DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Detroit District
1560 East Jefferson Avenue
Detroit, MI 48207-3179
Telephone: 313-226-6260

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CERTIFIED MAIL

RETURN RECEIPT REQUESTED

WARNING LETTER
2000-DT-27

July 11, 2000

Keith D. Gates
President and CEO
Integrity Pharmaceutical Corporation
9084 Technology Drive, Suite 600
Fishers, Indiana 46038

Dear Mr. Gates:

A March 15 through April 12, 2000 inspection of your firm's drug manufacturing operations found that your firm is operating in serious violation of the Federal Food, Drug, and Cosmetic Act (the Act). During the inspection, our investigators documented numerous significant deviations from the Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Part 211), which cause your drug products to be adulterated within the meaning of section 501(a)(2)(B) of the Act. While examples are as follows, we suggest you refer to the list of inspectional observations [the FDA-483] which was issued at the conclusion of the inspection for additional details:

1. Failure to have a quality control unit adequate to perform its functions and responsibilities, as required by 21 CFR 211.22. Your failure to have an adequate quality control unit is demonstrated by the number and types of inspectional observations made during this inspection.

2. Failure to have an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of a drug product and/or failure to ensure that each person engaged in such activities has the education, training, and experience, or any combination thereof, to enable them to perform their assigned functions, as required by 21 CFR 211.25. Your failure to have a staff adequate to perform their assigned functions, is demonstrated by the number and types of inspectional observations made during this inspection.

3. Failure of the quality control unit to review all drug product production and control records to determine compliance with established written procedures before a batch is released or rejected, and to perform an investigation when a batch or its components fails to meet specifications, as required by 21 CFR 211.192. For examples, see FDA-483 observations 8 and 9.

4. Failure to establish and to follow written control procedures designed to assure batch uniformity and the integrity of drug products, as required by 21 CFR 110. For example, see FDA-483 observations 5, 6 and 10.

5. Failure to have batch production and control records that include complete information relating to the production and control of each batch, as required by 21 CFR 211.188. For example, see FDA-483 observations 13, 17, 22 and 26.

6. Failure to have, to follow, and to have a record justifying any deviations from, procedures for production and process control designed to assure that drug products have the identity, strength, quality, and purity they purport or are represented to possess, as required by 21 CFR 211.100. For example, see FDA-483 observations 6, 14 and 15.

7. Failure to make an appropriate laboratory determination of satisfactory conformance of each batch of drug product to its final specifications prior to its release, as required by 21 CFR 211.165. For example, see FDA-483 observation 3.

8. Failure to have, and/or to follow, laboratory controls which include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality and purity, as required by 21 CFR 211.160. For example, see FDA-483 observations 1, 2, 4, 5, 10, & 18.

9. Failure to maintain laboratory records that include complete data from all tests necessary to assure compliance with established specifications and standards, as required by 21 CFR 211.194. For example, see FDA-483 observation 13.

10. Failure to adequately evaluate, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing and control procedures, as required by 21 CFR 211.180(e). For example, see FDA-483 observations 7 and 28.

11. Failure to have, and to follow, a stability testing program adequate to assess the stability characteristics of drug products, as required by 21 CFR 211.166. For example, see FDA-483 observations 11, 13 and 16.

12. Failure to maintain adequate control over air handling and exhaust systems, as required by 21 CFR 211.46. For example, see FDA-483 observations 19 and 21.

13. Failure to assure that equipment is routinely calibrated, inspected or checked according to a written program designed to assure proper performance, as required by 21 CFR 211.68(a). For example, see FDA-483 observations 20, 22, 23, 24 and 25.

14. Failure to have appropriate controls over computer or related systems to assure that changes in records are instituted only by authorized personnel, as required by 21 CFR 211.68(b). For example, see FDA-483 observation 12.

15. Failure to have and/or to follow written procedures for reprocessing, as required by 21 CFR 211.115. For example, see FDA-483 observation 15.

The above list of deviations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Good Manufacturing Practice Regulations. Other Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

We request that you take prompt action to correct these violations. Failure to promptly correct these violations may result in enforcement action being initiated by the Food and Drug Administration without further notice, such as seizure and/or injunction.

We acknowledge receipt of your various written and verbal responses to the list of inspectional observations and your commitments to take specific steps to correct the noted violations. We request that you thoroughly evaluate the adequacy of your procedures and controls, and that you take whatever actions are necessary to make systemic corrections and to assure that similar violations will not recur. Our review of your responses finds some of them appear to only address the specific examples noted on the list of inspectional observations, and we are not sure from these responses that you understand all of the specific and/or systemic deficiencies which may exist at your firm. Thus, we concur in your decision to seek the assistance of outside expertise, and we recommend that you have your consultants evaluate the adequacy of your various responses.

Please notify this office in writing, within fifteen (15) working days of receipt of this letter, as to any additional steps you have taken to correct these violations, including an explanation of each step being taken to identify and make corrections to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be implemented.

Your reply should be directed to Melvin O. Robinson, Compliance Officer, at the above address.

Sincerely,

John P. Dempster

for Raymond V. Mlecko
District Director
Detroit District

Cc via certified mail:
Mr. Matthew A. Szczesiul
Vice President of Operations
Integrity Pharmaceutical Corporation
5767 Thunderbird Road
Indianapolis, IN 46219