DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

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TRANSMITTED BY FACSIMILE

Joanna Waugh
Program Director
Drug Regulatory Affairs
Hoffman-LaRoche Inc.
Bldg. 1/2
340 Kingsland Street
Nutley, New Jersey 07110-1199

RE: NDA 18-662
Accutane (isotretinoin) Capsules
MACMIS ID # 10836

Dear Ms. Waugh:

This letter notifies Hoffman-LaRoche Inc. (Roche) that the Division of Drug Marketing, Advertising, and Communications (DDMAC) has identified promotional activities that are in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. Specifically, a representative of Roche made false or misleading oral statements about Accutane (isotretinoin) Capsules at Roche's promotional exhibit booth at the American Pharmaceutical Association's (APhA) Annual Meeting and Exposition held in Philadelphia, Pennsylvania in March 2002.

False or Misleading Statements and Minimization of Important Risk Information

Roche's representative engaged in false or misleading promotional activities about a bolded warning and other risk information relating to psychiatric disorders in Accutane's approved product labeling (PI). The representative's oral statements raise significant public health and safety concerns because they minimize the risk of psychiatric disorders that can occur with Accutane therapy and misleadingly suggest that the drug is safer than has been demonstrated by substantial evidence. The bolded Warnings section of the PI states:

> "Psychiatric Disorders: Accutane may cause depression, psychosis and, rarely, suicidal ideation, suicide attempts and suicide. Discontinuation of Accutane therapy may be insufficient; further evaluation may be necessary. No mechanism of action has been established for these events (see ADVERSE REACTIONS: Psychiatric)."

In addition, the adverse reactions section of the PI states:

> "Psychiatric: suicidal ideation, suicide attempts, suicide, depression, psychosis (see WARNINGS: Psychiatric Disorders), emotional instability"

One Roche representative was asked by two DDMAC reviewers at Roche's promotional exhibit booth at the APhA meeting if there was something in the PI (for Accutane) about psychosis. The representative failed to provide the risk information about psychosis and instead made the following false or misleading statements about the risk of psychiatric disorders with Accutane therapy:

> "We don't feel it's an issue."
> "News has hyped it up."
> "Like any drug used in patients with depression, such as penicillin, it could bring it out."

These oral statements made by the Roche representative are in violation of the Act because they minimize the risk described in the bolded warning for Accutane and misleadingly suggest that the drug may be safer than has been demonstrated by substantial evidence.

Requested Actions

Roche should immediately cease promotional activities such as those identified above that minimize the risk information associated with the use of Accutane. Roche should submit a written response to DDMAC on or before August 8, 2002, describing its intent and plans to comply with the above.

Roche should direct its response to me by facsimile at (301) 594-6771 or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-42, Room 17B-20, 5600 Fishers Lane, Rockville, MD 20857.

In all future correspondence regarding this matter, please refer to MACMIS ID #10836 in addition to the NDA number. DDMAC reminds Roche that only written communications are considered official.

Sincerely,

{See appended electronic signature page}

Warren Rumble
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications