



Bristol-Myers Squibb Company

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**Dockets Management Branch
Food and Drug Administration, HFA-305
5630 Fishers Lane, Room 1061
Rockville, MD 20852**

Re: Docket No. 2004N-0267; Proposed Rule: Applications for Approval to Market a New Drug; Complete Response Letter; Amendments to Unapproved Applications [69 *Federal Register* 43351 (July 20, 2004)]

Dear Sir or Madam:

Bristol-Myers Squibb (BMS), a diversified worldwide health and personal care company with principal businesses in pharmaceuticals, infant formulas, and nutritional products, is pleased to have the opportunity to offer comments on the proposed rule. Our company's mission is to extend and enhance human life by providing the highest-quality pharmaceutical and related health care products. For this reason, we are interested in commenting on the Proposed Rule: *Applications for Approval to Market a New Drug; Complete Response Letter; Amendments to Unapproved Applications*. Our comments are set forth below.

Summary of BMS Comments on Proposal

We commend the Food and Drug Administration for addressing this issue and, thus, ensuring FDA's compliance with the user fee performance goals. There are, however, a few aspects of the proposed rule that we at Bristol-Myers Squibb respectfully request be given additional consideration.

General Comment

Throughout the proposed rule the word response is often used without identifying whose response. An example of this can be found in § 314.101(ii) "Issue a notice of opportunity for hearing if the applicant asked FDA to provide it an opportunity for a hearing on an application in *response* to a complete response letter."

Recommendation: In order to clarify whose response is being referenced we recommend always identifying the respondent. For example, § 314.101 (ii), referenced above, could be clarified by adding "applicant response": "*Issue a notice of opportunity for hearing if the applicant asked FDA to provide it an opportunity for a hearing on an application in an applicant's response to a complete response letter.*"

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Specific Comments

Comment 1. Responses to complete response letters §314.110(c) "Failure to take action"

The proposed rule describes in §314.110(b) available actions for applicants following receipt of a complete response letter. These include resubmission [314.110(b)(1)], withdrawal [314.110(b)(2)], or request an opportunity for a hearing [314.110(b)(3)]. If an applicant fails to take any such action within 1 year after receiving a complete response letter, FDA may, under proposed §314.110(c), consider such failure to be a request by the applicant to withdraw the application.

The revision to the rule appears to rescind sponsor's opportunity to inform FDA of its intention to respond to the deficiencies described in the complete response letter that need to be corrected to put the application in condition for approval. This is a significant change from existing §314.110(a), which provides that applicants must respond within 10 days of receipt of an "approvable" letter in one of the following ways: (1) amend the application (or notify FDA of an intent to do so), (2) withdraw the application, (3) request an opportunity for a hearing, or (4) advise the agency that they agree to a specified extension while determining which response to make.

The benefit of the approach under the existing regulation is that it provides both the Agency and the Sponsor with a clear path on how to continue to communicate about the sponsor's application and the deficiencies that might exist. Additionally, there may be situations where an applicant needs to perform significant work (including in some instances further studies) to address the deficiencies cited in a complete response letter that may take longer than 1 year from the receipt of the complete response letter. This should not reasonably be characterized as failure to take action, and this result can be avoided by preserving the existing framework for communicating about deficiencies in the current regulation..

Recommendation: For these reasons we recommend modifying §314.110(c) to include a provision to allow applicants to notify FDA, within a prescribed time frame, of their intent to amend the application or to agree to a specified extension of the one year period to reflect an agreed-upon action plan to address deficiencies acknowledged in a complete response letter. In both instances this notification will allow the FDA to not consider the application as withdrawn. Absent such notification from the sponsor, FDA may consider the application withdrawn if it is not resubmitted within 1 year. Further, if an additional study is required to complete the response, an extension beyond 1 year should be allowed and negotiation of the timeline allowed.

Comment 2. Miscellaneous Revisions - Withdrawal by the Applicant of an Unapproved Application (proposed §314.65)

The agency writes that it proposes "to revise §314.65 ...to add a statement that if, by the time we receive a notice of withdrawal, we have identified any deficiencies in the application, we will list those deficiencies in the letter we send the applicant acknowledging the withdrawal."

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Recommendation: Further clarification should be included in the rule regarding public disclosure for situations in which an applicant chooses to withdraw an application. All communications prior to the issuance of an approval or tentative approval letter should remain confidential and, thus, the existence of such communications should not be disclosed. This would lend consistency to the approach the Agency is proposing under Section 314.430. For clarity we recommend using the following wording, " *that if, by the time we receive a notice of withdrawal, we have identified any deficiencies in the application, we will list those deficiencies in the letter we send the applicant acknowledging the withdrawal. This communications, like all communications, prior to approval or tentative approval will not be publicly disclosed.*"

Comment 3. Miscellaneous Revisions - Public Disclosure of Existence of Applications (proposed §314.430)

The proposed rule states FDA would disclose the existence of an application only after issuance of an approval letter or a tentative approval letter, unless the existence of the application has been previously publicly disclosed or acknowledged. This is consistent with the agency's long-standing position that the existence of an application is confidential commercial information under 21 CFR 20.61.

Recommendation: We agree with and support the agency's proposal not to publicly disclose the existence of an application unless as proposed in §314.430 (b) the applicant has received an approval letter under §314.105 or a tentative approval letter under §314.107, and unless the existence of the application has been previously publicly disclosed or acknowledged. BMS appreciates the opportunity to provide comment and respectfully requests that the FDA give consideration to our recommendations. We would be pleased to provide additional pertinent information as may be requested.

Sincerely,



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