Manufacturers Association (NDMA) (Ref. 1) to provide industry an opportunity to discuss its position on FDA's proposed rule for OTC vaginal contraceptive drug products. NDMA opposed the requirement of applications for these products and requested that FDA reconsider its position to reject monograph standards for OTC vaginal spermicides.

In the Federal Register of October 30, 1996 (61 FR 55990), FDA announced a joint meeting of the Nonprescription Drugs, Reproductive Health Drugs, Anti-Infective Drugs, and Antiviral Drugs Advisory Committees. The meeting took place on November 20–22, 1996, at the Holiday Inn-Gaithersburg, Two Montgomery Village Ave., Gaithersburg, MD. On November 22, 1996, the committees discussed proposals and guidance for clinical efficacy studies on marketed OTC vaginal spermicides. Issues for discussion included the type of data and quality of both in vitro and in vivo data needed to support and ensure spermicidal efficacy in final formulation.

Because the issues have a direct impact on FDA's rulemaking on OTC vaginal contraceptive drug products, the agency is reopening the administrative record to specifically allow for comments on the matters discussed at the November 22, 1996, meeting. Transcripts of the November 22, 1996, meeting may be requested (by mail or fax) from the Freedom of Information Staff (HFI–35), 5600 Fishers Lane, rm. 12A–16, Rockville, MD 20857, 301–443–6310; or FAX 301–443–1726. Requests should specify date of meeting, name of committee, and a description of document(s) requested. The agency requests data and information regarding clinical efficacy studies, and in vivo and in vitro data needed to support and ensure spermicidal efficacy in final formulation. Any individual or group may, on or before March 3, 1997, submit to the Dockets Management Branch (address above), comments and data specifically limited and relevant to the matters discussed at the November 22, 1996, meeting. Two copies of any comments are to be submitted, except that individuals may submit one copy. All comments are to be identified with the docket number found in brackets in the heading of this document. The administrative record will remain open until March 3, 1997.

Reference

(1) Minutes of meeting between FDA and NDMA, September 24, 1996, coded MM1, Docket No. 80N–0280, Dockets Management Branch.

Dated: December 3, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–32273 Filed 12–18–96; 8:45 am]

BILLING CODE 4160–01–F

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21 CFR Part 812

[Docket No. 96N–0299]

Investigational Device Exemptions; Treatment Use

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing procedures to allow for the treatment use of investigational devices. These procedures are intended to facilitate the availability of promising new therapeutic and diagnostic devices to desperately ill patients as early in the device development process as possible, i.e., before general marketing begins, and to obtain additional data on the device's safety and effectiveness. These procedures would apply to patients with serious or immediately life-threatening diseases or conditions for which no comparable or satisfactory alternative device, drug, or other therapy exists.

DATES: Submit written comments by March 19, 1997. Written comments on the information collection requirements should be submitted by January 21, 1997. FDA proposes that any final rule that may issue based on this proposal become effective 30 days after date of publication of the final rule.

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

FOR FURTHER INFORMATION CONTACT: Joanne R. Less, Office of Device Evaluation (HFZ–403), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–1190.

SUPPLEMENTARY INFORMATION:

I. Background

In the Federal Register of May 22, 1987 (52 FR 19466), FDA published a final rule that codified procedures authorizing the treatment use of investigational new drugs (IND's) (hereinafter referred to as the treatment IND regulation). In publishing the treatment IND regulation, FDA was responding to an increased demand from patients as well as from health professionals to permit broader availability of investigational drugs to treat serious diseases for which there were no satisfactory alternative treatments. For similar reasons, FDA is now proposing to amend its Investigational Device Exemption (IDE) regulations (part 812 (21 CFR part 812)). With minor exceptions, the proposed rule parallels the regulation for treatment use of investigational new drugs and extends those provisions to cover the treatment use of investigational devices, including diagnostic devices. The proposed rule is intended to facilitate the availability of promising new devices to patients as early in the device development process as possible while safeguarding against commercialization of the devices and ensuring the integrity of controlled clinical trials.

II. Summary of the Proposed Rule

The proposed rule amends part 812 by adding proposed § 812.36, which parallels the IND treatment use provisions contained in 21 CFR 312.34 and 312.35. The proposed rule consists of the following provisions.

A. Purpose

Proposed § 812.36(a) provides for the treatment use of investigational devices in order to facilitate the availability of promising new devices to desperately ill patients as early in the device development process as possible, before general marketing begins, and to obtain additional data on the device's safety and effectiveness.

B. Criteria

Proposed § 812.36(b) specifies that treatment use of an investigational device would only be considered when the following criteria are satisfied: (1) The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition; (2) there is no comparable or satisfactory alternative device or other therapy available to treat or diagnose that stage of the disease or condition in the intended patient population; (3) the device is under investigation in a controlled clinical trial under an approved IDE, or all clinical trials have been completed; and (4) the sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the

investigational device with due diligence.

An example of approved devices which would have met the proposed treatment IDE criteria are nonthoracotomy (transvenous) defibrillation leads. These leads would have met the proposed criteria because: (1) They are intended to treat immediately life-threatening conditions; i.e., sudden cardiac death and ventricular tachyarrhythmia; (2) there were no comparable or satisfactory alternative devices (no other leads could be placed in the patient without opening the chest cavity); (3) the devices were under investigation under controlled clinical trials under approved IDE's; and (4) the sponsors of the controlled clinical trials pursued marketing approval of the leads with due diligence.

1. Definitions

Proposed § 812.36(a) defines an ''immediately life-threatening disease or condition'' as a stage of a disease or condition in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. Generally, an immediately life-threatening illness or condition is one that poses a significant threat that the patient will die from the illness or condition unless the course of the disease is promptly altered to reduce that possibility.

As in the treatment IND regulation, this definition does not mean that a clinician would have to make a prognosis with exact precision, but is meant only to provide a general yardstick for decisionmaking purposes (for example, a reasonable expectation of death within 6 months). (See 52 FR 19466 at 19467.) FDA recognizes that the medical judgment of the treating physician must carry considerable weight in deciding whether an illness poses a sufficient threat to justify treating patients with a device for which safety or effectiveness has not yet been fully demonstrated. FDA's statutory responsibility with regard to investigational devices, however, necessitates that it retain authority to review the appropriateness of treatment use and to ensure that such use does not constitute commercialization of the investigational device. Therefore, FDA will apply a common sense interpretation of the term ''immediately life-threatening,'' in that the agency would not normally consider death within more than a year to be immediately life-threatening, but would consider death within several days or several weeks to be an overly restrictive interpretation of the term. (*Id.*)

The phrase ''or in which premature death is likely without early treatment'' is intended to describe those fatal illnesses or conditions where death itself may not be imminent but where immediate treatment is necessary to prevent premature death. For example, a ventricular septal defect can lead to overloading of the right ventricle, failure of the left ventricle, and ultimately result in myocardial infarction (heart attack). Use of a septal closure device would help to prevent this progression of events and could quality, therefore, for treatment IDE use.

The stage of a disease or condition is important in determining whether it should be considered immediately life-threatening, serious, or not serious within the context of this treatment IDE regulation. For diseases such as multiple sclerosis, where some stages of the disease would not be considered serious, the regulation would not be applicable to those stages. In approving a treatment IDE, FDA will seek to define the intended patient population and, in medically appropriate cases, will limit treatment use to particular stages of a disease or condition or to patients with a particular set of symptoms.

To illustrate these categories further, the following diseases or conditions or stages of diseases would normally be considered to be immediately life-threatening: (1) Certain cardiac arrhythmias; (2) arteriovenous malformations; and (3) intracranial aneurysms.

In addition, the following would normally be considered serious diseases or conditions or serious stages of diseases: (1) Early stages of breast cancer; (2) proliferative vitreoretinopathy; and (3) advanced Parkinson's disease.

FDA recognizes that these are illustrative and not complete lists. The agency solicits suggestions for additional diseases or conditions that would provide greater breadth to these illustrative lists.

2. No Comparable or Satisfactory Alternative Device or Other Therapy

Similar to the treatment IND regulation, the absence of an alternative therapy is proposed as a prerequisite to granting a treatment IDE because one of the major principles underlying the proposed treatment IDE policy is that these devices would be necessary to fill an existing gap in the medical therapies available. (See 52 FR 19466 at 19468.) FDA recognizes that there should be flexibility in applying this concept so as to best serve desperately ill patients. The fact that the disease in question has existing approved therapies does not mean that the approved treatments are satisfactory for all patients. FDA will not be unduly restrictive in interpreting this criterion. FDA would view the criterion of no comparable or satisfactory alternative therapy as being met when there are patients who are not adequately treated by available therapies, even if the particular disease does respond in some cases to available therapy. This criterion would be met, for example, if the intended population is patients who have failed on an existing therapy (i.e., the existing therapy did not provide its intended therapeutic benefit or did not fully treat the condition); patients who could not tolerate the existing therapy (i.e., it caused unacceptable adverse effects); or patients who had other complicating diseases that made the existing therapy unacceptable (e.g., concomitant disease that makes available therapy contraindicated). The key is that the device proposed for treatment use addresses an unmet medical need in a defined patient population.

3. The Device is Under Investigation in a Controlled Clinical Trial Under an Approved IDE or All Clinical Trials Have Been Completed

To ensure that progress is being made towards a marketing application, FDA will only permit treatment use of an investigational device if the device is being studied or has been studied in a controlled clinical trial for the same use under an approved IDE. As in the treatment IND regulation, FDA expects that clinical studies will be of the kind that can reasonably be expected to provide data acceptable to FDA in determining the safety and effectiveness of the investigational device for its intended use. (See 52 FR 19466 at 19470.) Therefore, the agency would interpret the proposed regulation to mean that the controlled trial that serves as the underpinning for the treatment IDE must be sufficiently well-designed to provide such data. The agency anticipates that the controlled clinical trial would often be a concurrently controlled trial but recognizes other trial designs may be equally appropriate to establish safety and effectiveness. In a recent analysis of IDE approvals, the agency found more than 40 percent of the key clinical trials used historically controlled or self controlled designs. Thus, the term ''controlled clinical trial'' is intended to incorporate a number of different trial designs, rather than to specify any one particular design.

4. The Sponsor of the Controlled Clinical Trial is Pursuing Marketing Approval of the Investigational Device With Due Diligence

The term ''due diligence'' is intended to refer to an applicant's good faith effort to seek timely and expeditious marketing approval through actions intended to advance the progress of the clinical study or the subsequent marketing application. Pursuing marketing approval with due diligence is necessary as a precaution against the artificial prolonging of the investigational status of a device. In deciding whether a sponsor is pursuing marketing approval with due diligence, FDA will take into consideration all relevant factors. For example, full enrollment and monitoring of ongoing clinical trials(s); compliance with all IDE obligations, especially adverse reaction and annual reporting requirements; preparation and filing of a marketing application; and moving into compliance with FDA's Current Good Manufacturing Practices (CGMP's) would be considered as evidence of a sponsor's due diligence to pursue marketing approval.

C. Interpretation of Treatment IDE Criteria

FDA intends to interpret the above proposed criteria for treatment use of investigational devices in the same way FDA's Center for Devices and Radiological Health (CDRH) applies the criteria for expedited review of premarket approval applications, with which CDRH has considerable experience. FDA expects that most requests for treatment use would meet the criteria for expedited review, i.e., the device: (1) Is intended for a life-threatening or irreversibly debilitating condition for which there is no alternative therapy or for which the device provides a significant advance in safety and effectiveness over the existing alternatives; or (2) meets a specific public health need.

In addition, however, regardless of whether the device is intended to treat an immediately life-threatening or serious disease or condition, such devices may be considered for distribution under a treatment IDE only when there is promising evidence of safety and effectiveness, i.e., relatively late in the IDE process. Therefore, information that is relevant to the safety and effectiveness of the device for the intended treatment use that is available to a sponsor at the time a treatment use is requested should be submitted to the agency for review. The evidence should include relevant data gathered under the controlled clinical trial, as well as other supporting information the sponsor may have.

The criteria in this proposed rule are independent of, and should not be confused with or substituted for, the criteria to categorize IDE devices for Medicare coverage purposes. (See 60 FR 48417 at 48425, September 19, 1995.) For Medicare coverage purposes, IDE's are designated as either Category A (Experimental) or Category B (Nonexperimental/Investigational). Accordingly, Category A devices, even if given treatment IDE status, would continue to be categorized as experimental, and Category B devices would be considered to be nonexperimental only when used within the context of an approved clinical trial protocol.

D. Applications for Treatment Use

As in the treatment IND regulation, the proposed requirements for applications for treatment use would be minimal, but must be consistent with patient safety and proper use. (See 48 FR 26720 at 26729.) Each application would include, among other things, an explanation of the rationale for the use of the device; the criteria for patient selection; a description of clinical procedures, laboratory tests, or other measures to be used to monitor the effects of the device and to minimize risk; written procedures for monitoring the treatment use; information that is relevant to the safety and effectiveness of the device for the intended treatment use; and a written protocol describing the treatment use. The protocol should be written by the device firm supplying the device, with input from the clinical community and FDA as necessary to aid patient safety and proper use.

The agency recognizes that most of the information needed for a treatment IDE should already be available in the sponsor's IDE. Therefore, the additional supporting information to be submitted by the sponsor of the treatment IDE should focus on the safety and effectiveness of the device for the proposed treatment use. Applications for treatment use of an investigational device should be clearly identified as a ''Treatment IDE.''

E. FDA Action on Treatment IDE Applications

1. Approval of Treatment IDE's

Similar to the treatment IND regulations, proposed § 812.36(d)(1) provides that treatment use may begin 30 days after FDA receives the treatment IDE submission, unless FDA notifies the sponsor in writing earlier than the 30 days that the treatment use may or may not begin. FDA may approve the treatment use as proposed or approve it with modifications.

2. Disapproval or Withdrawal of Approval of Treatment IDE's

Under proposed § 812.36(d)(2)(i), FDA would have the authority to disapprove a treatment IDE if the threshold criteria proposed in § 812.36(b) are not met or the treatment IDE is incomplete, i.e., does not contain all the information proposed in § 812.36(c). FDA may also disapprove or withdraw approval of a treatment IDE if any of the grounds for disapproval or withdrawal of approval listed in § 812.30(b)(1) through (b)(5) apply.

Two additional proposed reasons for disapproval or withdrawal of approval of a treatment IDE relate to the amount of evidence necessary to support the intended treatment use. Under proposed § 812.36(d)(2)(iii), FDA may disapprove or withdraw approval of a treatment IDE for a serious disease if there is insufficient evidence of safety and effectiveness to support such use. In addition, under proposed § 812.36(d)(2)(iv), FDA may disapprove or withdraw approval of a treatment IDE for an immediately life-threatening illness if the available scientific evidence, taken as a whole, fails to provide a reasonable basis for concluding that the device: (1) May be effective for its intended use in its intended patient population; or (2) would not expose the patients to whom the device is to be administered to an unreasonable or significant additional risk of illness or injury.

As in the treatment IND regulation, FDA believes that the severity of the disease or condition needs to weigh heavily in the decision on whether to approve the investigational device for treatment use. This is because of the different risk-benefit considerations involved in treating patients under different disease conditions; the consequences of denying treatment use for a patient in an immediately life-threatening situation are much graver than for a patient with a serious, but not immediately life-threatening condition. The agency believes that this standard needs to be interpreted so that the level of evidence needed to support treatment use in diseases that are immediately life-threatening is significantly less than that needed for device approval and may be less than what would be needed to support treatment use in diseases that are serious, but not immediately life-threatening.

In order to reflect this continuum, the agency is proposing that FDA may deny

a request for treatment use for an immediately life-threatening illness if the available scientific evidence, taken as a whole, fails to provide a reasonable basis for concluding that the device: (a) May be effective for its intended use in its intended patient population; or (b) would not expose the patients in whom the device is to be used to an unreasonable or significant additional risk of illness or injury. The agency is proposing that FDA may deny a request for treatment use for serious, but not immediately life-threatening, disease conditions based on a finding of insufficient evidence of safety and effectiveness to support such use. For any of these disease conditions, the proposed rule provides for a standard of medical and scientific rationality—a requirement for sufficient scientific evidence on the basis of which experts reasonably could conclude that the device may be effective for the intended patient population.

The scientific evidence to be submitted in support of a treatment IDE may arise from a variety of sources. FDA expects that at least an early analysis of the data from the controlled clinical trial will ordinarily be available at the time a treatment IDE is submitted. However, FDA is committed to reviewing and considering all available evidence, including results of domestic and foreign clinical trials, animal data, and, where pertinent, in vitro data or bench testing. FDA will also consider clinical experience from outside a controlled trial, where the circumstances surrounding such experience provide sufficient indicia of scientific value.

Under proposed § 812.36(d)(2)(v), FDA may disapprove or propose to withdraw approval of a treatment IDE if there is reasonable evidence that the treatment use is impeding enrollment in, or otherwise interfering with the conduct or completion of, a controlled investigation of the same or another investigational device. As in the treatment IND regulation, FDA is concerned that the treatment IDE process does not become either a substitute for the research necessary to bring a device to market or a substitute for marketing itself. Therefore, the proposed rule incorporates specific approval criteria as well as reasons for disapproval or withdrawal of approval of a treatment IDE that reflect these agency concerns. These provisions are intended to ensure that the premarket availability of devices for treatment use does not impede the controlled clinical trial of the device or delay the timely development and submission of marketing applications for promising therapies.

Under proposed § 812.36(d)(2)(vi), FDA may disapprove or propose to withdraw approval of a treatment IDE if the device has received marketing approval or a comparable device or therapy becomes available to treat or diagnose the same indication in the same patient population for which the investigational device is being used. As previously discussed in this document, FDA believes that the proposed treatment IDE regulation can facilitate the availability of therapeutic or diagnostic tools for patients that have no other alternative available to them. However, if the treatment use device gains marketing approval/clearance, or if an alternative device becomes available for this specific indication, FDA may determine that the treatment IDE is no longer medically necessary, or needs to be restricted to patients for whom the recently approved product is not medically appropriate.

Under proposed § 812.36(d)(2)(vii), FDA may disapprove or propose to withdraw approval of a treatment IDE if the sponsor of the controlled clinical trial is not pursuing marketing approval/clearance with due diligence. As discussed in section II.B.4. of this document, pursuing marketing approval/clearance with due diligence is necessary as a precaution against the artificial prolonging of the investigational status of a device by a sponsor that is unable or unwilling to complete the clinical trial(s) and prepare a marketing application. Thus, if FDA determines that a sponsor is not demonstrating due diligence in pursuing marketing approval/clearance, FDA may disapprove or propose to withdraw approval of the treatment IDE.

Under proposed § 812.36(d)(2)(viii), FDA may disapprove or propose to withdraw approval of a treatment IDE if approval of the IDE for the clinical trial for the device has been withdrawn for reasons related to safety and effectiveness of the device. In such a situation, if FDA has determined that it is contrary to public health to allow the clinical trial of the device to continue due to issues related to safety and/or effectiveness of the device, the agency believes that treatment use of the device should also be curtailed.

Under proposed § 812.36(d)(2)(ix), FDA may disapprove a treatment IDE if the investigator(s) named in the application are not qualified by reason of their scientific training and experience to use the investigational device for the intended treatment use. While it is primarily the sponsor's responsibility to select only those investigators who are qualified to use the device under the treatment IDE, FDA may also review the qualifications of a proposed investigator if the need arises.

As with all IDE's, in addition to FDA's authority to disapprove or withdraw approval of the treatment IDE, FDA reserves the right to impose limits on the number of sites and/or patients who may receive the investigational device under a treatment use protocol. If FDA determines that it is necessary to impose limits on treatment use or to withdraw approval of the treatment IDE, the treatment IDE sponsor is responsible for ensuring that no new patients are enrolled and that the patients that had already been enrolled are followed in accordance with the treatment use protocol.

3. Notice of Disapproval or Withdrawal of Approval of Treatment IDE

Under proposed § 812.36(d)(3), FDA will follow the procedures set forth in § 812.30 if FDA disapproves or proposes to withdraw approval of a treatment IDE. In accordance with § 812.30(c), FDA will notify the sponsor in writing of FDA's decision to disapprove or propose to withdraw approval of a treatment IDE. The notice of disapproval or proposed withdrawal of approval of a treatment IDE will contain a complete statement of the reasons for disapproval or proposed withdrawal and a statement that the sponsor has an opportunity to request a part 16 hearing. FDA will provide the opportunity for a hearing before withdrawal of approval, unless FDA determines and specifies in the notice that continuation of use of the device will result in an unreasonable risk to patients and orders withdrawal of approval before any hearing.

F. Safeguards

FDA's objectives in regulating the clinical testing of new devices is the same as in regulating the clinical testing of new drugs; that is to protect the rights, safety, and welfare of human subjects involved in such testing while, at the same time, to facilitate the development and marketing of beneficial device therapies. (See 52 FR 19466 at 19468.) In order to fulfill these objectives, FDA has included in the proposed rule certain safeguards that were already in place as part of the IDE regulations and other safeguards that have been specifically designed for the proposed treatment use.

Under proposed § 812.36(e), treatment use of an investigational device is conditioned upon the sponsor and investigators complying with the IDE regulations, including distribution of

the device through qualified experts, maintenance of adequate manufacturing facilities, the submission of certain reports, and with the regulations governing informed consent (part 50 (21 CFR part 50)) and institutional review boards (21 CFR part 56).

The most significant of these safeguards are the following:

1. *The IDE regulations*. The obligations and responsibilities of the sponsor of a clinical trial also apply to the sponsor of a treatment IDE. For example, treatment IDE sponsors are responsible for maintaining control of the device by ensuring that only qualified experts receive the device under the treatment IDE protocol. Similarly, the responsibilities of a clinician using an investigational device for treatment use are the same as those imposed on an investigator participating in a clinical trial. In addition, as with investigational devices, the methods, facilities, and controls used for the manufacturing, processing, packaging, storage, and when appropriate, installation of the treatment use device must be adequate. Finally, as with all investigational devices, treatment IDE sponsor(s) or any person(s) acting for or on behalf of the treatment IDE sponsor(s) may not charge the subjects or investigators a higher price than is necessary to recover costs of research, development, manufacturing, and handling. However, because FDA is concerned that the existence of treatment IDE's may increase the risk of commercialization of investigational devices, FDA is soliciting comment on the appropriate approach to take with respect to charging for devices under a treatment IDE. Specifically, do the IDE and proposed treatment IDE regulations provide sufficient protection against commercialization? Is it appropriate for sponsors to recover research and development costs in addition to the cost of manufacturing and handling an investigational device? Should prior FDA approval of charging be required? FDA wants to adopt an approach that facilitates the availability of promising new devices to treat serious diseases early in the device development process, but does not want to undermine the integrity of controlled clinical trials or increase the likelihood that investigational products will be commercialized before safety and efficacy have been established.

2. *Submission of progress reports*. Under proposed § 812.36(f), in lieu of the annual reports required under 812.150(b)(5), the sponsor of a treatment IDE shall submit progress reports on a quarterly basis to all reviewing IRB's and FDA. See section G below for further explanation.

3. *Informed consent*. As in the treatment IND regulation, authorization to use an investigational device for treatment use is conditioned upon the practitioner obtaining the legally effective informed consent of the patient. See 52 FR 19466 at 19469. Clearly, there are risks in using experimental devices. Patients must be informed of the device's potential benefits and risks to help them decide whether the risks are appropriate and acceptable for their particular situation. Thus, the regulations governing informed consent, part 50, apply to the use of devices under a treatment IDE.

4. *IRB review*. Compliance with the IRB regulations will help to ensure that the rights, safety, and welfare of human subjects treated with an investigational device are protected, whether it be during a clinical investigation or under a treatment IDE. Therefore, FDA has determined that an IRB, either local or national, shall review and have authority to approve, require modifications to, or disapprove the treatment use of an investigational device.

G. Reporting Requirements

Under proposed § 812.36(f), in lieu of the annual reports submitted under § 812.150(b)(5), the sponsor of a treatment IDE shall submit progress reports on a quarterly basis to all reviewing IRB's and FDA. Similar to IDE progress reports, treatment use progress reports shall contain a summary of the safety and effectiveness information gathered under the treatment IDE, a summary of anticipated and unanticipated adverse device effects, the number of patients treated with the device under the treatment IDE, the names of the investigators participating in the treatment IDE, and a brief description of the sponsor's efforts to pursue marketing approval/clearance of the device. The sponsor of a treatment IDE is also responsible for submitting all other reports required under § 812.150.

III. 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.

IV. Analysis of Impacts

FDA has examined the impacts of the 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). 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.

Treatment use of an investigational device will only be considered when the criteria set out in section II.B. of this document are met. FDA believes that these limitations are necessary to ensure that devices are not commercialized before FDA determines that they are reasonably safe and effective for wider distribution.

Given the limited circumstances in which a treatment use of an investigational device may be considered, FDA estimates that about six investigational devices per year will meet the criteria for treatment use. FDA believes that the requirements for applications for treatment use of an investigational device would be minimal, but must be consistent with patient safety and proper use. Because relevant information already should be available to FDA in the sponsor's IDE, limited additional information relative to the safety and effectiveness of the device for treatment use would be required in the treatment IDE application. In fact, applications for treatment use may be submitted as supplements to the IDE for the controlled clinical trial in order to eliminate the additional burden that could result if sponsors were required to submit new applications. FDA estimates that the annual cost of submitting an application for treatment use and the necessary progress reports would be about $8,000 per application. Treatment use would benefit the public health by permitting wider distribution of life-saving devices while marketing approval is pending.

The proposed rule contains very specific provisions regarding the approval criteria as well as the reasons for disapproval or withdrawal of approval of a treatment IDE. This will assist sponsors in determining whether they have met the criteria for initial and continued approval of a treatment use IDE well in advance of their applications.

For the reasons set forth above, the Commissioner of Food and Drugs 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.

V. Paperwork Reduction Act of 1995

This proposed rule contains information collections which are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995. The title, description, and respondent description of the information collection are shown below with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, gathering and maintaining the data needed, and completing and reviewing the collection of information.

With respect to the following collection of information, FDA invites comments on: (1) Whether the proposed collection of information is necessary for 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: Investigational Device Exemptions; Treatment Use.

Description: The proposed rule is intended to permit broader availability of investigational devices to treat serious diseases for which there are not satisfactory alternative treatments. Under the proposed rule, treatment use of an investigational device would only be considered when the following criteria are satisfied: (1) The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition; (2) there is no comparable or satisfactory alternative device or other therapy available to treat or diagnose that stage of the disease or condition in the intended patient population; (3) the device is under investigation in a controlled clinical trial under an approved IDE, or all clinical trials have been completed; and (4) the sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

The proposed requirements for applications for treatment use would be minimal, but must be consistent with patient safety and proper use. Each application would include, among other things, an explanation of the rationale for the use of the device; the criteria for patient selection; a description of clinical procedures, laboratory tests, or other measures to be used to monitor the effects of the device and to minimize risk; written procedures for monitoring the treatment use; information that is relevant to the safety and effectiveness of the device for the intended treatment use; and a written protocol describing the treatment use. Sponsors of an approved treatment IDE would be required to submit quarterly progress reports.

Description of Respondents: Businesses or other for profit organizations.

ESTIMATED ANNUAL REPORTING BURDEN

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
812.36(c)	6	1	6	120	720
812.36(f)	6	4	24	20	480
Total					1,200

There are no operating and maintenance costs or capital costs associated with this information collection.

As required by section 3507(d) of the Paperwork Reduction Act of 1995, FDA has submitted the collections of information contained in the proposed rule to OMB for review. Other organizations and individuals should submit comments on the information collection requirements by January 21, 1997, and should direct them to the Office of Information and Regulatory Affairs, OMB (address above).

Lists of Subjects in 21 CFR Part 812

Health records, Medical devices, Medical research, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 812 be amended as follows:

Part 812—Investigational Device Exemptions

1. The authority citation for 21 CFR part 812 continues to read as follows:

Authority: Secs. 301, 501, 502, 503, 505, 506, 507, 510, 513–516, 518–520, 701, 702, 704, 721, 801 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331, 351, 352, 353, 355, 356, 357, 360, 360c–360f, 360h–360j, 371, 372, 374, 379e, 381); secs. 215, 301, 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 262, 263b–263n).

2. New § 812.36 is added to subpart B to read as follows:

§ 812.36 Treatment use of an investigational device.

(a) *General.* A device that is not approved for marketing may be under clinical investigation for a serious or immediately life-threatening disease or condition in patients for whom no comparable or satisfactory alternative device or other therapy is available. During the clinical trial or prior to final action on the marketing application, it may be appropriate to use the device in the treatment of patients not in the trial under the provisions of a treatment investigational device exemption (IDE). The purpose of this section is to facilitate the availability of promising new devices to desperately ill patients as early in the device development process as possible, before general marketing begins, and to obtain additional data on the device's safety and effectiveness. In the case of a serious disease, a device ordinarily may be made available for treatment use under this section after all clinical trials have been completed. In the case of an immediately life-threatening disease, a device may be made available for treatment use under this section prior to the completion of all clinical trials. For the purpose of this section, an ''immediately life-threatening'' disease means a stage of a disease in which there is a reasonable likelihood that

death will occur within a matter of months or in which premature death is likely without early treatment. For purposes of this section, ''treatment use'' of a device includes the use of a device for diagnostic purposes.

(b) *Criteria*. FDA shall consider the use of an investigational device under a treatment IDE if:

(1) The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;

(2) There is no comparable or satisfactory alternative device or other therapy available to treat or diagnose that stage of the disease or condition in the intended patient population;

(3) The device is under investigation in a controlled clinical trial under an approved IDE, or such clinical trials have been completed; and

(4) The sponsor of the investigation is actively pursuing marketing approval/clearance of the investigational device with due diligence.

(c) *Applications for treatment use*. (1) A treatment IDE application shall include, in the following order:

(i) The name, address, and telephone number of the sponsor of the treatment IDE;

(ii) The intended use of the device, the criteria for patient selection, and a written protocol describing the treatment use;

(iii) An explanation of the rationale for use of the device, including, as appropriate, either a list of the available regimens that ordinarily should be tried before using the investigational device or an explanation of why the use of the investigational device is preferable to the use of available marketed treatments;

(iv) A description of clinical procedures, laboratory tests, or other measures that will be used to evaluate the effects of the device and to minimize risk;

(v) Written procedures for monitoring the treatment use and the name and address of the monitor;

(vi) Instructions for use of the device and all other labeling as required under § 812.5(a) and (b);

(vii) Information that is relevant to the safety and effectiveness of the device for the intended treatment use. Information from other IDE's may be incorporated by reference to support the treatment use;

(viii) A statement of the sponsor's commitment to meet all applicable responsibilities under this part and part 56 of this chapter and to assure compliance of all participating investigators with the informed consent requirements of part 50 of this chapter; and

(ix) An example of the agreement to be signed by all investigators participating in the treatment IDE and certification that no investigator will be added to the treatment IDE before the agreement is signed.

(2) A licensed practitioner who receives an investigational device for treatment use under a treatment IDE is an ''investigator'' under the IDE and is responsible for meeting all applicable investigator responsibilities under this part and parts 50 and 56 of this chapter.

(d) *FDA action on treatment IDE applications*. (1) Approval of treatment IDE's. Treatment use may begin 30 days after FDA receives the treatment IDE submission at the address specified in § 812.19, unless FDA notifies the sponsor in writing earlier than the 30 days that the treatment use may or may not begin. FDA may approve the treatment use as proposed or approve it with modifications.

(2) Disapproval or withdrawal of approval of treatment IDE's. FDA may disapprove or withdraw approval of a treatment IDE if:

(i) The criteria specified in § 812.36(b) are not met or the treatment IDE does not contain the information required in § 812.36(c);

(ii) FDA determines that any of the grounds for disapproval or withdrawal of approval listed in § 812.30(b)(1) through (b)(5) apply;

(iii) The device is intended for a serious disease or condition and there is insufficient evidence of safety and effectiveness to support such use;

(iv) The device is intended for an immediately life-threatening disease or condition and the available scientific evidence, taken as a whole, fails to provide a reasonable basis for concluding that the device:

(A) May be effective for its intended use in its intended population; or

(B) Would not expose the patients to whom the device is to be administered to an unreasonable or significant additional risk of illness or injury;

(v) There is reasonable evidence that the treatment use is impeding enrollment in, or otherwise interfering with the conduct or completion of, a controlled investigation of the same or another investigational device;

(vi) The device has received marketing approval clearance or a comparable device or therapy becomes available to treat or diagnose the same indication in the same patient population for which the investigational device is being used;

(vii) The sponsor of the controlled clinical trial is not pursuing marketing approval/clearance with due diligence;

(viii) Approval of the IDE for the controlled clinical investigation of the device has been withdrawn; or

(ix) The clinical investigator(s) named in the treatment IDE are not qualified by reason of their scientific training and/or experience to use the investigational device for the intended treatment use.

(3) Notice of disapproval or withdrawal. If FDA disapproves or proposes to withdraw approval of a treatment IDE, FDA will follow the procedures set forth in § 812.30(c).

(e) *Safeguards*. Treatment use of an investigational device is conditioned upon the sponsor and investigators complying with the safeguards of the IDE process and the regulations governing informed consent (part 50 of this chapter) and institutional review boards (part 56 of this chapter).

(f) *Reporting Requirements*. In lieu of the annual reports required under § 812.150(b)(5), the sponsor of a treatment IDE shall submit progress reports on a quarterly basis to all reviewing IRB's and FDA. These reports shall be based on the period of time since initial approval of the treatment IDE and shall include a summary of the safety and effectiveness information gathered under the treatment IDE, a summary of anticipated and unanticipated adverse device effects, the number of patients treated with the device under the treatment IDE, the names of the investigators participating in the treatment IDE, and a brief description of the sponsor's efforts to pursue marketing approval/clearance of the device. The sponsor of a treatment IDE is responsible for submitting all other reports required under § 812.150.

§ 812.150 [Amended]

3. Section 812.150 *Reports* is amended by revising paragraph (b)(5) to read as follows:

* * * * *

(b) * * *

(5) *Progress reports*. At regular intervals, and at least yearly, a sponsor shall submit progress reports to all reviewing IRB's. In the case of a significant risk device, a sponsor shall also submit progress reports to FDA. In lieu of the annual reports, a sponsor of a treatment IDE shall submit

progress reports on a quarterly basis to all reviewing IRB's and FDA in accordance with § 812.36(f).

* * * * *

Dated: December 11, 1996.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 96–32186 Filed 12–18–96; 8:45 am]

BILLING CODE 4160–01–F

FEDERAL MINE SAFETY AND HEALTH REVIEW COMMISSION

29 CFR Part 2704

Implementation of Equal Access to Justice Act in Commission Proceedings

AGENCY: Federal Mine Safety and Health Review Commission.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Federal Mine Safety and Health Review Commission is proposing to revise its rules providing for the award of attorneys' fees and other expenses under the Equal Access to Justice Act (EAJA), 5 U.S.C. 504, applicable to eligible individuals and entities who are parties to administrative proceedings before the Commission. The proposed revisions to the rules are in response to amendments to the EAJA, enacted pursuant to Public Law 104–121, 110 Stat. 862 (1996), and effective on March 29, 1996. The proposed rules authorize fee awards under a newly-defined standard—when the Secretary of Labor's demand is substantially in excess of the decision of the Commission and is unreasonable when compared to that decision. The proposed rules also expand the definition of a ''party'' eligible for an award under this new standard to include ''a small entity'' as defined by 5 U.S.C. 601. The maximum hourly rate for attorneys' fees in all EAJA cases before the Commission is increased to $125. Finally, the Commission is revising its rules to provide that parties submit EAJA applications to the Chief Administrative Law Judge instead of the Chairman. The Commission invites public comments on these proposed rules.

DATES: Comments should be received by January 21, 1997.

ADDRESSES: Comments should be sent to Richard L. Baker, Executive Director, Federal Mine Safety and Health Review Commission, 1730 K Street, NW, 6th Floor, Washington, DC 20006. For the convenience of persons who will be reviewing the comments, it is requested that commenters provide an original and three copies of their comments.

FOR FURTHER INFORMATION CONTACT: Norman M. Gleichman, General Counsel, Office of the General Counsel, 1730 K Street, NW, 6th Floor, Washington, DC 20006, telephone 202–653–5610 (202–566–2673 for TDD Relay). These are not toll-free numbers.

SUPPLEMENTARY INFORMATION:

I. Background

Under the Commission's present rules, the EAJA applies to administrative adjudications, brought pursuant to the Federal Mine Safety and Health Act of 1977, 30 U.S.C. 801 *et seq.*, in which an eligible party prevails over the Department of Labor's Mine Safety and Health Administration. 29 CFR 2704.100 and 2704.103. Prior to the enactment of Public Law 104–121, prevailing parties could receive awards if they met the EAJA's eligibility standards (which set ceilings on the net worth and number of employees) and if the government's position was not ''substantially justified.''

Public Law 104–121 creates an additional standard under which eligible parties can obtain fees in administrative adjudications. The EAJA amendments authorize an award when a government ''demand'' is both ''substantially in excess of the decision of the adjudicative officer'' and ''unreasonable.'' *Id.* at 231(a). Under this standard, if the demand by the Secretary of Labor is substantially in excess of the judgment finally obtained by the Secretary and is unreasonable when compared with that judgment under the facts and circumstances of the case, the Commission shall award to the opposing party the fees and other expenses related to defending against the excessive demand, unless the party has committed a willful violation of law or otherwise acted in bad faith, or special circumstances make an award unjust. *Id.*

Public Law 104–121 also establishes a separate definition of a ''party'' for fee awards under the new standard. Parties that are eligible to apply for awards include ''small entit[ies] as defined in section 601 [of title 5].'' *Id.* at 231(b)(2). Title 5 U.S.C. 601(6) provides that ''small entity'' has ''the same meaning as the term[ ] 'small business'. . . .'' In turn, a ''small business'' is defined at 5 U.S.C. 601(3) as a ''small business concern'' under section 3 of the Small Business Act (15 U.S.C. 632). Section 632(a) authorized the Small Business Administration (SBA) to establish standards to specify when a business concern is ''small.'' The SBA has recently issued updated size standards for various types of economic activity, categorized by the Standard Industrial Classification System (SIC). 13 CFR 121.105. In defining the standards for small businesses engaged in mining, the SBA regulations count either annual receipts or numbers of employees. The number of employees or annual receipts specified is the maximum allowed for a concern and its affiliates to be considered small. 13 CFR 121.201. The standards for the mining industry are as follows:

DIVISION B—MINING:	
MAJOR GROUP 10—METAL MINING.	500 employees.
MAJOR GROUP 12—COAL MINING.	500 employees.
MAJOR GROUP 14—MINING AND QUARRYING OF NON-METALLIC MINERALS, EXCEPT FUELS.	500 employees.
EXCEPT:	
1081 Metal Mining Services.	$5 million.
1241 Coal Mining Services.	$5 million.
1481 Nonmetallic Minerals Services, Except Fuels.	$5 million.

13 CFR 121.201.

Finally, Public Law 104–121 increases the maximum fee award of an attorney or agent from $75.00 to $125.00 per hour. *Id.* at 231(b)(1).

II. Analysis of the Regulations

The present language of § 2704.100 providing for fee awards to prevailing parties when the Secretary's position is not substantially justified is unchanged. The Commission proposes to add new language to the rule to provide that an eligible party may receive an award if the demand of the Secretary is substantially in excess of the decision of the Commission and is unreasonable when compared with that decision, unless the applicant party has committed a willful violation of law or otherwise acted in bad faith or special circumstances make an award unjust. For purposes of this part, a decision of the Commission includes not only a decision by the Commission but also a decision by an administrative law judge that becomes final by operation by law.

The present language of § 2704.102 is revised to specify that recovery under the prevailing party standard is available for any adversary adjudication commenced before the Commission after August 5, 1984. Proposed language provides that, where an applicant seeks an award based on a substantially excessive and unreasonable demand of