

**Bristol-Myers Squibb  
Pharmaceutical Research Institute**

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June 25, 1999

Ms. Jennie Butler  
Food and Drug Administration,  
Dockets Management  
5630 Fishers Lane  
Rockville, MD 20857

Dear Ms. Butler:

We would like to submit comments on the FDA's revised proposal on site-specific stability data. We are aware the comment period has lapsed and apologize for the delay in sending our comments. Your consideration in reviewing our proposals is appreciated.

Sincerely,

*Richard Marclani*  
Richard Marclani  
Associate Director  
CMC for North American  
Marketed Products

98D-0362



A Bristol-Myers Squibb Company

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## Comments Referring to Table 2:

Example Major - Drug substance characteristics are controlled by the specifications of the material going into manufacture; not by stability.

Amount of SSS Data, Major and Moderate - We feel strongly that if a product meets the release specifications, the fact that it was made at a different geographic location does not affect its stability. If the release specifications cannot determine a difference, then they need to be changed. Stability does not contribute to the process.

The amount of SSS data required for both and majors and moderate changes are the same.

## Comments Referring to Table 3:

Stability does not control the product. Input specifications and manufacturing controls, control the product. The FDA appears to be focused on the wrong point in the process. Concerning NDA's vs. ANDA's, we feel the FDA's proposal is scientifically flawed. The method of the filing should not determine what one needs to review to be comfortable with the data. Industry should insist on good science for any proposal.

For NDA's Major: definition needed for primary data. It is not clear why a longer (12 month) body of data are needed.

Consideration should be given to placing sterile solution and sterile powder products under the "Minor" classification. A site transfer for these dosage forms should not result in stability issues different than those associated with the non-sterile solutions and powders (assuming that all of the process validation work has been completed and equivalence shown to the process used at the primary site).

## General Issues and Approaches

### 1. Drug Substance

Comment - If the degradation pathway always remains the same when you start with the same substance, then release data is all that is needed.

### IV. Further Research

Comment - Industry should be able to quickly provide data on a successful transfer. Further research should not be considered until the issue is addressed from a scientific basis. Political research is not needed, scientific data is needed. Again if the manufacturing process produces the same product, its degradation will be the same no matter where it was produced. Geography will be of no impact. If the product is not adequately defined to know if two products are different then product characteristic testing needs to be improved, not stability testing.

**Subject: Re: Site-Specific Stability Expert Panel**

**Date:** Thu, 24 Jun 1999 17:29:19 -0400 (EDT)

**From:** Kimberly Topper 301-827-7001 FAX 301-827-6776 <TOPPERK@cder.fda.gov>

**To:** Richard J Marciani <marcianr@bms.com>

Richard,

The Docket officially closed 14 June - even though it is late we accept all comments - Comments must be submitted to the Docket. You might get a form letter back telling you the docket closed, but your comment will be put in for future consideration. Technically we do not have to consider the late comments in this go-round but we always do - after all we asked you for your input! I will alert them I am expecting your comments so they watch for it.

The snail mail address is:

Food and Drug Administration,  
Dockets Management  
(Building 5630)  
ATTN: Jennie Butler  
5600 Fishers Lane  
Rockville, MD 20857

If you send it FedEx or other rapid delivery method change:

5600 Fishers to 5630 Fishers Lane

We have begun looking at the comments and would like to consider yours ASAP if you wouldn't mind please e-mail it to me and we can use it until the formal dockets copy gets to us.

If you have any questions please give me a call at (301) 827-6755.

Kimberly

>Dear Kimberly,

>

>On March 31, 1999 at Bethesda, Maryland, an FDA panel along with representatives of the pharmaceutical industry met to discuss site-specific stability data. A revised proposal was issued which we would like to comment on. Are you still accepting comments? If so, is there an e-mail address to send comments? If an e-mail address is not available, could you please let me know what the mailing address is?

>

>Sincerely,

>

>Richard Marciani Bristol-Myers Squibb Co.