

### **HYPOTHETICAL CASE STUDY 3: AGENCY DECISIONS ABOUT PENDING PRODUCT APPLICATIONS.**

Company X has developed a biological product that it believes will be a significant therapeutic advance compared to current therapies available to patients with a serious condition Y that frequently results in death. There is an ongoing Phase 3 clinical trial being conducted under an investigational new drug application (IND).

During the Phase 3 trial, a report of the Phase 2 trial, which had favorable results, has been published in the literature by the clinical investigators, resulting in significant public interest. However, this article does not provide sufficient detail to permit readers to assess (1) aspects of the clinical trial design that may render the results less conclusive than they appear; or (2) the totality of the data on this drug, which, though unmentioned in the article, includes negative, but unpublished, study results. The IND reviewers at FDA familiar with the clinical data believe that the article provides a more optimistic view of the drug's safety and effectiveness than is warranted at this time. Based on the article, FDA receives a number of inquiries from the public regarding when the product will be available.

#### **Issues for Discussion:**

(Note: Because the purpose of the discussion is to elucidate the policy considerations that should be weighed in deciding whether changes to current practice, laws, or regulations are warranted, the issues should be discussed without regard for current practice, laws, or regulations.)

Response to public inquiries: How should FDA respond to these inquiries from the public about the availability of the product? Should FDA acknowledge the information that is already in the public domain? Should FDA provide additional information about the clinical trials than what is in the published literature? If so, what information should the agency provide? If the trials are listed in [clintrials.gov](http://clintrials.gov), how does that affect the analysis?

Application status: Should FDA disclose that the company has an ongoing IND and that the company hasn't submitted a BLA? Should FDA disclose when the company submits a biological license application (BLA) to FDA for approval? What are the factors that should be considered in deciding whether to do so? Should FDA consider affirmative disclosure or only disclose the information in response to a request?

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After completing two pivotal multi-center clinical studies, the company submits a BLA to FDA for approval of the product to treat condition Y. Following the agency's review of the application, FDA issues a letter to Company X (a "complete response letter") identifying numerous deficiencies in Company X's application. In the letter, the agency sets forth its significant concerns about the effectiveness of the product in treating condition Y, and recommends a clinical study of at least one year.

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Fact that decision not to approve at this time has been made: Should the agency publicly disclose that it sent a complete response letter to the applicant? What are the factors that should be considered in deciding whether to do so? Should FDA consider affirmative disclosure or only disclose the information in response to a request?

Disclosure of information in complete response letter: Should the agency disclose any of the information in the complete response letter? What are the factors that should be considered in deciding whether to do so? Should FDA consider affirmative disclosure or only disclose the information in response to a request?

Response to complete response letter: Should the agency publicly disclose any of the contents of Company X's response? What are the factors that should be considered in deciding whether to do so? Should FDA consider affirmative disclosure or only disclose the information in response to a request?

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In addition to proposing that the product be used in patients with condition Y, the applicant's BLA submission also proposes use in patients with condition Z, and provides data from clinical trials for these uses. FDA determines that the product is safe and effective for treating condition Y, but that the product is not effective for treating condition Z. FDA approves the product for condition Y.

After approval, physicians use the product off-label for condition Z. Neither the company nor the investigators publish articles about the clinical studies for condition Z. FDA receives questions about the effectiveness of the product to treat condition Z.

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Disclosure of information about unapproved use: Should FDA disclose any of the efficacy information for the unapproved use? What are the factors that should be considered in deciding whether to do so?