DEPARTMENT OF HEALTH & HUMAN SERVICES

ic Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

MAY - 6 1998

Kathryn A. Roberts
Senior Manager
Rhone-Poulenc Rorer
500 Arcola Road
P.O. Box 1200
Collegeville, PA 19426-0107

RE: NDA# 20-599
Rilutek (riluzole) Tablets
MACMIS ID# 5697

Dear Ms. Roberts:

Through routine monitoring and surveillance, the Division of Drug Marketing, Advertising and Communications (DDMAC) has become aware of certain claims and promotional activities by Rhone-Poulenc Rorer (RPR) for Rilutek (riluzole) Tablets that are false, misleading, and in violation of the Federal Food, Drug, and Cosmetic Act. The materials include, but are not limited to, a convention booth flashcard, a mailer, a brochure, and reprint carriers with the following identification numbers: RTJ797(15-25)A, RT4971J(10)A, RT497(12.5-25)A, RT1296J(5-25)A, and RT197J(5-25)A. Further, DDMAC refers to the promotional materials and practices by RPR at the American Academy of Neurology (AAN) meeting held in Minneapolis, Minnesota (April 25-May 2, 1998).

Specifically, DDMAC objects to the following:

1. The flashcard and the mailer present a highly prominent hypothetical "example" of Rilutek's "survival advantage" that implies that 210/1000 Rilutek-treated have survived at a specific point in time when those on placebo had no survivors. This example is false and misleading because mortality benefit associated with Rilutek treatment has not been demonstrated. Similarly, the claim that the probability of survival while taking Rilutek improved by 21% is false and misleading. The approved product labeling states that Rilutek "extends survival and/or time to tracheostomy" early in the treatment period (i.e., possibly a two-month advantage). Further, the statistically significant difference between Rilutek-treated and placebo-treated patients was determined for the entire study period (i.e., 18 months) and does not pertain to any one time point. There is no statistically significant

difference in overall mortality at one year. None of this qualifying information is included in the materials in question and the prominence of the example misleads the viewer to believe that a significant number of patients taking Rilutek will survive.

2. The reprint carriers are misleading because they promote a mortality benefit of Rilutek that is not considered to be a substantiated claim. Specifically, the carriers state claims such as "significant effects on rates of survival" and "statistically significant survival advantage." This is not supported by the clinical studies for Rilutek.

   Similarly, the convention panels and materials presented at the AAN meeting carry out-of-context, unsubstantiated claims that Rilutek has demonstrated a "survival advantage." Where they exist, footnotes claiming that survival was "defined as time to death or tracheostomy" are not prominent and not detailed enough to clarify the misleading message.

DDMAC notes that this is RPR's fourth notification of the violative nature of this type of campaign:

> In our letter dated February 28, 1996, DDMAC commented that claims regarding survival benefit must be qualified with an indication of the magnitude of the effect and that claims of statistical significance for certain time points were not substantiated.
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> In our letter dated July 1, 1996, RPR was notified of violative materials that implied that Rilutek offered a mortality benefit.
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> In our letter dated August 2, 1996, RPR was again advised that claims regarding survival benefits must be accompanied by appropriate information qualifying such statements (i.e., "Rilutek can extend survival and/or time to tracheostomy for about two to three months").

DDMAC is concerned about the repetitive violative claims by RPR concerning the survival benefits for Rilutek. In the absence of substantial evidence to show survival benefits, such claims are considered false or misleading.

To address the objections noted in this letter, RPR should immediately discontinue the use of these materials and all other promotional materials for Rilutek that contain the same or similar presentations. Please respond to this letter, in writing, by May 21, 1998. This response should include a list of all violative promotional materials and RPR's methods for discontinuing their use.

If RPR has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or 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 particular matter, please refer to MACMIS ID #5697 in addition to the NDA number.

Sincerely,

Lisa L. Stockbridge, Ph.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications