DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAY 16 2003

Frank R. Sisto
Executive Vice President
Regulatory Affairs and Generic Drug Development
Mylan Pharmaceuticals Inc.
781 Chestnut Ridge Road
P. O. Box 4310
Morgantown, West Virginia 26504

Docket Nos. 03P-0107/CP1 and 03P-0113/CP1

Dear Mr. Sisto:

This letter responds to your petitions dated March 18 and March 19, 2003, asking the Food and Drug Administration (FDA) to amend our *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book) to designate two additional reference listed drugs (RLDs) for levothyroxine sodium oral tablets: Abbott Laboratories' Synthroid (Docket No. 03P-0107) and Jones Pharma's Levoxyl (Docket No. 03P-0113). For the reasons stated below, your petitions are granted.

Section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) allows the marketing of generic versions of previously approved drug products when the generic version is the subject of an approved abbreviated new drug application (ANDA). To gain approval, the ANDA must show, among other things, that the generic version has the same active ingredient in the same strength, that its labeling is essentially identical, and that it is bioequivalent to a listed drug, i.e., a previously approved drug product. The specific drug product to which an ANDA refers is the reference listed drug.

FDA's policy on the designation of reference listed drugs is described in the preamble to the final rule establishing the requirements for ANDAs, published in the *Federal Register* of April 28, 1992 (57 FR 17950, 17958):

> . . . FDA will designate all reference listed drugs. Generally, the reference listed drug will be the NDA drug product for a single source drug product. For multiple source NDA drug products or multiple source drug products without an NDA, the reference listed drug

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> generally will be the market leader as determined by FDA on the basis of commercial data. FDA recognizes that, for multiple source products, a product not designated as the listed drug and not shown bioequivalent to the listed drug may be shielded from direct generic competition. If an applicant believes that there are sound reasons for designating another drug as a reference listed drug, it should consult FDA.

FDA has examined the issues presented in your petition and has determined that Synthroid and Levoxyl have substantial shares of the market for levothyroxine sodium oral tablets, and that each share represents significant sales of the drug product, in terms of both the value of those sales and the number of prescriptions filled. The Agency has further determined that it would not be in the public interest to have Synthroid and Levoxyl "shielded from direct generic competition." Accordingly, FDA will designate Synthroid and Levoxyl as reference listed drugs in the Orange Book.

Sincerely yours,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research