DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

March 23, 1999

TRANSMITTED VIA FACSIMILE

Anthony F. Rogers
Director, Marketed Products Group
Drug Regulatory Affairs
Zeneca Pharmaceuticals
1800 Concord Pike
Wilmington, DE 19850-5437

RE: NDA 19-627
Diprivan (propofol) Injectable Emulsion
MACMIS ID #7617

Dear Mr. Rogers:

This letter concerns Zeneca Pharmaceuticals' (Zeneca) dissemination of certain promotional materials for Diprivan (propofol) injectable emulsion. The promotional materials at issue are "Dear Valued Customer" letters signed by Robert C. Black, President of Zeneca, and glossy brochures containing selected information from a lawsuit that Zeneca recently filed against the Food and Drug Administration (FDA). The letters, dated February 8, and March 12, 1999 and respective brochures, are currently being distributed by Zeneca by mail or by Zeneca's sales representatives throughout the U.S. In these promotional materials, you object to the FDA's January 4, 1999, approval of an abbreviated new drug application (ANDA) for propofol injectable emulsion submitted by GensiaSicor Pharmaceuticals, Inc. (GensiaSicor). The Division of Drug Marketing, Advertising, and Communications (DDMAC) has determined that these materials contain statements, or suggestions that are misleading. We have concluded that these promotional labeling pieces are in violation of the Federal Food, Drug, and Cosmetic Act (Act), and thus misbrand Diprivan. In addition, you failed to submit these promotional labeling pieces to the FDA as required by the post-marketing reporting requirements, 21 CFR §314.81(b)(3)(i).

This action addresses your dissemination of the letters and brochures to health care providers and facilities to promote the use of Diprivan and to influence product selection by these "customers." It is not intended to and does not address your petition to the FDA or your right to seek judicial review of FDA's decision.

1. Safety and Effectiveness

Your February, 8, 1999, letter and glossy promotional brochure state or suggest that GensiaSicor's formulation of propofol injectable emulsion is not therapeutically equivalent to Zeneca's Diprivan (propofol) injectable emulsion. Such suggestions are false or misleading. As you know, FDA has reviewed GensiaSicor's application and has determined that GensiaSicor's propofol and Zeneca's Diprivan are therapeutically equivalent, and therefore, were granted an "A" rating. This rating means that these products are bioequivalent and therapeutically equivalent, and can be substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the prescribed product.

You allege in your promotional materials that GensiaSicor's propofol product is not therapeutically equivalent to Diprivan and should not be substituted for Diprivan because GensiaSicor's product contains sodium metabisulfite as a preservative whereas your product contains EDTA. You also allege that GensiaSicor's product is neither safe nor effective. These allegations are false or misleading. The criteria for bioequivalence and therapeutic equivalence are well established. Under these criteria, bioequivalent and therapeutically equivalent parenteral products such as propofol, may differ in a variety of ways including, but not limited to, the preservatives, buffers, or antioxidants used in the formulation. There also may be labeling differences, as in the case of propofol, to the extent that the inclusion or exclusion of an inactive ingredient requires modification of the product label.

In the March 12, 1999 letter and brochure, you allege various types of stability problems associated with GensiaSicor's product. Since GensiaSicor's product was not available to Zeneca, you prepared a product that you allege is similar to the approved product. You conducted some tests on the product you prepared and state or suggest that the results you obtained are representative of quality, safety, and efficacy issues regarding the GensiaSicor propofol formulation. Such allegations are clearly false or misleading and misbrand Diprivan, 21 CFR 201.6(a).

2. Failure to Submit Promotional Materials

You failed to submit these promotional labeling pieces to FDA as is required by the post-marketing reporting requirements, 21 CFR § 314.81(b)(3)(i). This failure to submit promotional labeling to FDA at the time of initial dissemination also violated the Act and regulations.

3. Conclusions and Requested Actions

In order to address these objections, we recommend that you take the following actions:

- Immediately cease the dissemination of all promotional labeling and the publication of any advertisements that state, suggest, or imply that

GensiaSicor's propofol product is not equivalent and substitutable for Diprivan.

- Provide a written response stating your agreement to comply with paragraph .
- Submit a list of all promotional labeling and advertising that you will discontinue as a result of this letter.

Your response should be received not later than April 5, 1999. If you have 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. We remind you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #7617 in addition to the NDA number.

Sincerely,

/S/

Mark W. Askine, R.Ph.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications