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DEPARTMENT OF HEALTH & HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

PHILADELPHIA DISTRICT

WARNING LETTER

900 U.S. Customhouse
2nd and Chestnut Streets
Philadelphia, PA 19106

Telephone: 215-597-4390

February 22, 2002

02-PHI-03

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

David R. Brennan, President and CEO
AstraZeneca Pharmaceuticals LP
1800 Concord Pike
Wilmington DE 19850

Dear Mr. Brennan:

From October 10, 2001 through January 14, 2002, Food and Drug Administration (FDA) Investigators Vlada Matusovsky, Tammy L. Chavis, Debra L. Pagano, and Donald L. Lech conducted an inspection of AstraZeneca Pharmaceuticals LP, located at 587 Old Baltimore Pike, Newark, Delaware. During this inspection deviations from current Good Manufacturing Practice (cGMP) regulations codified at Title 21 Code of Federal Regulations (21 CFR) Part 211 were documented. The following deviation causes your [REDACTED] drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Food, Drug, and Cosmetic Act (the Act).

The Quality Unit failed to adequately investigate the impact of the presence of [REDACTED] in [REDACTED] drug products when environmental monitoring samples taken in the [REDACTED] facility were found positive for [REDACTED] [21 CFR 211.22]. For example, your firm possessed no validated analytical method to determine if [REDACTED] drug products were cross-contaminated with [REDACTED].

We note that in your letter dated February 6, 2002, Elvin M. Clausen, V.P. Quality Assurance, indicated that you subsequently tested retain samples of [REDACTED] drug products for the presence of [REDACTED] he reported no cross-contamination with [REDACTED] was found. However, he did not submit documentation to support his conclusion, e.g., analytical records, nor did he submit documentation to indicate the method(s) used was validated. Please provide this office with your analytical results to date as well as methodology and related validation work.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. FDA inspections are audits which are not intended to determine all deviations from cGMPs. It is

Page 2

Warning Letter: AstraZeneca Phramaceuticals LP

not the role of FDA to inspect a firm into compliance. As top management, it is your responsibility to ensure that all requirements of the cCGMP regulations are being met as well as all other requirements of the Act. The specific violation noted in this letter and in form FDA 483, Inspectional Observations, issued at the conclusion of the inspection by the FDA investigators may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems.

The aforementioned February 6, 2002 letter responding to form FDA-483, reports corrections have been made to additional, significant cGMP deviations. The adequacy of these corrective actions will be reviewed during the next FDA inspection of AstraZeneca.

You should take prompt action to correct the deviations with respect to all products where these deficiencies in controls apply. Failure to promptly take corrective action may result in regulatory action without further notice. Possible regulatory actions include seizure and/or injunction.

Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts. Additionally, new drug applications (NDA's), abbreviated new drug applications (ANDA's), and export approval requests may not be approved until the aforementioned violations are corrected.

Please advise this office in writing within fifteen (15) days of receipt of this letter as to any additional specific actions you have taken or intend to take to correct these violations and prevent their recurrence. Your reply should be directed to the attention of James C. Illuminati, Compliance Officer, at the address noted in the letterhead.

Sincerely,



Thomas D. Gardine
District Director
Philadelphia District

jci