

Bristol-Myers Squibb Pharmaceutical Research Institute

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September 18, 2002

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

Re: Docket No. 00N-1663; Proposed Rule, Investigational New Drugs: Export Requirements for Unapproved New Drug Products, 67 *Federal Register* 41642 (June 19, 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 proposal regarding the exportation of investigational new drugs.

Summary of BMS Comments on Proposal

We commend the U.S. FDA for proposing the provisions that would implement changes in FDA's export authority resulting from the FDA Export Reform and Enhancement Act of 1996. Specifically, we commend the agency's proposal in §312.110 (b) (4) to streamline the requirements of the 312 program by eliminating the requirement of prior FDA authorization. The agency's proposal to require a person seeking to export an unapproved new drug for investigational use without an IND to send a written certification to FDA that affirms the safety, and quality of exporting investigational new drugs, without having to receive prior FDA authorization, is a prudent recommendation. Particularly in light of the fact that it is our understanding that "very few investigational new drug exports under the existing program raise any safety, quality, or other public health concerns,"¹ making this program an unnecessary burden to the agency.

However, there are several aspects of the proposed rule/guidance that need clarification or appear contrary to the FDA's stated objectives, which we have noted below.

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¹ *Federal Register*, Vol. 67, No. 118/June 19, 2002



Specific Comments

Section II. Description of Proposed Rule

FDA states in the proposed rule that it interprets section 802(c) of the FDA Export Reform and Enhancement Act of 1996 (FEREA) as permitting investigational drugs to be sent to principal investigators in a listed country for use by him or her in an unlisted country. FDA's interpretation stipulates that investigational drug transshipped for such studies, in the unlisted country are conducted in accordance with the laws of both the listed and the unlisted countries. BMS does not support this interpretation. Further, this interpretation conflicts with the FDA's previously stated position in this proposed rule that the agency has interpreted 802 (c) to mean that "... the provision does not allow transshipment."² FDA further interprets 802 (c) as "permitting investigational new drugs to be sent to principal investigators in a listed country who use the investigational new drug in an unlisted country if the principal investigator conducts the clinical investigations in accordance with the requirements of both the listed country and the unlisted country where the investigation is conducted."³

BMS Response/Recommendations:

BMS does not concur with FDA's interpretation of 802(c) as noted above. Once a drug is exported from a listed country, even the most conscientious investigator may have little ability to control how the drug is moved, stored, and used. It is unrealistic to expect investigators to adhere and enforce the laws, regulations and practices of the listed country in an unlisted country, where there would be no guarantee of control. Furthermore, such a practice potentially exposes the investigator, the sponsor, and patients to significant risks. In conclusion, BMS believes that transshipment by clinical investigators of investigational new drug from a listed country to an unlisted country should be prohibited. In our view, transshipment of investigational new drugs should be the responsibility of the sponsor alone.

We further ask the agency to clarify the process whereby transshipment could take place. It is our understanding that, under the provisions of the new rule, transshipment from an unlisted or listed country could be allowed if the sponsor would amend its original certification requesting shipment of an investigational new drug product from either a listed or unlisted country A to unlisted country B where the protocol is unchanged and all applicable laws are met. BMS would therefore recommend that under these circumstances only product under direct control of the sponsor be permitted for transshipment.

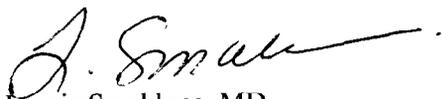
Lastly, in proposed section 312.110(b)(4), the agency writes that the written certification statements submitted to the agency should confirm that the "the drug is promoted in accordance with the labeling." We asked for clarification on this requirement since the proposed rule addresses exports of investigational new drugs, which can not be the subject of promotion. Without further clarification or justification for this requirement we propose that the requirement be removed from this rule.

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 or any clarification that may be requested.

² Ibid, pg. 41643

³ Ibid

Sincerely,

A handwritten signature in black ink, appearing to read "L. Smaldone", with a long horizontal flourish extending to the right.

Laurie Smaldone, MD
Senior Vice President
Global Regulatory Sciences