Proposed Actions

Since an unsafe condition has been identified that is likely to exist or develop on other engines of the same type design registered in the United States, the proposed AD would require installation of module TU63, at the earliest of the following: the next shop visit after the effective date of this AD, 120 cycles-in-service after the effective date of this AD, or within 30 days after the effective date of this AD. The actions would be required to be accomplished in accordance with the SB described previously.

Economic Analysis

There are approximately 100 engines of the affected design in the worldwide fleet. The FAA estimates that 9 engines installed on aircraft of US registry would be affected by this proposed AD, that it would take approximately 1 work hour per engine to accomplish the proposed actions, and that the average labor rate is $60 per work hour. Required parts would cost approximately $5,500.00 per engine. Based on these figures, the total cost impact of the proposed AD on US operators is estimated to be $ $50,040. The manufacturer has advised the DGAC that they may provide module TU63 at no cost to the operator, thereby substantially reducing the cost impact of this proposed rule.

Regulatory Impact

This proposal does not have federalism implications, as defined in Executive Order No. 13132, because it would not have a substantial direct effect on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the FAA has not consulted with state authorities prior to publication of this proposal.

For the reasons discussed above, I certify that this proposed regulation: (1) Is not a ''significant regulatory action'' under Executive Order 12866; (2) is not a ''significant rule'' under the DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979); and (3) if promulgated, will not have a significant economic impact, positive or negative, on a substantial number of small entities under the criteria of the Regulatory Flexibility Act. A copy of the draft regulatory evaluation prepared for this action is contained in the Rules Docket. A copy of it may be obtained by contacting the Rules Docket at the location provided under the caption **ADDRESSES**.

List of Subjects in 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Safety.

The Proposed Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration proposes to amend part 39 of the Federal Aviation Regulations (14 CFR part 39) as follows:

PART 39—AIRWORTHINESS DIRECTIVES

1. The authority citation for part 39 continues to read as follows:

Authority: 49 U.S.C. 106(g), 40113, 44701.

§ 39.13 [Amended]

2. Section 39.13 is amended by adding the following new airworthiness directive:

Turbomeca: Docket No. 99–NE–42–AD.

Applicability: Turbomeca Arrius 1A series turboshaft engines, installed on but not limited to Ecureuil AD355 series helicopters.

Note 1: This airworthiness directive (AD) applies to each engine identified in the preceding applicability provision, regardless of whether it has been modified, altered, or repaired in the area subject to the requirements of this AD. For engines that have been modified, altered, or repaired so that the performance of the requirements of this AD is affected, the owner/operator must request approval for an alternative method of compliance in accordance with paragraph (c) of this AD. The request should include an assessment of the effect of the modification, alteration, or repair on the unsafe condition addressed by this AD; and, if the unsafe condition has not been eliminated, the request should include specific proposed actions to address it.

Compliance: Required as indicated, unless accomplished previously.

To prevent unexpected power loss, which could result in an uncommanded in-flight engine shutdown, autorotation, and forced landing, accomplish the following:

Installation of Module TU63

(a) Install module TU63 in accordance with the Instructions for Incorporation of Turbomeca Service Bulletin (SB) No. 319 72 0016, Revision 1, dated December 22, 1997, at the earliest of the following after the effective date of this AD:

- The next shop visit, or
- Within 120 cycles-in-service, or
- Within 30 days.

Definition

(b) For the purpose of this AD, a shop visit is defined as whenever the engine is removed from the helicopter for maintenance.

Alternative Methods of Compliance

(c) An alternative method of compliance or adjustment of the compliance time that provides an acceptable level of safety may be used if approved by the Manager, Engine Certification Office. Operators shall submit their request through an appropriate FAA Principal Maintenance Inspector, who may add comments and then send it to the Manager, Engine Certification Office.

Note 2: Information concerning the existence of approved alternative methods of compliance with this airworthiness directive, if any, may be obtained from the Engine Certification Office.

Ferry Flights

(d) Special flight permits may be issued in accordance with §§ 21.197 and 21.199 of the Federal Aviation Regulations (14 CFR 21.197 and 21.199) to operate the aircraft to a location where the requirements of this AD can be accomplished.

Issued in Burlington, Massachusetts, on October 24, 1999.

David A. Downey,

Assistant Manager, Engine and Propeller Directorate, Aircraft Certification Service.

[FR Doc. 99–31171 Filed 11–30–99; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 314 and 601

[Docket No. 99N–1852]

RIN 0910–AB83

Postmarketing Studies for Human Drugs and Licensed Biological Products; Status Reports

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to revise the status reports section of the postmarketing annual reporting requirements for drug and biological products, and to require applicants to submit annual status reports for certain postmarketing studies of licensed biological products. This proposed rule would describe the types of postmarketing studies covered by these status reports, the information to be included in the reports, and the type of information that FDA would consider appropriate for public disclosure. The agency is taking this action to implement section 130 of the Food and Drug Administration Modernization Act of 1997 (FDAMA).

DATES: Submit written comments on the proposed rule by February 14, 2000. Submit written comments on the information collection provisions by January 3, 2000.

ADDRESSES: Submit written comments to the Dockets Management Branch

(HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit written comments on the information collection provisions to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB), New Executive Office Bldg., 725 17th St. NW., Washington, DC 20503, Attn: Wendy Taylor, Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT:

Paula S. McKeever, Center for Biologics Evaluation and Research (HFM–17), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448, 301–827–6344; or

Audrey A. Thomas, Center for Drug Evaluation and Research (HFD–7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5625.

SUPPLEMENTARY INFORMATION:

I. Introduction

On November 21, 1997, the President signed the FDAMA into law (Public Law 105–115). Section 130(a) of the FDAMA amended the Federal Food, Drug, and Cosmetic Act (the act) by adding a new provision on reports of postmarketing studies) (section 506B of the act (21 U.S.C. 356b)). Section 506B of the act provides FDA with additional authority for monitoring the progress of postmarketing studies that companies have made a commitment to conduct and also requires the agency to make information that pertains to the status of these studies publicly available.

Under section 506B(a) of the act, applicants that have committed to conduct a postmarketing study for a drug or biological product that is approved for marketing must submit to FDA a report on the progress of the study or the reasons for the failure of the applicant to conduct the study. This provision directs FDA to issue regulations that prescribe the content of these reports.

Section 506B(a) of the act also states that these reports must be submitted to FDA within 1 year after the approval of the product and annually thereafter until the study is completed or terminated. This provision applies to commitments for postmarketing studies that were made on or after enactment of FDAMA, as well as those made prior to enactment of FDAMA. For commitments made prior to enactment of FDAMA, the act requires that an initial report be submitted to FDA within 6 months after the date of issuance of the final rule implementing section 506B of the act. Section 506B(b) of the act specifies which information in a status report may be considered public information. Under section 506B(b) of the act, FDA may publicly disclose any information pertaining to a status report under section 506B(a) to the extent that the information is necessary to identify the applicant, or to establish the status of a study and the reasons, if any, for failure to conduct, complete, and report the study.

Section 506B(c) of the act directs FDA to develop and publish annually in the **Federal Register** a report concerning this activity. This report must provide information on the status of postmarketing studies that applicants have committed to conduct under this provision and for which reports have been submitted.

FDAMA also directs FDA, under section 130(b), to submit a specific report to Congress by October 1, 2001. This report must contain a summary of the status reports submitted under section 506B of the act, an evaluation of the performance of applicants in fulfilling their commitments to conduct postmarketing studies under this provision and of FDA's timeliness in reviewing these postmarketing studies, and any legislative recommendations regarding postmarketing studies.

Under the agency's existing postmarketing reporting regulations for human drug products, at § 314.81(b)(2) (21 CFR 314.81(b)(2)), each applicant holding an approved new drug application (NDA) or abbreviated new drug application (ANDA) must submit an annual report to FDA for the drug product. This annual report is required to contain, among other information, a section on status reports that includes a statement on the current status of any postmarketing studies of the drug product performed by, or on behalf of, the applicant (§ 314.81(b)(2)(vii)). This section also permits applicants to include a list of any open regulatory business with FDA concerning the drug product. In the **Federal Register** of December 2, 1998 (63 FR 66632), FDA issued a final rule amending these postmarketing reporting regulations to require that annual reports contain, among other information, specific information about the status of postmarketing clinical studies in pediatric populations. In this proposed rule, FDA is proposing to amend these regulations, including the new provisions issued in the final rule of December 2, 1998, to implement the requirements of section 506B of the act for human drug products. In a separate rulemaking, FDA plans to propose additional amendments to the annual report requirements pertaining to the nonclinical laboratory studies and clinical data sections of the annual report. However, these amendments are beyond the scope of this proposed rule.

Each applicant holding a biologics license application (BLA) must submit an annual report to FDA describing any minor changes that may relate to the safety or effectiveness of the product (§ 601.12(d) (21 CFR 601.12(d)) and must also submit a separate annual report, in accordance with the final rule of December 2, 1998 (63 FR 66632), regarding postmarketing pediatric studies (§ 601.37 (21 CFR 601.37)). In this proposed rule, FDA is proposing to amend the biologics regulations at part 601 (21 CFR part 601) by revising the postmarketing annual reporting requirement at § 601.37 and by adding a new postmarketing annual reporting requirement, § 601.70, to implement the requirements of section 506B of the act for licensed biological products. Proposed § 601.70 would only apply to licensed biological products that meet the definition of ''drug'' under the act; it would not apply to biological products that also meet the definition of ''medical device'' under the act, since section 506B does not cover medical devices.

This proposed rule would only apply to human drug and biological products; it would not apply to animal drug products. FDA intends to amend its regulations to implement section 506B of the act for animal drug products in a separate rulemaking.

In May 1996, the Office of Inspector General of the Department of Health and Human Services issued a report regarding FDA's oversight of postmarketing study commitments for prescription drugs (Ref. 1). This study found that the number of postmarketing study commitments was increasing and that the agency did not have formal standards or procedures for monitoring postmarketing studies or for establishing whether a postmarketing study commitment had been met. At the same time, FDA was developing formal procedures for tracking the progress of postmarketing study commitments, an effort that began in February 1995 when the agency recognized the need for such procedures. These procedures were implemented in October 1996. The proposed revisions to the human drug and biologics regulations in this rule will facilitate FDA's current system for tracking postmarketing study commitments.

In addition to the regulatory changes proposed in this rule, FDA will issue guidance regarding section 506B of the act. This guidance will describe in greater detail the type of information

that applicants should submit to the agency in a status report for a postmarketing study of an approved drug or licensed biological product, the implementation schedule for submission of these status reports to the agency, how FDA will track information obtained for postmarketing studies, and the schedule for FDA review of status reports and final study reports for postmarketing studies. In accordance with the agency's Good Guidance Practices (62 FR 8961, February 27, 1997), FDA will make the guidance available in draft form for public comment before issuing a final guidance. FDA is also in the process of reviewing and revising, as necessary, its internal operating procedures related to tracking commitments made for the conduct of postmarketing studies under this provision for approved drug and licensed biological products.

II. Description of the Proposed Rule

A. Introduction

The proposed rule would amend the postmarketing annual reporting requirements for human drug products under § 314.81(b)(2) by reorganizing the status reports section, at § 314.81(b)(2)(vii), to require that the information contained in this section be provided to FDA in a different format. FDA is proposing that this information be included in the annual report in three different sections. One section would contain, as described below (see section II.B of this document), status reports for those postmarketing studies of the drug product (i.e., clinical safety, clinical efficacy, clinical pharmacology and nonclinical toxicology) that are required by FDA (e.g., pediatric studies) or that an applicant has committed, in writing, to conduct either at the time of approval of an application or a supplement to an application, or after approval of an application or a supplement consistent with section 506B of the act (proposed § 314.81(b)(2)(vii)). This section would also include, for pediatric studies, a statement that indicates whether postmarketing clinical studies in pediatric populations were required by FDA under § 201.23 (21 CFR 201.23). Another section would contain status reports for any other postmarketing studies of the drug product (proposed § 314.81(b)(2)(viii)) (e.g., chemistry, manufacturing, and controls, stability of the product), and the third section would contain, at the applicant's discretion, a list of any open regulatory business with FDA concerning the drug product (proposed § 314.81(b)(2)(ix)). FDA would use the information provided under proposed § 314.81(b)(2)(vii) to meet its reporting obligations under section 506B of the act (annual report in the **Federal Register**) and section 130(b) of FDAMA (report to congressional committees by October 1, 2001). FDA does not intend to use information provided under proposed § 314.81(b)(2)(viii) for this purpose. This proposed change in the structure of the annual report would facilitate FDA's preparation of its annual reports and its report to Congress without imposing a new reporting burden on applicants with approved NDA's and ANDA's because these applicants are currently required to report such information to FDA.

The proposed rule would also create a new subpart G under part 601 entitled ''Postmarketing Studies'' and a new § 601.70 under subpart G. Proposed § 601.70 would require, as described in section II.B of this document, annual reports of the status of postmarketing studies for licensed biological products (i.e., clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology) that are required by FDA (e.g., pediatric studies) or that an applicant has committed, in writing, to conduct either at the time of approval of an application or a supplement to an application, or after approval of an application or a supplement. Proposed § 601.37(c) would require that the status of postmarketing pediatric studies that are covered under proposed § 601.70 be reported to FDA under proposed § 601.70 rather than under § 601.37. FDA notes that biological products previously approved under the product license application and establishment license application process are included wherever BLA, the new form of application for biological products, is used in this preamble.

B. Scope of Proposed Rule

Postmarketing studies for marketed human drug and licensed biological products are conducted for a variety of purposes (e.g., new indication, safety, medication errors, pharmacokinetics, pharmacology, chemistry, marketing, stability, use in special populations such as children). Some of these postmarketing studies are conducted by an applicant on its own initiative. Other postmarketing studies are required by FDA to be conducted by applicants such as assessing the safety and effectiveness of new drugs and biologics in pediatric patients (§ 314.55 (21 CFR 314.55) and § 601.27. Others result from an applicant's commitment, in writing, to the agency to conduct the study at the time of approval of an application (e.g, an NDA, ANDA, BLA, or supplement), after approval of an application (e.g., as a result of suspected adverse drug reaction reports), as a condition of accelerated approval of new drugs and biological products for serious or life–threatening illnesses (subpart H of part 314 (21 CFR part 314), and subpart E of part 601 respectively), or as a deferred submission of pediatric studies (§§ 314.55(b) and 601.27(b)). Studies that applicants commit to conduct at the time of approval of an application are usually intended to address concerns about the risks, benefits, or optimal use of a drug or biological product that do not warrant delaying approval of the application.

This proposed rule would define postmarketing studies for which status reports must be submitted under section 506B of the act as those that concern clinical safety, clinical efficacy, clinical pharmacology or nonclinical toxicology studies and that are required by FDA (e.g., pediatric studies) or that are committed to, in writing, either at the time of approval of an application or a supplement or after approval of an application or supplement. FDA is proposing to include clinical studies such as safety, efficacy, and pharmacology studies within the scope of this rule because these types of studies provide the most relevant and useful additional information about the risks, benefits, and optimal use to patients and consumers of an approved drug or licensed biological product. In addition, FDA is proposing to include nonclinical toxicology studies within the scope of this rule, although such studies typically cannot be performed on human subjects, because they are very useful to further evaluate the safety of a marketed drug or biological product.

For the purpose of this rule, clinical safety and clinical efficacy studies would include human epidemiological studies. Examples of clinical pharmacology studies are pharmacokinetic and pharmacodynamic studies. For all of the postmarketing studies described previously, §§ 314.81(b)(2)(vii) and 601.70 would require applicants to provide status reports to FDA regarding the progress of such studies.

Postmarketing studies designed to evaluate other types of issues such as manufacturing and control issues (e.g., stability of the product, development of new tests or specifications) and medication errors (e.g., attributable to the labels, labeling and/or packaging of the product) would be reported for drug products, as described below, under proposed § 314.81(b)(2)(viii) rather than under proposed § 314.81(b)(2)(vii), and

would not be required to be reported under § 601.70 for licensed biological products.

This proposed rule would require, as stated previously, status reports, under proposed §§ 314.81(b)(2)(vii) and 601.70, for postmarketing studies that either are required by FDA (e.g., pediatric studies) or that applicants commit, in writing, to conduct either at the time of approval of an application or a supplement to an application, or after approval of an application or a supplement.

Under proposed § 314.81(b)(2)(viii), applicants with approved NDA's and ANDA's would be required to provide status reports for any postmarketing study not reported under proposed § 314.81(b)(2)(vii) (e.g., chemistry, manufacturing, and controls, stability of the product, medication errors). These would include postmarketing studies performed by, or on behalf of, the applicant, whether or not the studies are required or subject to commitments. Proposed § 314.81(b)(2)(viii) does not represent a new reporting burden for applicants with approved NDA's or ANDA's because these applicants are currently required to provide status reports for these studies in their postmarketing annual reports. FDA is not proposing a similar reporting requirement for postmarketing studies of licensed biological products in this proposed rule. Applicants with licensed biological products may voluntarily submit status reports to FDA for postmarketing studies that are not required to be reported under proposed § 601.70.

The agency is committed to harmonizing its reporting requirements for drugs and biologics as much as possible. Section 123(f) of FDAMA requires FDA to take measures to minimize differences in the review and approval of products required to have approved BLA's under section 351 of the Public Health Service Act (42 U.S.C. 262) and products required to have approved NDA's under section 505(b)(1) of the act (21 U.S.C. 355(b)(1)). At the present time, FDA is considering whether to amend its biologics regulations in a separate rulemaking to require the submission of information in postmarketing annual reports currently submitted to the agency by applicants with approved NDA's and ANDA's under § 314.81(b)(2)(i) through (b)(2)(vi). FDA requests comment on whether the postmarketing annual report for licensed biological products under § 601.12(d), (changes to an approved application), § 601.37 (annual reports of postmarketing pediatric studies), and proposed § 601.70 should be combined into a single annual report and whether such a report should include additional information as required in § 314.81(b)(2)(i) through (b)(2)(vi). However, FDA has determined that requiring such additional information is beyond the scope of this proposed rulemaking and that it is appropriate, at this time, to harmonize only the drugs and biologics postmarketing annual reporting requirements as they relate to section 506B of the act.

C. Content of Status Reports

Current regulations (§ 314.81(b)(2)(vii)) do not prescribe the content of status reports of postmarketing studies. In this proposed rule, FDA is proposing to set forth the format and content of these reports, as described in section 506B of the act, which requires sufficient information to identify the applicant of the postmarketing study, the specific study being conducted, the status of the study, and the reasons, if any, for the applicant's failure to complete the study. Under proposed § 314.81(b)(2)(vii) and (b)(2)(viii) and § 601.70(b), a status report for a postmarketing study would be required to contain the following information:

1. Applicant's name.

2. Product name. This would include the approved product's established/proper name and proprietary name, if applicable.

3. NDA number, ANDA number, BLA/reference number, or supplement number of the approved product.

4. Date of product's U.S. approval.

5. Date of postmarketing study commitment. This date would be the same as the date of the product's U.S. approval for commitments made, in writing, at the time of U.S. approval of an application; would be the date of U.S. approval of the supplement for commitments made, in writing, at the time of U.S. approval of a supplement; and would be the date of written commitment for commitments made after U.S. approval of an application or supplement.

6. Description of postmarketing study commitment. For clinical studies, this section would include the purpose of the postmarketing study, the patient population addressed by the study, the number of patients and/or subjects to be included in the study, and the indication and dosage(s) that are to be studied. For nonclinical studies, this section would include the type and purpose of the study (e.g., carcinogenicity study to determine effects of chronic dosing).

7. Schedule for conduct, completion, and reporting of the postmarketing study commitment. This section would include projected dates for initiation of the different phases of the study, for completion of the study, and for submission of the final study report to FDA. This schedule should reflect a reasonable, but aggressive timetable for completing the postmarketing study commitment. Although some delays in a study may be unanticipated, it is expected that studies would progress as originally scheduled. If the original schedule is revised under section 9 of this status report, the revised schedule would also be reported in this section (i.e., section 7) in the next report with a note indicating that the schedule has been revised as reported in the previous status report.

8. Current status of the postmarketing study commitment. Applicants would categorize the status of each postmarketing study using one of the following terms that describe the study's status on the U.S. anniversary date of approval of the application or other agreed upon date:

a. *Pending*. The study has not been initiated (i.e., first patient has not been enrolled).

b. *Ongoing*. The study is proceeding according to or ahead of the original schedule described in section 7 of the status report. If a study has been completed but the final study report has not been submitted to FDA, the date the study was completed would be provided.

c. *Delayed*. The study is proceeding but is behind the original schedule described in section 7 of the status report. The original schedule would serve as the basis for defining a study as ''delayed,'' even if a revised schedule is provided.

d. *Terminated*. The study was ended before completion.

e. *Submitted*. The study has been completed (i.e., last patient finished the protocol) or terminated and a final study report has been submitted to FDA. This category would include the date the final study report was submitted to FDA.

9. Explanation of the study's status. This section would include a brief description of the status of the study, including the number of patients and/or subjects enrolled to date and an explanation of the study's status identified under section 8 of the status report (e.g., delayed due to difficulty in patient accrual, terminated because study would no longer provide useful information, terminated because study is no longer feasible, terminated because of adverse events or other safety issues associated with the use of the product). This section would also include a

revised schedule, as well as the reason(s) for the revision, if the schedule under section 7 of the status report has changed since the last annual report. This revised schedule would be included, as noted previously, under section 7 of the next report.

FDA believes that the information proposed to be required in status reports would provide the agency with sufficient data for review of the progress of ongoing postmarketing studies under this section. These reports would also provide FDA with sufficient information to meet the agency's reporting obligations under section 130 of FDAMA (i.e., annual report in the **Federal Register** on the status of postmarketing studies, report to congressional committees by October 1, 2001).

D. Log of Outstanding Regulatory Business

Current regulations (§ 314.81(b)(2)(vii)), as noted previously (see section I of this document), permit applicants with approved NDA's and ANDA's to include in the status reports section of annual reports a list of any open regulatory business with FDA concerning the drug product that is the subject of the annual report. FDA would continue to permit applicants to submit such information in annual reports under proposed § 314.81(b)(2)(ix). For clarification, FDA is proposing to provide examples of the types of open regulatory business that would be reported under proposed § 314.81(b)(2)(ix). These would include a list of the applicant's unanswered correspondence with the agency and a list of the agency's unanswered correspondence with the applicant.

Proposed § 601.70 does not contain a similar provision for outstanding regulatory business. However, as noted previously (see section II.B of this document), FDA is considering a separate rulemaking that would require the same postmarketing annual reporting requirements for drugs and biologics.

E. Report Submission Requirements

Current regulations at § 314.81(b), require applicants with approved drug products to submit two copies of an annual report to FDA. Under § 314.81(b)(2), these annual reports are required to be submitted within 60 days of the anniversary date of U.S. approval of the application to the FDA division responsible for reviewing the application and these reports. Each annual report is required to be accompanied by a completed transmittal Form FDA–2252 (Transmittal of Periodic Reports for Drugs for Human Use) that includes all the information required under § 314.81(b)(2) that the applicant received or otherwise obtained during the annual reporting interval, which ends on the U.S. anniversary date. FDA is proposing to amend these regulations by replacing the phrase ''Periodic Reports'' with the phrase ''Annual Reports'' to correct an error and by making other minor changes to provide clarity.

Currently, applicants with licensed biological products must submit reports, under § 601.12(d), describing certain minor changes to an approved BLA, and under § 601.37, providing information on postmarketing pediatric studies, each year within 60 days of the anniversary date of approval of the application. Proposed § 601.70(c) and (d) would require applicants with licensed biological products to submit a separate annual report to FDA describing the status of certain postmarketing studies using submission requirements similar to those required for drugs under § 314.81(b)(2) and for licensed biologics under §§ 601.12(d) and 601.37. Applicants with licensed biological products would submit two copies of an annual progress report to FDA within 60 days of the anniversary date of the U.S. approval of the application for the product. Each annual progress report would be accompanied by a completed transmittal Form FDA–2252 that includes all the information required under proposed § 601.70 that the applicant received or otherwise obtained during the annual reporting interval, which ends on the U.S. anniversary date. These annual progress reports would be submitted for all postmarketing studies of a licensed biological product covered under the scope of this proposed rule including those that are required by FDA (e.g., pediatric studies) and those that an applicant committed, in writing, to conduct on or after the effective date of any final rule that may issue based on this proposed rule and prior to the effective date.

For drugs and biologics with approved NDA's, ANDA's, and BLA's, FDA intends, as noted previously (see section II.A of this document), to fulfill its annual reporting requirement mandated by section 506B(c) of the act by publishing in the **Federal Register**, the status of postmarketing study commitments reported under proposed §§ 314.81(b)(2)(vii) and 601.70. Furthermore, FDA will post additional information on the agency's web page (see section G.2 of this document). This additional information will include an applicant's failure to submit a status report under proposed §§ 314.81(b)(2)(vii) and 601.70 for any postmarketing study commitment that the agency has formally tracked (i.e., commitments included in agency databases which were made, in writing, at the time of approval or after approval of an application or a supplement to an application, and commitments made as a condition of accelerated approval, or required studies for assessing the safety and effectiveness of drugs and biologics in pediatric patients).

A status report under proposed §§ 314.81(b)(2)(vii) and 601.70 would be submitted to FDA until the agency notifies the applicant, in writing, that the study commitment has been fulfilled or acknowledges that the study is either no longer feasible or would no longer provide useful information. Applicants may indicate in their status report that a study has been terminated because it is either no longer feasible or would no longer provide useful information. However, these applicants would be required to submit a final study report to FDA and continue to submit status reports for the study until the agency evaluates the final study report and concurs, in writing, with the applicant's determination. To expedite the process, FDA encourages applicants to submit a final study report to the agency as soon as they have determined that a postmarketing study commitment is to be terminated.

F. Public Disclosure of Information

Section 506B(b) of the act requires FDA to publicly disclose any information pertaining to a status report described in section 506B(a) of the act to the extent that such information is necessary to: (1) Identify the sponsor or (2) establish the status of the postmarketing study and the reasons, if any, for any failure to carry out the study. Therefore, FDA is proposing to state in the rule its authority to disclose any information contained within or relating to postmarketing studies under proposed § 314.81(b)(2)(vii) or proposed § 601.70, if the information is necessary to establish the identity of the applicant or the status of the study, including the reasons, if any, for the applicant's failure to conduct, complete, and report the study. However, FDA would not disclose trade secrets as defined in 21 CFR 20.61(a) or information described in 21 CFR 20.63, the disclosure of which would constitute an unwarranted invasion of personal privacy. Information necessary to establish the status of a postmarketing study would include the study protocol, patient accrual rates, reports of unexpected (i.e., unlabeled) suspected adverse drug

reactions, and study results. Some of these types of information such as study protocols for certain postmarketing studies and adverse event reports for certain postmarketing studies are currently publicly available. Section 130(b) of FDAMA provides FDA with statutory authority to disclose data and information, including certain information that may be considered to constitute confidential commercial information. Section 130(b) of FDAMA constitutes authorization by law for the purposes of 18 U.S.C. 1905 to disclose certain information that could otherwise be considered nondisclosable confidential commercial information.

G. Proposed Implementation Scheme

1. Effective Dates

FDA proposes that any final rule that may issue based on this proposed rule become effective 90 days after its date of publication in the **Federal Register**. Applicants with approved applications for human drug and licensed biological products (that are not medical devices) would be subject to the annual reporting requirements in this proposed rule. In addition, applicants that have entered into a commitment prior to November 21, 1997, to conduct a postmarketing study described under proposed § 314.81(b)(2)(vii) or proposed § 601.70 would be required, as mandated by FDAMA, to submit an initial report to FDA within 6 months after the effective date of any final rule that may issue based on this proposed rule. Thus, in some cases, an applicant would be required to submit two reports to FDA in the first year after the effective date of the final rule (i.e., an initial report containing only information required under proposed § 314.80(b)(2)(vii) or proposed § 601.70 due within 6 months after the effective date and a complete annual report based on the product's anniversary date of U.S. approval due in the 7th to 12th month after the effective date). After the first year, applicants would only be required to submit one annual report to FDA each year.

This proposed rule does not affect the existing reporting requirements issued in the final rule of December 2, 1998 (63 FR 66632). Any changes to the provisions in the final rule of December 2, 1998, that are proposed in this rule would be in effect on the effective date of any final rule that may issue based on this proposed rule.

2. Annual **Federal Register** Report

Consistent with section 506B(c) of the act, FDA will publish annually a report in the **Federal Register**. This report will provide a brief summary of the status of postmarketing study commitments for approved drugs and licensed biological products that applicants have submitted to FDA under proposed §§ 314.81(b)(2)(vii) and 601.70. The report will include the number of pending, ongoing, delayed, and terminated postmarketing study commitments, as well as the number of final study reports that have been submitted to FDA, the number of study commitments that FDA has deemed fulfilled, and the number of applicants that failed to submit a status report to the agency for unfulfilled postmarketing study commitments. Detailed information regarding the status of these postmarketing studies will be posted on FDA's web page at ''http://www.fda.gov''. The web site will contain, at a minimum, the following information for each postmarketing study commitment: Name of the applicant, application number, product name, dosage form, product use category, type of study, commitment description, commitment date, projected study completion date, current status of commitment, applicant summary of status, annual report due date, and date annual report received.

III. Request for Comments

Interested persons may, on or before February 14, 2000, 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.

IV. Environmental Impact

The agency has determined under 21 CFR 25.30(h) 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.

V. Analysis of Impacts

FDA has examined the impact of this proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612). 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). Under the Regulatory Flexibility Act, if a rule would have a significant economic impact on a substantial number of small entities, the agency must analyze regulatory options that would minimize any significant impact of the rule on small entities. Title II of the Unfunded Mandates Reform Act (2 U.S.C. 1501 *et seq.*) requires that agencies prepare a written statement and economic analysis before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector of $100 million (adjusted annually for inflation) in any 1 year.

The agency believes that this rule is consistent with the principles set out in the Executive Order and in these two statutes. OMB has determined that the proposed rule is a significant regulatory action as defined by the Executive Order and so is subject to review. The rule would require applicants that have committed, in writing, to conduct a postmarketing study for an approved drug or biologic product to submit annual reports on the progress of the study or on the reasons for the failure of the applicant to conduct, complete, and report the study. The rule would permit FDA to publicly disclose information concerning these postmarketing studies, thereby providing patients, consumers, and the medical community with access to important and useful information.

A. Nature of Impact

Currently, applicants holding approved NDA's or ANDA's are required to submit annual reports to the agency that include information on the current status of any postmarketing studies of the drug product performed by, or on the behalf of the applicant. Although the proposed rule prescribes the format for the required information, this requirement would add no new economic burden for the majority of NDA and ANDA applicants. About half of the applicants holding approved NDA's or ANDA's with outstanding postmarketing study commitments made prior to the enactment of FDAMA may incur a small cost the first year, if their annual report is due within the last 6 months after the effective date of issuance of the final rule and they must submit one initial report within the first 6 months after the effective date. FDA estimates that there will be approximately 116 such reports submitted, which will require about 16 hours per report to complete. Assuming an average wage rate of $35 per hour,

the estimated, one-time cost of this provision is $64,960.

Applicants with licensed biological products are currently required to submit information on postmarketing studies in pediatric populations in annual reports to the agency. These applicants will incur additional costs to comply with the proposed requirements in this proposed rule. The agency estimates that about 33 applicants will submit approximately 43 postmarketing status reports annually for approved licensed biological products. As the reporting requirements are not extensive and the information is readily accessible to the applicant, FDA estimates that establishments will require about 16 hours to complete the required information. Assuming an average wage rate of $35 per hour, the estimated incremental cost of the annual reporting requirement will be $560 per report, for an industry total of $24,080 per year. As with applicants holding NDA's or ANDA's, a few applicants with licensed biological products with outstanding postmarketing study commitments may also incur an additional, one-time cost because they must submit their initial report within the first 6 months after the effective date of the final rule and an annual report within the last 6 months of the year. FDA estimates there will be approximately seven such reports, for a total one-time cost of about $4,000.

B. Small Business Impacts

The requirements in this proposed rule will not have a significant economic impact on a substantial number of small entities. Although it is possible that some firms may feel added pressure to honor the agreed upon commitments, the agency does not expect the proposed rule to result in an increased number of completed postmarketing studies. Nor does it believe that applicants will incur significantly increased costs from completing studies earlier than intended, as a result of the reporting, tracking, and disclosure activities implemented by the agency. Because affected applicants holding NDA's and ANDA's must currently submit annual reports to the agency, they already have procedures in place to monitor their postmarketing studies. The additional reporting requirement for applicants holding approved BLA's and the reformatting of the annual reports for applicants holding NDA's and ANDA's would be minimal. To simplify the reporting requirement further, however, the agency will publish a guidance for industry to aid applicants in preparing reports in the proper format.

C. Conclusion

The previous cost estimates demonstrate that this rule is not economically significant under Executive Order 12866. The Unfunded Mandates Reform Act does not require a cost-benefit analysis of this rule, because the rule will not result in an expenditure by State, local, or tribal governments, in the aggregate, or by the private sector of $100 million in any 1 year. Finally, the agency certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities.

VI. The Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by OMB under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). A description of these provisions is shown below with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing the instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Reporting the Status of Postmarketing Studies for Human Drugs and Licensed Biological Products.

Description: Section 506B of the act provides FDA with additional authority for monitoring the progress of postmarketing studies that companies have made a commitment to conduct and also requires the agency to make the status of these studies publicly available.

Under section 506B(a) of the act, applicants that have committed to conduct a postmarketing study for an approved human drug or biological product must submit to FDA a report of the progress of the study or the reasons for the failure of the applicant to conduct the study. This report must be submitted within 1 year after the U.S. approval of the product and annually thereafter until the study is completed or terminated. Under §§ 314.81(b)(2)(vii) and (b)(2)(viii), and 601.70(b), information submitted in a status report would be limited to that which is needed to sufficiently identify each applicant that has committed to conduct a postmarketing study, the status of the study that is being reported, and the reasons, if any, for the applicant's failure to conduct, complete, and report the study.

Currently under § 314.81(b)(2), applicants holding an NDA or an ANDA must submit status reports on postmarketing studies for the approved human drug product as part of an annual report to FDA. The agency is proposing to amend § 314.81(b)(2)(vii) to specify information that must be included in status reports submitted under section 506B of the act (studies of clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology that are required by FDA or that an applicant commits, in writing, to conduct either at the time of approval of an application or a supplement to an application or after approval of an application or supplement). Proposed § 314.81(b)(2) also adds paragraph (b)(2)(viii) which would require status information on any postmarketing study commitments not reported under paragraph (b)(2)(vii) that are being performed by, or on behalf of, the applicant; and paragraph (b)(2)(ix) which would allow the applicant to list any open regulatory business with FDA concerning the drug product subject to the application. For licensed biological products, FDA proposes to create § 601.70 to require postmarketing status reports for studies of clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology that are required by FDA or that an applicant of a BLA commits to conduct, in writing, at the time of approval of an application or a supplement to an application or after approval of an application or a supplement. FDA is also proposing to revise § 601.37(c) to require that the status of postmarketing pediatric studies described in proposed § 601.70 be reported under proposed § 601.70 rather than § 601.37.

This proposed rule is intended to provide FDA with specific procedures for monitoring the progress of postmarketing studies that companies have made a commitment, in writing, to conduct and also to permit the agency to make the status of these studies publicly available.

Description of Respondents: Applicants holding approved

applications for human drugs and biological products that have committed to conduct postmarketing studies.

Under current § 314.81(b)(2), applicants with approved NDA's and ANDA's for human drugs are required to submit to the agency two copies of the annual reports that must include information on the current status of any postmarketing study (OMB No. 0910–0001).

Proposed § 314.81(b)(2)(vii), (b)(2)(viii), and (b)(2)(ix) would expressly require status information to be provided in a specific format as part of the status reports of postmarketing study commitments (clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology), a subpart of the annual report. Based on past experience, the agency estimates that each applicant holding an approved NDA or ANDA would expend an additional 8 hours, to reformat the annual report. This is a one-time burden required under proposed § 314.81(b)(2)(vii). Based on the number of drug applicants in past years who have committed to conduct postmarketing studies, the agency estimates that this provision would apply to approximately 183 applicants and approximately 462 postmarketing studies.

Based upon information obtained from the Center for Biologics Evaluation and Research's computerized application and license tracking database, the agency estimates that approximately 33 applicants with 43 approved BLA's have committed to conduct approximately 86 postmarketing studies (clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology) and would be required to submit an annual progress report on those postmarketing studies under proposed § 601.70. Proposed § 601.70 requires postmarketing studies status reports for the first time for biological products. Based on past experience with reporting under § 314.81(b)(2), the agency estimates that approximately 8 hours annually is required for an applicant to gather, complete, and submit the appropriate information for each report (approximately two studies per report). Included in these 8 hours is the time necessary to initially format the status report.

Applicants holding NDA's, ANDA's, and BLA's whose anniversary date of U.S. approval of the application falls within the latter half of the year after the effective date of any final rule that may issue based on this proposed rule are required under section 506B of the act to submit an initial report to FDA for postmarketing studies committed to be conducted prior to November 21, 1997, within 6 months after the effective date of any final rule in addition to the reports required by the final rule. This information collection is a statutory requirement for which the proposed regulations add no additional burden other than prescribing the format. The burden of setting up the format is calculated under §§ 314.81(b)(2)(vii) and 601.70(b).

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
314.81(b)(2)(vii), (b)(2)(viii), (b)(2)(ix)[2]	183	2.5	462	8	3,696
601.70(b) and (d)	33	2.6	86	8	688
Total					4,384

[1] There are no capital costs or operating and maintenance costs with this collection of information.
[2] One-time burden for reformatting annual report.

In compliance with section 3507(d) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)), the agency has submitted the information collection provisions of this proposed rule to OMB for review. Interested persons are requested to send comments regarding this information collection by January 3, 2000, to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Desk Officer for FDA.

VII. Reference

The following reference has been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. ''Postmarketing Studies of Prescription Drugs,'' Department of Health and Human Services, Office of the Inspector General Final Report, May 1996.

List of Subjects

21 CFR Part 314

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

21 CFR Part 601

Administrative practice and procedure, Biologics, Confidential business information.

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 314 and 601 be amended as follows:

PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG

1. The authority citation for 21 CFR part 314 is revised to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 356b, 371, 374, 379e.

2. Section 314.81 is amended by revising the introductory text of paragraph (b)(2), by revising paragraph (b)(2)(vii), and by adding paragraphs (b)(2)(viii) and (b)(2)(ix) to read as follows:

§ 314.81 Other postmarketing reports.

* * * * *

(b) * * *

(2) *Annual report.* The applicant shall submit the following information each year within 60 days of the anniversary date of U.S. approval of the application. The applicant shall submit two copies of the report to the FDA division responsible for reviewing the application. Each annual report is required to be accompanied by a completed transmittal Form FDA–2252 (Transmittal of Annual Reports for Drugs for Human Use), which may be obtained from the PHS Forms and Publications Distribution Center, 12100 Parklawn Dr., Rockville, MD 20857, and is required to include all the information required under this section that the applicant received or otherwise obtained during the annual reporting interval, which ends on the U.S. anniversary date. The report is required to contain in the order listed:

* * * * *

(vii) *Status reports of postmarketing study commitments.* A status report of each postmarketing study of the drug product concerning clinical safety, clinical efficacy, clinical pharmacology,

and nonclinical toxicology that is required by FDA (e.g., pediatric studies) or that the applicant has committed, in writing, to conduct either at the time of approval of an application for the drug product or a supplement to an application, or after approval of an application or a supplement. For pediatric studies, the status report shall include a statement indicating whether postmarketing clinical studies in pediatric populations were required by FDA under § 201.23 of this chapter. The status of these postmarketing studies shall be reported annually until FDA notifies the applicant, in writing, that the agency concurs with the applicant's determination that the study commitment has been fulfilled or that the study is either no longer feasible or would no longer provide useful information.

(*a*) *Content of status report.* The following information shall be provided for each postmarketing study reported under this paragraph:

(*1*) *Applicant's name.*

(*2*) *Product name.* Include the approved drug product's established name and proprietary name, if applicable.

(*3*) *NDA, ANDA (abbreviated new drug application), or supplement number.*

(*4*) *Date of product's U.S. approval.*

(*5*) *Date of postmarketing study commitment.*

(*6*) *Description of postmarketing study commitment.* For clinical studies, include the purpose of the postmarketing study, the patient population addressed by the study, the number of patients and/or subjects to be included in the study, and the indication and dosage(s) that are to be studied. For nonclinical studies, include the type and purpose of the study.

(*7*) *Schedule for conduct, completion, and reporting of the postmarketing study commitment.* Include projected dates for initiation of the different phases of the study, for completion of the study, and for submission of the final study report to FDA. Provide a revised schedule, in addition to the original schedule, if the original schedule was revised in the previous report.

(*8*) *Current status of the postmarketing study commitment.* Categorize the status of each postmarketing study using one of the following terms that describes the study's status on the anniversary date of U.S. approval of the application or other agreed upon date:

(*i*) *Pending.* The study has not been initiated.

(*ii*) *Ongoing.* The study is proceeding according to or ahead of the original schedule described under paragraph (b)(2)(vii)(*a*)(*7*) of this section. Include the date the study was completed, if a study has been completed but the final study report has not been submitted to FDA.

(*iii*) *Delayed.* The study is proceeding but is behind the original schedule described under paragraph (b)(2)(vii)(*a*)(7) of this section.

(*iv*) *Terminated.* The study was ended before completion.

(*v*) *Submitted.* The study has been completed or terminated and a final study report has been submitted to FDA. Include the date the final study report was submitted to FDA.

(*9*) *Explanation of the study's status.* Provide a brief description of the status of the study, including the number of patients and/or subjects enrolled to date and an explanation of the study's status identified under paragraph (b)(2)(vii)(*a*)(*8*) of this section. Provide a revised schedule, as well as the reason(s) for the revision, if the schedule under paragraph (b)(2)(vii)(*a*)(*7*) of this section has changed since the last report.

(*b*) *Public disclosure of information.* Except for the information described in this paragraph, FDA may publicly disclose any information concerning a postmarketing study, within the meaning of paragraph (b)(2)(vii) of this section, if the agency determines that the information is necessary to identify the applicant or to establish the status of the study including the reasons, if any, for failure to conduct, complete, and report the study. Information necessary to establish the status of a postmarketing study includes the study protocol, patient accrual rates, reports of unexpected suspected adverse drug reactions, and study results. Under this section, FDA will not publicly disclose trade secrets, as defined in § 20.61 of this chapter, or information, described in § 20.63 of this chapter, the disclosure of which would constitute an unwarranted invasion of personal privacy.

(viii) *Status of other postmarketing studies.* A status report of any postmarketing study not included under paragraph (b)(2)(vii) of this section that is being performed by, or on behalf of, the applicant. The applicant shall provide information as prescribed under paragraphs (b)(2)(vii)(*a*)(*1*) through (b)(2)(vii)(*a*)(*9*) of this section for each of the postmarketing studies required to be reported under this paragraph.

(ix) *Log of outstanding regulatory business.* To facilitate communications between FDA and the applicant, the report may, at the applicant's discretion, also contain a list of any open regulatory business with FDA concerning the drug product subject to the application (e.g., a list of the applicant's unanswered correspondence with the agency, a list of the agency's unanswered correspondence with the applicant).

PART 601—LICENSING

3. The authority citation for 21 CFR part 601 is revised to read as follows:

Authority: 15 U.S.C. 1451–1561; 21 U.S.C. 321, 351, 352, 353, 355, 356b, 360, 360c–360f, 360h–360j, 371, 374, 379e, 381; 42 U.S.C. 216, 241, 262, 263, 264; sec. 122, Pub. L. 105–115, 111 Stat. 2322 (21 U.S.C. 355 note).

4. Section 601.37 is amended by revising the second sentence in paragraph (c) to read as follows:

§ 601.37 Annual reports of postmarketing pediatric studies.

* * * * *

(c) * * * The statement shall include whether postmarketing clinical studies in pediatric populations were required or agreed to, and, if so, the status of these studies shall be reported to FDA in annual progress reports of postmarketing studies under § 601.70 rather than under this section.

5. Subpart G, consisting of § 601.70, is added to part 601 to read as follows:

Subpart G—Postmarketing Studies

§ 601.70 Annual progress reports of postmarketing studies

(a) *General requirements.* This section applies to all required postmarketing studies (e.g., pediatric studies) and postmarketing studies that an applicant has committed, in writing, to conduct either at the time of approval of an application or a supplement to an application, or after approval of an application or a supplement. Postmarketing studies within the meaning of this section are those that concern:

(1) Clinical safety;

(2) Clinical efficacy;

(3) Clinical pharmacology; and

(4) Nonclinical toxicology.

(b) *What to report.* Each applicant of a licensed biological product shall submit a report to FDA on the status of postmarketing studies for each approved product application. The report shall include the status of each study which is required by FDA (e.g., pediatric studies) or which the applicant has committed, in writing, to conduct, including any reasons for the applicant's failure to conduct or to progress with the study. The status of these postmarketing studies shall be

reported annually until FDA notifies the applicant, in writing, that the agency concurs with the applicant's determination that the study commitment has been fulfilled, or that the study is either no longer feasible or would no longer provide useful information. Each annual progress report shall be accompanied by a completed transmittal Form FDA–2252, which may be obtained from the PHS Forms and Publications Distribution Center, 12100 Parklawn Dr., Rockville, MD 20857, and shall include all the information required under this section that the applicant received or otherwise obtained during the annual reporting interval, which ends on the U.S. anniversary date. The report shall provide the following information for each postmarketing study:

(1) *Applicant's name.*

(2) *Product name.* Include the approved product's proper name and the proprietary name, if applicable.

(3) *Biologics license application (BLA)/reference or supplement number.* The biologics license application number, reference number, or supplement number of the approved product.

(4) *Date of product's U.S. approval.*

(5) *Date of postmarketing study commitment.*

(6) *Description of postmarketing study commitment.* For clinical studies, include the purpose of the postmarketing study, the patient population addressed by the postmarketing study, the number of patients and/or subjects to be included in the study, and the indication and dosage(s) that are to be studied. For nonclinical studies, include the type and purpose of the study.

(7) *Schedule for conduct, completion, and reporting of the postmarketing study commitment.* Include projected dates for initiation of the different phases of the study, for completion of the study, and for submission of the final study report to FDA. Provide a revised schedule, in addition to the original schedule, if the original schedule was revised in the previous report.

(8) *Current status of the postmarketing study commitment.* Categorize the status of each postmarketing study using one of the following terms that describes the study's status on the anniversary date of the U.S. approval of the application or other agreed date:

(i) *Pending.* The study has not been initiated.

(ii) *Ongoing.* The study is proceeding according to or ahead of the original schedule described under paragraph (b)(7) of this section. Include the date the study was completed, if a study has been completed but the final study report has not been submitted to FDA.

(iii) *Delayed.* The study is proceeding but is behind the original schedule described under paragraph (b)(7) of this section.

(iv) *Terminated.* The study was ended before completion.

(v) *Submitted.* The study has been completed or terminated, and a final study report has been submitted to FDA. Include the date the final study report was submitted to FDA.

(9) *Explanation of the study's status.* Provide a brief description of the status of the study, including the number of patients and/or subjects enrolled to date and an explanation of the study's status identified under paragraph (b)(8) of this section. Provide a revised schedule, as well as the reason(s) for the revision, if the schedule under paragraph (b)(7) of this section has changed since the previous report.

(c) *When to report.* Annual progress reports for postmarketing study commitments entered into by applicants shall be reported to FDA within 60 days of the anniversary date of the U.S. approval of the application for the product.

(d) *Where to report.* Submit two copies of the annual progress report of postmarketing studies to the Food and Drug Administration, Center for Biologics Evaluations and Research, Document Control Center (HFM–99), suite 200N, 1401 Rockville Pike, Rockville, MD 20852–1448.

(e) *Public disclosure of information.* Except for the information described in this paragraph, FDA may publicly disclose any information concerning a postmarketing study, within the meaning of this section, if the agency determines that the information is necessary to identify an applicant or to establish the status of the study including the reasons, if any, for failure to conduct, complete, and report the study. Information necessary to establish the status of a postmarketing study includes the study protocol, patient accrual rates, reports of unexpected suspected adverse drug experiences, and study results. Under this section, FDA will not publicly disclose trade secrets, as defined in § 20.61 of this chapter, or information described in § 20.63 of this chapter, the disclosure of which would constitute an unwarranted invasion of personal privacy.

Dated: August 9, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 99–31123 Filed 11–30–99; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1309

[DEA NUMBER 185–P]

RIN 1117–AA50

Chemical Registration and Reregistration Fees

AGENCY: Drug Enforcement Administration (DEA), Justice.

ACTION: Proposed rule.

SUMMARY: The Drug Enforcement Administration (DEA) proposes to amend its application fees for registration and reregistration of manufacturers, distributors, importers, and exporters of List I chemicals, as authorized by section 3(a) of the Domestic Chemical Diversion Control Act of 1993 (DCDCA), reducing the fees from $595 to $326 for initial registration, and the reregistration fees from $477 to $171. Fees for retail registrants will increase from $255 to $326 for registration, and from $116 to $171 for reregistration. Office of Management and Budget (OMB) Circular A–25 requires a periodic review of user charges for agency programs. This review will bring fees into alignment with current changes in costs or market values.

DATES: Written comments or objections must be submitted on or before January 31, 2000.

ADDRESSES: Comments and objections should be submitted in quintuplicate to the Deputy Assistant Administrator, Office of Diversion Control, Drug Enforcement Administration, Washington, DC 20537, Attention: DEA Federal Register Representative/CCR.

FOR FURTHER INFORMATION CONTACT: Patricia Good, Chief, Liaison and Policy Section, Office of Diversion Control, Drug Enforcement Administration, Washington, DC 20537. Telephone (202) 307–7297.

SUPPLEMENTARY INFORMATION:

Impact of the Proposed Rule

What Is the Effect of This Proposed Rule, and to Whom Does It Apply?

The Drug Enforcement Administration (DEA) proposes to reduce the registration and