

Bristol-Myers Squibb Pharmaceutical Research Institute

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19-Sep-2002

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

Re: Docket No. 02D-0350; Draft Guidance, Handling and Retention of BA and BE Testing Samples, 67 Federal Register, 54219 (August 21, 2002)

Dear Sir or Madam:

Bristol-Myers Squibb is a diversified worldwide health and personal care company with principal businesses in pharmaceuticals, consumer medicines, nutritionals and medical devices. We are a leader in the research and development of innovative therapies for cardiovascular, metabolic and infectious diseases, neurological disorders, and oncology. In 2001 alone, Bristol-Myers Squibb dedicated \$2.1 billion for pharmaceutical research and development activities. The company has nearly 6,000 scientists and doctors committed to discover and develop best in class therapeutic and preventive agents that extend and enhance human life. Our current pipeline comprises more than 50 compounds under active development.

For these reasons, we are very interested in and well qualified to comment on this FDA draft guidance regarding Handling and Retention of BA and BE Testing Samples.

Summary of BMS Comments on Proposal

We commend the U.S. FDA for working to refine the rules to assure that test and reference products for BA/BE studies are randomly selected and retained at investigational sites.

However, there are several aspects of the draft guidance which are unclear, particularly those related to Part IV, Section D (Studies Conducted In-House by a Study Sponsor and/or Drug Manufacturer). We provide those comments below seeking further clarification because Bristol-Myers Squibb does conduct some BA/BE studies at an in-house facility.

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Specific Comments to Part IV, Section D

1. The draft guidance contains inconsistent text in last sentence of the first paragraph and last sentence of Point 3 (lines 349 and 367). In line 349 it is stated that it is "RECOMMENDED" that a third party be used for sample retention while in line 367 the same statement becomes it is "ADVISED" that a third party be used for sample retention. Which term does the agency want to use for this activity? We understand RECOMMENDED to say BMS will use a third party while ADVISED says to us we might consider using same. For this important point we request that FDA use consistent and more precise language.

2. The draft guidance states in Section D, Point 2 that an independent third party "BE AVAILABLE" to witness dosing and random selection of reserve samples (lines 361-362). The term "BE AVAILABLE" is very ambiguous. Does this mean that a third party was invited to witness those activities or does a third party actually need to be present during sample selection and to witness dosing? For this important point we also recommend FDA use more precise language.

3. Further comment to Section D, Point 2 as it pertains to this sponsor. The Bristol-Myers Squibb Clinical Pharmacology Unit (our in-house facility) is staffed by a combination of company and hospital employees. If, as noted in the previous comment, a third party witness for dosing and random selection of reserve samples is required, could those hospital employees serve as the third party witness assuming their actions are properly documented? We submit that the hospital employees who work at our in-house facility could serve in that role so long as they were not responsible for that particular BA/BE study. In this respect their actions would not be substantially different that those of employees at an external study facility who have been contracted to conduct a BMS-sponsored BA/BE study. However, if FDA's intention for this guidance is that the third party witness must be totally independent of in-house staff (company or hospital employees) this point should be clarified to state same.

BMS appreciates the opportunity to provide comment and respectfully requests that FDA give consideration to our recommendations. We would be pleased to provide additional pertinent information as may be requested.

Sincerely,



Laurie Smaldone, MD
Senior Vice President
Global Regulatory Sciences