DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

M2819n

WARNING LETTER

19900 MacArthur Blvd., Ste 300
Irvine, California 92612-2445
Telephone (949) 798-7600

July 21, 1999

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Frank Becker, Executive Vice President
Chief Operating Officer
Gensia Sicor Pharmaceuticals, Inc.
19 Hughes
Irvine, CA 92618

W/L 37 - 9

Dear Mr. Becker:

During an inspection of your pharmaceutical manufacturing facility conducted on June 14 to 24, 1999, our investigators found significant deviations from the Good Manufacturing Practice for Finished Pharmaceuticals regulations (Title 21, Code of Federal Regulations (CFR), Parts 210 and 211). Such deviations cause human drugs manufactured by your company to be adulterated within the meaning of Section 501 (a)(2)(B) of the Federal Food, Drug and Cosmetic Act (Act).

Our investigation revealed that there is no assurance that the methods used in or the facilities and controls used for the manufacture, processing, packing, or holding of your finished pharmaceuticals are in conformance with the GMP requirements as follows:

1. Failure to establish procedures to assure equipment and utensils are sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of drugs beyond the official or other established requirements [21 CFR 211.67]. Specifically, your firm does not have sufficient evidence demonstrating that the sanitizing processes used to clean production equipment and areas are valid and that all residues have been reduced to acceptable levels.

2. Failure to maintain laboratory records to include complete data derived from all tests necessary to assure compliance with established specifications and standards [21 CFR 211.194]. Specifically, your firm failed to properly maintain electronic files containing data secured in the course of tests from 20 HPLCs and 3 GLCs. Additionally, no investigation was conducted by your company to determine the cause of missing data and no corrective measures were implemented to prevent the recurrence of this event.

We have received your firm's letter dated July 12, 1999 which you provided in response to the form FDA 483, issued to your firm on June 24, 1999. We must advise you that your response does not adequately address the problems disclosed during our inspection. Your response does not provide sufficient documentation to eliminate our concerns regarding your weaknesses in your cleaning validation of your production equipment. Additionally, please provide copies of your written procedures describing system security, system maintenance, and data file backup procedures for assuring backed up automated laboratory files are retrievable. Your proposed corrections will be verified during our future inspections(s).

The above listed violations are not intended to be construed as all inclusive of those existing at your firm. It is your responsibility to ensure that all requirements of the Federal Food, Drug, and Cosmetic Act and regulations promulgated thereunder are being met.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such action includes, but is not limited to, 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, pending Antibiotic Form 6, NDA, ANDA, or expert approval requests may not be approved until the above violations are corrected.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you plan to take to assure that each of the noted violations will be corrected. Your response should also include an explanation of the specific steps which will be taken to prevent the recurrence of similar violations. If you have any questions you may contact Dannie E. Rowland, Compliance Officer, at (949) 798-7648.

Your written reply should be addressed to:

Thomas L. Sawyer
Director of Compliance
U. S. Food and Drug Administration
19900 MacArthur Boulevard, Suite 300
Irvine, CA 92715-2445

Sincerely,

Thomas L. Sawyer

Acting District Director

cc: Carlo Salvi, President
Chief Executive Officer
Sicor Inc.
19 Hughes
Irvine, CA 92618

State Department of Public Health
Environmental Health Services
Attn: Chief, Food and Drug Branch
601 North 7th Street
P.O. Box 942732
Sacramento, CA 94234