DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC 16 1999

TRANSMITTED VIA FACSIMILE

Ellen R. Westrick
Executive Director
Office of Medical/Legal
Merck & Co., Inc.
P.O. Box, WP37C-116
West Point, PA 19486

RE: NDA 21-042
Vioxx (rofecoxib) tablets
MACMIS ID #8410, 8506

Dear Ms. Westrick:

Reference is made to Merck & Co., Inc.'s (Merck) letters, dated November 30, 1999, and December 15, 1999, in response to letters from the Division of Drug Marketing, Advertising, and Communications (DDMAC) dated, November 12, 1999, and December 1, 1999. Our letters concerned the alleged dissemination of two "homemade" promotional pieces, entitled "TEN REASONS WHY VIOXX IS BETTER THAN CELEBREX," and "Vioxx vs. Celebrex Poem" distributed by or on behalf of Merck, that promoted Vioxx (rofecoxib) capsules in violation of the Federal Food, Drug and Cosmetic Act (Act) and its regulations. DDMAC requested that Merck investigate the extent to which these "homemade" pieces were used to promote Vioxx, and the number of health care professionals who received these pieces.

In your letter, you described that in both cases one sales representative distributed these "homemade" pieces in their respective geographic regions. Your letter also described Merck's policy for prohibiting dissemination of homemade materials by your sales force, and specified the corrective actions taken to ensure that this activity will not continue.

We have reviewed these promotional pieces and have determined that they are false or misleading because they contain misrepresentations of Vioxx's safety profile, unsubstantiated comparative claims, and are lacking in fair balance.

Misrepresentation of Safety Information

- You present claims that misrepresent the safety profile for Vioxx, including but not limited to, "VIOXX HAS ENDOSCOPY STUDIES SHOWING A SAFER THAN PLACEBO INCIDENCE RATE OF GASTRODUODENAL ULCERS." However, this claim is in direct contrast with the approved product labeling (PI) that states, "...the studies cannot rule out at

least some increase in the rate of endoscopic gastroduodenal ulcers when comparing Vioxx to placebo." Furthermore, this claim suggests that Vioxx is safer than placebo in regards to clinically significant gastroduodenal events. However, the PI states, "The correlation between findings of endoscopic studies, and the relative incidence of clinically serious upper GI events that may be observed with different products, has not been fully established." Moreover, this claim minimizes the warning in the PI that states, "Serious gastrointestinal toxicity such as bleeding, ulceration, and perforation of the stomach, small intestine or large intestine, can occur at any time, with or without warning symptoms...," and omits material fact in the PI which states, "Serious clinically significant upper GI bleeding has been observed in patients receiving VIOXX in controlled trials...." Therefore, we object to this claim because it minimizes the GI warning associated with Vioxx and is inconsistent with the data in the PI.

Unsubstantiated Comparative Claims

Promotional materials are false or misleading if they contain representations or suggestions that a drug's safety or effectiveness is comparable or superior to another drug when such has not been demonstrated by substantial evidence. Some examples of misleading comparative claims in your "homemade" promotional pieces include:

- In the Vioxx vs. Celebrex Poem you claim, "Your patients in pain – they give you their grief; A Cox-II is the answer for their pain relief." This claim makes a broad superiority claim comparing Vioxx to not only the class of NSAIDs, of which it is a member, but to all analgesic and anti-inflammatory therapies available for the management of pain. However, this global superiority claim has not been demonstrated by substantial evidence, and therefore, is false or misleading. Moreover, PI states that Vioxx is indicated, "For the management of acute pain in adults." (emphasis added). Therefore, this claim lacks important contextual information concerning Vioxx's approved indication, and consequently, is misleading.

- You also presents several unsubstantiated comparative claims to Celebrex (celecoxib), including but not limited to, "Vioxx of course – the answer again, It's stronger, lasts longer, is faster, and then its safer...." This claim suggests Vioxx is more efficacious and has a superior safety profile compared to Celebrex, when such has not been demonstrated by substantial evidence. Therefore, this unsubstantiated comparative claim is misleading.

Fair Balance

Overall, Merck's "homemade" promotional pieces are lacking in fair balance with respect to the content and presentation of risk information related to the use of Vioxx. In general, promotional materials must present information about the risks associated with the use of a drug with a prominence and readability reasonably comparable to that of claims for the drug.

- Although these pieces contain numerous claims for the efficacy and safety of Vioxx, you have not presented any risk information concerning the contraindications, warnings,

precautions, or adverse events associated with Vioxx's use. (emphasis added). Therefore, we consider these promotional pieces to be lacking in fair balance. Furthermore, these promotional pieces are in violation of the Act because the approved product labeling for Vioxx did not accompany them.

In addition, promotional materials must be submitted to the FDA, under Form FDA 2253, at the time of initial dissemination. However, our records indicate these promotional materials were not submitted at the time of initial use. This failure to submit promotional materials at the time of initial dissemination is in violation of the Act.

We have reviewed your response and actions taken in response to the dissemination of this violative promotional piece. We do not wish to comment your internal processes, however we do acknowledge your investigation and the corrective actions taken to prevent reoccurrence of this type of violative promotional activity. At this time, we have no further questions and consider this matter closed.

If you have any further questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or by written communication at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. We remind you that only written communications are considered official.

In all future correspondence regarding this matter, please refer to the MACMIS # 8506 and 8410, in addition to the NDA number.

Sincerely,

/S/

Spencer Salis, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications