apply to any person (other than the applicant) whose name appears on the label of an approved drug product as a manufacturer, packer, or distributor. However, in order to avoid unnecessary duplication in the submission to FDA, and followup to, reports required by paragraph (c)(1)(i) of this section, obligations of a nonapplicant may be met by submission of all reports of serious adverse drug experiences to the applicant. \* \* \*

\* \* \* \* \*

(f) *Reporting Form FDA-1639.* (1) Except as provided in paragraph (f)(3) of this section, the applicant shall complete a Form FDA-1639 (Adverse Reaction Report) for each report of an adverse drug experience.

\* \* \* \* \*

(l) \* \* \* For purposes of this provision, the term "applicant" also includes any person reporting under paragraph (c)(1)(ii) of this section.

\* \* \* \* \*

#### PART 600—BIOLOGICAL PRODUCTS: GENERAL

5. The authority citation for 21 CFR part 600 continues to read as follows:

Authority: Secs. 201, 501, 502, 503, 505, 510, 519, 701, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, 360i, 371, 374); secs. 215, 351, 352, 353, 361, 2125 of the Public Health Service Act (42 U.S.C. 216, 262, 263, 263a, 264, 300aa–25).

6. Section 600.80 is amended by removing the definition for *Increased frequency* in paragraph (a), by removing paragraph (c)(1)(ii), by redesignating paragraphs (c)(1)(iii) and (c)(1)(iv) as paragraphs (c)(1)(ii) and (c)(1)(iii), respectively, by revising the first sentence in the introductory text of newly redesignated paragraph (c)(1)(ii), by removing the last sentence in paragraph (d)(1), by revising paragraph (f)(1), and by revising the last sentence in paragraph (m) to read as follows:

#### § 600.80 Postmarketing reporting of adverse experiences.

\* \* \* \* \*

(c) \* \* \*

(1) \* \* \*

(ii) The requirements of paragraph (c)(1)(i) of this section, concerning the submission of 15-day Alert reports, shall also apply to any person other than the licensed manufacturer of the final

product whose name appears on the label of a licensed biological product as a manufacturer, packer, distributor, shared manufacturer, joint manufacturer, or any other participant involved in divided manufacturing.

\* \* \* \* \*

(f) *Reporting forms.* (1) Except as provided in paragraph (f)(3) of this section, the licensed manufacturer shall complete the reporting form designated by FDA (FDA-3500A, or, for vaccines, a VAERS form) for each report of an adverse experience.

\* \* \* \* \*

(m) \* \* \* For purposes of this provision, this paragraph also includes any person reporting under paragraph (c)(1)(ii) of this section.

Dated: October 17, 1996.

William B. Schultz,

*Deputy Commissioner for Policy.*

[FR Doc. 96-27593 10-25-96; 8:45 am]

BILLING CODE 4160-01-F

## DEPARTMENT OF THE INTERIOR

### Minerals Management Service

#### 30 CFR Part 290

#### RIN 1010-AC21

### Administrative Appeals Process

**AGENCY:** Minerals Management Service, Interior.

**ACTION:** Proposed rule.

**SUMMARY:** The Minerals Management Service (MMS) proposes to amend the regulations governing its administrative appeals process. These amendments are in response to MMS's own initiatives to speed up the appeals process, and are in response to statutory requirements recently enacted which require the Department of the Interior to decide certain administrative appeals within 33 months from the commencement of the appeal. Under these proposed regulations, the MMS Director generally would be required to decide an appeal within 16 months of commencement of the appeal or the appeal would automatically be deemed denied. The appellant then could continue its appeal before the Interior Board of Land Appeals (IBLA). The IBLA then would have to complete its action on the appeal before the recently enacted 33-month deadline on deciding appeals involving Federal oil and gas leases. (The 33-month deadline for the IBLA would not apply to appeals involving Indian leases or to Federal leases for minerals other than oil or gas.) In addition, MMS's proposed regulations

would impose a new \$100.00 filing fee on appeals to the Director.

**DATES:** Comments must be received on or before December 27, 1996.

**ADDRESSES:** Comments should be sent to: Bettine Montgomery, Office of Policy and Management Improvement, Minerals Management Service, 1849 C Street, N.W., MS 4013, Washington, D.C. 20240; courier delivery to Department of the Interior, 1849 C Street, N.W., Washington, D.C. 20240, telephone (202) 208-3976; fax (202) 208-3118, e-Mail Elizabeth.Montgomery@smtp.mms.gov.

**FOR FURTHER INFORMATION CONTACT:** Hugh Hilliard, Office of Policy and Management Improvement, U.S. Department of the Interior, Mineral Management Service, 1849 C Street, N.W., Room 4013, Washington, D.C. 20240; telephone (202) 208-3398; fax (202) 208-4891; e-Mail Hugh\_Hilliard@smtp.mms.gov.

**SUPPLEMENTARY INFORMATION:** The principal author of this proposed rule is Chris Thomson at (202) 208-7551 in Washington, D.C.

#### I. Background

In May 1994, MMS began a comprehensive review of its administrative appeals process, particularly as it relates to appeals involving orders or decisions issued by the Royalty Management Program. As part of that review, MMS held several informal meetings with state, tribal, and industry representatives to discuss the problems and possible solutions within the appeals process. The principal problems identified included the length of the appeals process, sometimes taking several years to resolve a case, and the excessive costs of the process to both MMS and appellants. These proposed regulations to amend 30 CFR Part 290 are based in part on ideas developed through that review process. Subsequent to that review, the Royalty Policy Committee (advisory committee to the Secretary of the Interior composed of representatives of states, Indian tribes, industry, other Federal agencies and the general public) established a Subcommittee on Appeals and Alternative Dispute Resolution. MMS expects the Royalty Policy Committee to consider the work of that subcommittee during the pendency of this proposed rule and will consider the recommendations of the Royalty Policy Committee as part of this rulemaking process.

One of the primary ideas developed in the review was that MMS establish both strict time limits on the appeals process and an overall time limitation for

appeals as a whole. On August 13, 1996, the Federal Oil and Gas Royalty Simplification and Fairness Act, Pub. L. 104-185, 110 Stat. 1700, was enacted. Section 4 of the new Act amended the Federal Oil and Gas Royalty Management Act of 1982 (FOGRMA), 30 U.S.C. § 1701 *et seq.*, and added a new FOGRMA section 115(h) governing the Department's process for resolving appeals of MMS orders or decisions involving royalties and other payments due on Federal oil and gas leases. For appeals involving Federal oil and gas leases covered by this new provision, the Department has 33 months from the date a proceeding is commenced to complete all levels of administrative review or the appeal will be deemed decided. The 33-month deadline does not apply to appeals involving Indian leases or Federal leases for minerals other than oil and gas.

Therefore, it is necessary that MMS design its administrative appeal process to accommodate the new limitation. Although that limitation does not apply to Indian leases, or to Federal coal or other solid minerals leases, or to orders or decisions signed by the MMS Offshore Minerals Management Program, MMS proposes to apply the same time limit on all appeals to the Director for uniformity of administration.

These regulations propose in § 290.6 that all appeals to the MMS Director will be decided within 16 months of the date the appeal is commenced. The regulations also specify the date on which the Department deems an appeal to have commenced, namely, the date on which MMS receives a notice of appeal, including a statement of the reasons the appellant offers in support of the appeal and a one-page summary of the issues presented in the statement of reasons, and payment of a filing fee. MMS chose a time period shorter than 33 months in order to accelerate the process for all appeals and to provide time for IBLA's further review of MMS decisions. If the 16-month time limitation is reached and a decision has not been issued, then the appeal will automatically be deemed denied by the Director, allowing the appellant to continue its appeal before IBLA.

In addition, the overall 16-month time limitation period for resolving appeals to the MMS Director was derived from an overview of the steps of the appeals process. As noted above, an appeal to the Director of an order or decision issued by a program office of MMS would only "commence" with the proper filing of a notice of appeal, including a statement of reasons the appellant offers in support of the appeal