

Ellen R Westrick
Senior Director
Office of Medical/Legal
U.S. Human Health

Merck & Co., Inc.
P.O. Box 4, WP37C-116
West Point PA 19486
Fax 215 652 2178
Tel 215 652 3476

July 22, 1998
(via Federal Express)



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

Re: Docket No. 98N-0222
Dissemination of Information on Unapproved/
New Uses for Marketed Drugs, Biologics, and Devices

Dear Sir or Madam:

General Comments:

Merck & Co., Inc. is a worldwide leader in the research, development, production, and marketing of human health products used in the prevention and treatment of a variety of diseases. As mandated by Corporate policy, we continually strive to ensure that all Company product communications are supported by extensive scientific and clinical research and presented in compliance with FDA regulations.

Merck believes that, as part of the passage of the Food and Drug Administration Modernization Act of 1997 (FDAMA), it was the intent of Congress to facilitate greater access by healthcare providers to peer-reviewed research on off-label uses. Merck fully endorses Agency efforts to implement the provisions of FDAMA in general and specifically as they pertain to the dissemination of information not described in approved product labeling. A free flow of information is essential to ensure continued improvements in healthcare. Equally essential is the development of specific industry guidance that will facilitate these improvements via the appropriate dissemination of off-label information in a manner that retains the spirit and integrity of the Act as intended by Congress.

Merck believes, however, that in certain circumstances, the proposed regulations are unnecessarily restrictive and, in fact, may actually impede the flow of information regarding new and/or alternate treatment strategies -- a process that is at the heart of product innovation.

98N-0222

C43

Specific Comments:

Merck offers the following comments on specific issues included in the proposed regulation.

Section 99.3. Definitions

“New Use”

While Merck agrees that FDA should define “new use” broadly to allow for broad dissemination of new information from clinical investigations, the proposed definition is too broad. In effect, when read in conjunction with Section 99.405, it would limit the use of certain subpopulation claims or comparative studies not in the package circular to dissemination under Section 401 contrary to current regulations. Subpopulation claims are permissible even if not in the circular, if supported by substantial evidence or substantial clinical experience. [See 21 CFR 202.1(e)(6)(i).] Also, comparisons of safety or effectiveness are permissible for use in promotion if supported by substantial evidence or substantial clinical experience and if otherwise consistent with the circulars for both products, even if the comparisons are not in the circulars. [See 21 CFR 202.1(e)(6)(ii).] In order to remedy this inconsistency, a new use should be deemed to be one that would require approval of a supplemental application in order to be included in the product labeling and that must be included in product labeling in order to be used in advertising or promotional labeling. Claims about uses that are otherwise permitted independent of Section 401 should not be subjected to the requirements for dissemination under that section.

Section 99.101. Information That May Be Disseminated

Section Overview

Merck assumes the intention of this section is to prohibit the dissemination of information regarding a product which has never been studied, or which has been inadequately studied, for safety and efficacy as required under FDA’s NDA policy. As written, this point is adequately communicated. However, the proposed language does not address the reality of the marketplace and the time required to develop and clear appropriate resources. Therefore, Merck recommends the inclusion of a 60-day window in advance of the product’s PDUFA date during which time the manufacturer could submit proposed materials for review. Any submission would be made with the understanding that materials could not be used until receipt of final product approval.

“False or Misleading” Information

Proposed Section 99.101 states, among other things, that information may be considered false or misleading if it includes only favorable publications. Many new uses may only have favorable publications and would not, therefore, be misleading. A more appropriate manner in which to state the issue would be to cite the exclusion of unfavorable publications as the example. Also, Merck questions whether these examples, in any event, are relevant to this section. Rather, they appear to be examples relating to lack of objectivity or balance under proposed Section 99.103(a)(4) that can be corrected by Agency action under that section rather than rejection of a paper under Section 99.101(a)(4).

“Scientifically Sound” Articles

Merck believes that the level of detail that is specified in proposed Section 99.101(b)(1) to qualify articles and reference texts for dissemination goes far beyond what was intended by Congress and could, in effect, exclude high quality articles and texts which FDAMA was designed to allow. A simple statement requiring that an article include enough information to determine that it is scientifically sound would be more in keeping with the spirit of the Act as approved by Congress.

Accompanying Promotional Labeling

Proposed Section 99.101(b)(2) states that material that can be disseminated under Section 401 of FDAMA, “shall not be disseminated with any information that is promotional in nature.” The preamble at page 31147 states that the material “cannot be accompanied by information that is promotional in nature.” This language is too broad and could be interpreted to prohibit a company representative from providing a reprint disseminated under this section to a physician during the same discussion at which a detail piece was also provided. Nothing in the statute authorizes such an approach. Rather, FDA should revise the proposal to state, as it does in its reference text guidance of October 8, 1996, that product promotional information should not be “physically appended” to the disseminated material.

Section 99.105 Recipients of Information

Pharmacists

Proposed Section 99.105 identifies who may receive information under this section. Neither the statute nor the proposed regulations define the cited term “pharmacy benefit manager” or mention pharmacists. Merck agrees with FDA that it is essential that this information be provided only to persons who have the education, training, and experience to interpret its meaning and

relevance. Clearly, pharmacists are so qualified and, in fact, it would seem essential that they receive such information since they will be filling prescriptions and counseling patients on such new uses. Merck recommends that FDA include "pharmacists" in the discussion of persons qualified to receive this information and also to revise Section 99.3 to include a definition of "pharmacy benefits manager."

Section 99.201 Manufacturer's Submission to the Agency

Start of the 60-day Review Period

Proposed Section 99.201(d) indicates that the 60-day review period for materials proposed for dissemination will begin upon FDA's receipt of a "complete submission," with the explanation that "a submission shall be considered to be complete if FDA determines that it is sufficiently complete to permit a substantive review." While Merck agrees with FDA's intent to ensure that all materials are available prior to the start of their review, we recommend that this section be amended to require official FDA acknowledgment of the receipt of a complete submission. A set time period should be established (e.g., 2 weeks) within which time FDA would be required to notify the manufacturer that a submission is complete and the 60-day review period has begun or to advise what information is still outstanding.

Preamble, page 31156

Reference Text Guidance

In the preamble to this proposed rule at page 31156, FDA states that it plans to develop draft guidance on reference publications that do not fall within Section 401. The Agency should clarify that until said guidance is finalized the industry may continue to distribute reference texts that comply with the FDA guidance of October 8, 1996.

Merck appreciates the opportunity to comment on this important issue.

Sincerely,



Ellen R. Westrick
Senior Director, Office of Medical/Legal

ELLEN WESTRICK
MERCK & COMPANY
SUMNEYTOWN PIKE
WEST POINT PA 19486
(215)652-3476

SHIP DATE: 22JUL98
ACCOUNT # 019146740
MAN-WGT:1 LBS

TO: DOCKETS MGMT BRANCH, HFA-305
FOOD AND DRUG ADMINISTRATION
5630 FISHERS LANE, ROOM 1061
ROCKVILLE, MD 20852

HFA-305

385 7171 814

FedEx.

POWERSHIP 3

RELEASE#:4697309

REF: 60266.7746.010

PRIORITY OVERNIGHT

**THU
AA**

CAD # 679410 22JUL98

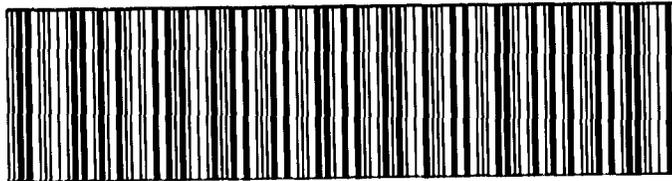
Trk# **385 7171 814**

FedEx Letter

20852-MD-US

I AD

ZMEDG



1d On Time

PART # 147923 FORMAT # 077 RIT 09/97