DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC - 1 1999

TRANSMITTED VIA FACSIMILE

Carol Patterson, MS
Manager, Regulatory Affairs
Endo Pharmaceuticals Inc.
500 Endo Blvd.
Garden City, NY 11530

RE: NDA 40-288
Zydone (hydrocodone bitartrate and acetaminophen tablets, USP 5mg/ 400 mg, 7.5 mg/ 400 mg, 10 mg/400 mg)
MACMIS ID # 8490

Dear Ms. Patterson:

This letter is in reference to Endo Pharmaceuticals Inc.'s (Endo) submission, dated August 24, 1999, of promotional materials under cover of Form FDA 2253 for Zydone. This submission included a professional direct mail piece, identified as ZY-1015. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed this professional direct mail piece and has concluded that it is in violation of the Federal Food, Drug and Cosmetic Act (Act) and its implementing regulations. Our specific objections follow:

Fair Balance

Promotional materials are misleading if they fail to 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. The efficacy claims for Zydone are prominently presented in large print and occupy the majority of the promotional piece. In contrast, information relating to Zydone's risks is presented in small print confined to the bottom of the page. Therefore, we object to the lack of fair balance with respect to the presentation of risk information in this professional direct mail piece.

Misleading Safety Claims

- You present the claim, "Just 400 mg of acetaminophen per tablet for reduced potential of hepatic toxicity," beneath the headline, "Take The Bite Out Of Pain And The Teeth Out Of Hepatic Toxicity." These claims suggests that the amount of acetaminophen in this product is associated with a reduced risk of hepatic toxicity, as compared to other products, when

such has not been demonstrated by substantial evidence. Therefore, we would consider these claims to be misleading.

You should immediately cease distribution of this professional direct mail piece and other similar promotional materials for Zydone that contain the same or similar claims or presentations. You should submit a written response on or before December 3, 1999, describing your intent and plans to comply with the above. Your letter should include a list of materials discontinued and the date on which these materials were discontinued.

You should direct your response to the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, Rm. 17B-17, 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 #8490 in addition to the NDA number.

Sincerely,

/S/

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