

(ii) Require the manufacturer to disseminate an objective statement prepared by FDA that is based on data or other scientifically sound information available to the agency and bears on the safety or effectiveness of the drug or device for the new use; and

(3) Require the manufacturer to maintain records that will identify individual recipients of the information that is to be disseminated when such individual records are warranted due to special safety considerations associated with the new use.

(b) *Protocols/Studies*. Within 60 days after receiving a submission under this part, FDA shall:

(1) If the manufacturer has planned studies that will be needed for the submission of a supplemental application for the new use, review the manufacturer's proposed protocols and schedule for completing such studies and determine whether the proposed protocols are adequate and whether the proposed schedule for completing the studies is reasonable. FDA shall notify the manufacturer of its determination; or

(2) If the manufacturer has completed studies that the manufacturer believes would be an adequate basis for the submission of a supplemental application for the new use, conduct a review of the protocols submitted for such studies to determine whether they are adequate. FDA shall notify the manufacturer of its determination.

§ 99.303 Extension of time for completing planned studies.

(a) Upon review of a drug or device manufacturer's proposed protocols and schedules for conducting studies needed for the submission of a supplemental application for a new use, FDA may, with or without a request for an extension from the manufacturer, determine that such studies cannot be completed and submitted within 36 months. The agency may exercise its discretion in extending the time period for completing the studies and submitting a supplemental application. Extensions under this paragraph are not subject to any time limit, but shall be made before the manufacturer begins the studies needed for the submission of a supplemental application for the new use.

(b) The manufacturer may, after beginning the studies needed for the submission of a supplemental application for a new use, request in writing that FDA extend the time period for conducting studies needed for the submission of a supplemental application for a new use and submitting a supplemental application to FDA. FDA may grant or deny the request or, after consulting the manufacturer, grant an extension different from that requested by the manufacturer. FDA may grant a manufacturer's request for an extension if FDA determines that the manufacturer has acted with due diligence to conduct the studies needed for the submission of a supplemental application for a new use and to submit such a supplemental application to FDA in a timely manner and that, despite such actions, the manufacturer needs additional time to complete the studies and submit the supplemental application. Extensions under this paragraph shall not exceed 24 months.

(c) If FDA extends the time period for completing the studies and submitting a supplemental application under paragraph (a) of this section after the manufacturer has submitted a certification under § 99.201(a)(4)(ii)(B), or if FDA grants a manufacturer's request for an extension under paragraph (b) of this section, the manufacturer shall submit a new certification under § 99.201(a)(4)(ii)(B) that sets forth the timeframe within which clinical studies will be completed and a supplemental application will be submitted to FDA.

§ 99.305 Exemption from the requirement to file a supplemental application.

(a) Within 60 days after receipt of an application for an exemption from the requirement of a supplemental application, FDA shall approve or deny the application.

(1) If FDA does not act on the application for an exemption within the 60-day period, the application for an exemption shall be deemed to be approved.

(2) If an application for an exemption is deemed to be approved, FDA may, at any time, terminate such approval if it determines that the requirements for

granting an exemption have not been met. FDA shall notify the manufacturer if the approval is terminated.

(b) In reviewing an application for an exemption, FDA shall consider the materials submitted by the manufacturer and may consider any other appropriate information, including, but not limited to, any pending or previously approved applications for exemption submitted by the manufacturer.

(c) FDA may grant an application for an exemption if FDA determines that:

(1) It would be economically prohibitive for the manufacturer to incur the costs necessary to submit a supplemental application for a new use, which at a minimum requires:

(i) That existing data characterizing the safety and effectiveness of the drug or device, including data from the study described in the information to be disseminated are not adequate to support the submission of a supplemental application for the new use; and

(ii) That the cost of the study or studies for the new use reasonably exceeds the expected revenue from the new use minus the cost of goods sold and marketing and administrative expenses attributable to the new use of the product, and there are not less expensive ways to obtain the needed information; or

(2) It would be unethical to conduct clinical studies needed to support the submission of a supplemental application for the new use because:

(i) Existing data characterizing the safety and effectiveness of the drug or device, including data from the study described in the information to be disseminated are not adequate to support the submission of a supplemental application for the new use; and

(ii) Although available evidence would not support the submission of a supplemental application for the new use, the data are persuasive to the extent that withholding the drug or device in a controlled study would pose an unreasonable risk of harm to human subjects and no studies in different populations or of modified design can be utilized. In determining whether it would be unethical to conduct clinical studies, the agency shall consider, in addition to the persuasiveness of available evidence of effectiveness, whether

the new use of the drug or device is broadly accepted as current standard medical treatment or therapy.

Subpart E—Corrective Actions and Cessation of Dissemination

§ 99.401 Corrective actions and cessation of dissemination of information.

(a) *FDA actions based on post dissemination data.* If FDA receives data after a manufacturer has begun disseminating information on a new use and, based on that data, determines that the new use that is the subject of information disseminated under this part may not be effective or may present a significant risk to public health, FDA shall consult the manufacturer and, after such consultation, take appropriate action to protect the public health. Such action may include ordering the manufacturer to cease disseminating information on the new use and to take appropriate corrective action.

(b) *FDA actions based on information disseminated by a manufacturer.* If FDA determines that a manufacturer is disseminating information that does not comply with the requirements under this part, FDA may:

(1) Provide to the manufacturer an opportunity to bring itself into compliance with the requirements under this part if the manufacturer's noncompliance constitutes a minor violation of these requirements; or

(2) Order the manufacturer to cease dissemination of information and to take corrective action. FDA shall issue such an order only after it has:

(i) Provided notice to the manufacturer regarding FDA's intent to issue an order to cease dissemination; and

(ii) Provided to the manufacturer an opportunity for a meeting. FDA need not provide an opportunity for a meeting if the manufacturer certified that it will submit a supplemental application for the new use within 6 months of the date that dissemination can begin and the noncompliance involves a failure to submit such supplemental application.

(c) *FDA actions based on a manufacturer's supplemental application.* FDA may