

Such approval will be conditioned upon the applicant incorporating the specified labeling changes exactly as directed and upon the applicant submitting to FDA a copy of the final printed labeling before marketing. The notice of approval of an HDE will be published in the FEDERAL REGISTER in accordance with the rules and policies applicable to PMA's submitted under § 814.20. Following the issuance of an approval order, data and information in the HDE file will be available for public disclosure in accordance with § 814.9(b) through (h), as applicable.

(c) *Approvable letter.* FDA will send the applicant an approvable letter if the application substantially meets the requirements of this subpart and the agency believes it can approve the application if specific additional information is submitted or specific conditions are agreed to by the applicant. The approvable letter will describe the information FDA requires to be provided by the applicant or the conditions the applicant is required to meet to obtain approval. For example, FDA may require as a condition to approval:

(1) The submission of certain information identified in the approvable letter, e.g., final labeling;

(2) Restrictions imposed on the device under section 520(e) of the act;

(3) Postapproval requirements as described in subpart E of this part; and

(4) An FDA inspection that finds the manufacturing facilities, methods, and controls in compliance with part 820 of this chapter and, if applicable, that verifies records pertinent to the HDE.

(d) *Not approvable letter.* FDA will send the applicant a not approvable letter if the agency believes that the application may not be approved for one or more of the reasons given in § 814.118. The not approvable letter will describe the deficiencies in the application and, where practical, will identify measures required to place the HDE in approvable form. The applicant may respond to the not approvable letter in the same manner as permitted for not approvable letters for PMA's under § 814.44(f).

§ 814.118 Denial of approval or withdrawal of approval of an HDE.

(a) FDA may deny approval or withdraw approval of an application if the applicant fails to meet the requirements of section 520(m) of the act or of this part, or of any condition of approval imposed by an IRB or by FDA, or any postapproval requirements imposed under § 814.126. In addition, FDA may deny approval or withdraw approval of an application if, upon the basis of the information submitted in the HDE or any other information before the agency, FDA determines that:

(1) There is a lack of a showing of reasonable assurance that the device is safe under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(2) The device is ineffective under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(3) The applicant has not demonstrated that there is a reasonable basis from which to conclude that the probable benefit to health from the use of the device outweighs the risk of injury or illness, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment;

(4) The application or a report submitted by or on behalf of the applicant contains an untrue statement of material fact, or omits material information;

(5) The device's labeling does not comply with the requirements in part 801 or part 809 of this chapter;

(6) A nonclinical laboratory study that is described in the HDE and that is essential to show that the device is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling, was not conducted in compliance with the good laboratory practice regulations in part 58 of this chapter and no reason for the noncompliance is provided or, if it is, the differences between the practices used in conducting the study and the good laboratory practice regulations do not support the validity of the study;

(7) Any clinical investigation involving human subjects described in the

HDE, subject to the institutional review board regulations in part 56 of this chapter or the informed consent regulations in part 50 of this chapter, was not conducted in compliance with those regulations such that the rights or safety of human subjects were not adequately protected;

(8) The applicant does not permit an authorized FDA employee an opportunity to inspect at a reasonable time and in a reasonable manner the facilities and controls, and to have access to and to copy and verify all records pertinent to the application; and

(9) The device's HUD designation should be revoked in accordance with § 814.102(c).

(b) If FDA issues an order denying approval of an application, the agency will comply with the same notice and disclosure provisions required for PMA's under § 814.45(b) and (d), as applicable.

(c) FDA will issue an order denying approval of an HDE after an approvable or not approvable letter has been sent and the applicant:

(1) Submits a requested amendment but any ground for denying approval of the application under § 814.118(a) still applies;

(2) Notifies FDA in writing that the requested amendment will not be submitted; or

(3) Petitions for review under section 515(d)(3) of the act by filing a petition in the form of a petition for reconsideration under § 10.33 of this chapter.

(d) Before issuing an order withdrawing approval of an HDE, FDA will provide the applicant with notice and an opportunity for a hearing as required for PMA's under § 814.46(c) and (d), and will provide the public with notice in accordance with § 814.46(e), as applicable.

(e) Unless FDA otherwise determines that continued marketing under the HDE is inconsistent with the intent of section 520(m) of the act, FDA will not withdraw approval of an HDE solely because it is subsequently determined that the disease or condition for which the HUD is intended affects or is manifested in more than 4,000 people in the United States per year. However, this fact may serve as a basis for disapproving an extension request.

§ 814.120 Requests for extension.

(a) *Eligibility.* In response to a request by the holder of an HDE, FDA may extend the HDE for an additional 18-month term. An exemption may be extended more than once, and may be extended after the expiration of the 5-year period that began on October 24, 1996, as provided by section 520(m)(5) of the act. If the approval term for an HDE has lapsed, the HDE is ineligible for extension under this section and the applicant must cease marketing the device until a new HDE has been submitted and approved in accordance with this part.

(b) *Submission.* In order to avoid the risk of a lapse in marketing approval, the holder of an HDE wishing to obtain an extension shall submit such a request to FDA at least 90 days prior to the expiration of the HDE. A request for extension must be submitted in writing, together with a new, separately bound, request for HUD designation. The request for extension and the request for HUD designation shall be submitted to the Office of Device Evaluation, CDRH at the address specified for the submission of original HDE's (§ 814.104(e)), and the outside envelope should be plainly marked: "Request for Extension of HDE Approval." The submission shall state the applicant's name and address, the HDE number, and shall include the following information based upon the first 12 months of experience with the device following the most recent HDE approval or extension:

(1) An update of the information required under § 814.102(a) in a separately bound volume;

(2) An update of the information required under §§ 814.104(c)(2), (c)(3), and (c)(5);

(3) The number of devices that have been shipped or sold since initial marketing approval under this subpart and, if the number shipped or sold exceeds 4,000, an explanation and estimate of the number of devices used per patient. If a single device is used on multiple patients, the applicant shall submit an estimate of the number of patients treated or diagnosed using the device together with an explanation of the basis for the estimate;