recommendations for the clinical investigations required to achieve marketing approval, FDA may require that the results of the nonclinical laboratory studies or completed early clinical studies be submitted to FDA for agency review.

§ 316.14 Refusal to provide written recommendations.
(a) FDA may refuse to provide written recommendations concerning the nonclinical laboratory studies and clinical investigations necessary for approval of a marketing application for any of the following reasons:
(1) The information required to be submitted by §316.10(b) has not been submitted, or the information submitted is incomplete.
(2) There is insufficient information about:
   (i) The drug to identify the active moiety and its physical and chemical properties, if these characteristics can be determined; or
   (ii) The disease or condition to determine that the disease or condition is rare in the United States; or
   (iii) The reasons for believing that the drug may be useful for treating the rare disease or condition with that drug; or
   (iv) The regulatory and marketing history of the drug to determine the scope and type of investigations that have already been conducted on the drug for the rare disease or condition; or
(3) The specific questions for which the sponsor seeks the advice of the agency are unclear or are not sufficiently specific.
(4) On the basis of the information submitted and on other information available to the agency, FDA determines that the disease or condition for which the drug is intended is not rare in the United States.
(5) On the basis of the information submitted and on other information available to the agency, FDA determines that there is an inadequate basis for permitting investigational use of the drug under part 312 of this chapter for the rare disease or condition.
(6) The request for information contains an untrue statement of material fact.
(b) A refusal to provide written recommendations will be in writing and will include a statement of the reason for FDA’s refusal. Where practicable, FDA will describe the information or material it requires or the conditions the sponsor must meet for FDA to provide recommendations.
(c) Within 90 days after the date of a letter from FDA requesting additional information or material or setting forth the conditions that the sponsor is asked to meet, the sponsor shall either:
(1) Provide the information or material or amend the request for written recommendations to meet the conditions sought by FDA; or
(2) Withdraw the request for written recommendations. FDA will consider a sponsor’s failure to respond within 90 days to an FDA letter requesting information or material or setting forth conditions to be met to be a withdrawal of the request for written recommendations.

Subpart C—Designation of an Orphan Drug

§ 316.20 Content and format of a request for orphan-drug designation.
(a) A sponsor that submits a request for orphan-drug designation of a drug for a specified rare disease or condition shall submit each request in the form and containing the information required in paragraph (b) of this section. A sponsor may request orphan-drug designation of a previously unapproved drug, or of a new use for an already marketed drug. In addition, a sponsor of a drug that is otherwise the same drug as an already approved drug may seek and obtain orphan-drug designation for the subsequent drug for the same rare disease or condition if it can present a plausible hypothesis that its drug may be clinically superior to the first drug. More than one sponsor may receive orphan-drug designation of the same drug for the same rare disease or
§ 316.21 Verification of orphan-drug status.

(a) So that FDA can determine whether a drug qualifies for orphan-drug designation under section 526(a) of