DEPARTMENT OF HEALTH & HUMAN SERVICES

FOI

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

JUN 4 1999

Michele M. Hardy
Director, Advertising and Labeling Policy
Glaxo Wellcome Inc.
Five Moore Drive PO Box 13398
Research Triangle Park, North Carolina 27709

Re: NDA 21-007
Agenerase (amprenavir) Capsules
NDA 21-039
Agenerase (amprenavir) Oral Solution
Macmis # 7971

Dear Ms. Hardy:

The Division of Drug Marketing, Advertising, and Communications ("DDMAC") is concerned with the promotional activities of Glaxo Wellcome, Inc. ("Glaxo") in support of Agenerase (amprenavir). Glaxo has conducted promotional activities in violation of the Federal Food, Drug, and Cosmetic Act, and applicable regulations.

The Food and Drug Administration gave accelerated approval to Agenerase on April 15, 1999, for the treatment of HIV-1 infection in combination with other antiretroviral agents. The indication was based on the analyses of plasma HIV RNA levels and CD4 cell counts in controlled studies up to 24 weeks in duration. Presently, there are no results from controlled trials evaluating long-term suppression of HIV RNA or disease progression with Agenerase. Approved labeling for Agenerase states that the "clinical relevance of the genotypic and phenotypic changes associated with [Agenerase] therapy has not been established." It further states that "[v]arying degrees of HIV-1 cross-resistance among protease inhibitors have been observed," and the "potential for protease inhibitor cross-resistance in HIV-1 isolates from [Agenerase]-treated patients has not been fully evaluated."

On May 13, 1999, DDMAC received information that Glaxo, or an individual on its behalf, ("representative") made telephone calls to physicians. If the physicians were not available, then the representative provided a toll free telephone number so the physicians could return the calls. The purpose of the calls appears to have been to provide these physicians with information about Agenerase.

DDMAC called the toll free telephone number on May 13th and asked for information about Agenerase. The representative that answered the call provided a promotional message that included several false or misleading statements about the resistance profile

of Agenerase. Specifically, the representative stated, among other things, that Agenerase offers a "unique resistance profile, better resistance, and lower resistance." He further stated that Agenerase is "not cross-resistant with other protease inhibitors."

These claims are false or misleading, and inconsistent with the approved labeling for Agenerase. Overall, the claims wrongly imply that the resistance profile of Agenerase is completely understood. Further, the claims imply that the resistance profile offers some clinical benefit. However, it has not been demonstrated by substantial evidence that the resistance profile of Agenerase is better than other protease inhibitors, or that the resistance profile is clinically unique, or that it offers clinical benefits to patients.

The representative also made a misleading claim about the tolerability of Agenerase, by stating that Agenerase is "well tolerated." Although, he mentioned some of the warnings, precautions, and adverse events that are associated with Agenerase therapy, his characterization of these conditions as "well tolerated" was misleading. Further, his characterization minimized the significance of the risks that are associated with use of Agenerase.

In addition, the promotional message that was presented to DDMAC appeared to have been read from previously prepared promotional labeling. If this was the case, we note that the promotional labeling was not submitted to DDMAC prior to dissemination, as is required by 21 C.F.R. 314.550.

By telephone, on May 14, 1999, DDMAC informed Glaxo of the violative activity and stated that Glaxo should immediately cease such activity. In your letter of May 14, 1999, you confirmed that Glaxo had ceased the above promotional activity, and that Glaxo would conduct a "thorough internal investigation, including an evaluation of current internal policies relating to similar practices." DDMAC notes your response and actions to date, and considers this matter closed. However, we will continue to closely monitor these issues.

Should you have any questions, please contact the undersigned by facsimile at (301) 594-6771, or by mail at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-40, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. In all future correspondence regarding this matter, please refer to MACMIS #7971, and the NDA numbers. As a reminder, only written communications are considered official.

Sincerely,

Sherrie Shade, R.Ph., J.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications