



10/7/97

HAND DELIVERED

WARNING LETTER

1990 MacArthur Blvd., Ste 300
Irvine, California 92715-2445
Telephone (714) 798-7600

July 23, 1997

WL-30-7

Wanjun Li
President
Biokwitech, Inc.
4204L Sorrento Valley Blvd.
San Diego, CA 92121

Dear Dr. Li:

During an inspection of your facility conducted between July 3 to July 9, 1997, our investigators determined that your firm manufactures and distributes a wide variety of in vitro diagnostic products, including HIV 1/2, HBsAg, and HBsAb tests. These in vitro diagnostic products are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above stated inspection revealed that these device are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to establish procedures describing any process controls necessary to ensure that devices conform to their specifications. For example, there are no written instructions which describe the production processes or monitoring steps of process parameters of devices during production. Additionally, there is no documentation which describes any of the production equipment or production processes or written procedures for storage, handling, acceptance and use of mice colonies used to produce hybridomas used in your antibody and antigen production of in vitro diagnostic products.
2. Failure to establish procedures for validation of production processes and major equipment used in the production of your in vitro diagnostic products. For example, there are no procedures describing the production or controls for proteins 41 and 36 including growth and harvesting of recombinant E. coli and purification of proteins used in your HIV 1/2 test kits. Also, there are no procedures describing the production or controls used in the production monoclonal antibodies which are used in the production of your in vitro diagnostic products.
3. Failure to establish any procedures for receiving, reviewing, and evaluating complaints. For example, there is no documentation of complaint evaluations.

Reports of false positives involving HIV and HCV test kits were not evaluated.

4. Failure to establish any procedures for implementing corrective and preventive action for nonconformities. For example, there is no documentation of any investigations the ascertain to reason for 5 nonconforming lots of HIV test kits.

5. Failure to establish any procedures to control product that does not conform to their specified requirement nor have any investigations been conducted of products failing to meet their specifications. For example, our investigation determined that upwards to 5 lots of HIV test kits failed to meet their specifications yet no investigation was conducted.

6. Failure to establish any procedures for finished device acceptance to ensure that each production run of finished devices meets its acceptance criteria.

7. Failure to prepare and maintain any device master records for any of your in vitro diagnostic products.

8. Failure to establish any procedures for acceptance of incoming products. For example, there are no records of acceptance or rejection of components.

9. Failure to establish any procedures to prevent contamination of equipment or product by substances that could have an adverse effect on product. For example, there is no written procedures for sanitization/sterilization of glassware used in the production of monoclonal antibodies and protein materials used in the production of in vitro diagnostic devices.

10. Failure to establish any procedures to ensure that measurement and production equipment is routinely calibrated, inspected, checked and maintained. For example, there is no documentation describing any maintenance, inspection, or calibration activities conducted on your incubators, deionized water system, vacuum chambers, laminar flow workstation, sterilizer, or electrophoresis equipment.

11. Failure to establish any procedures for quality audits nor has any quality audits been conducted by firm since the company was founded in 1992.

12. Failure to designate any individual(s) or establish any procedures to control all documents that are required by this regulation. For example, written production records and written procedures have not been signed nor approved by a individual. Also, you have not established any procedures for identifying training needs to ensure that all personnel are properly trained to perform their assigned functions nor is there any documentation of any training provided to any of the firm's employees.

13. Failure to designate a representative of management to ensure that the quality

system requirements are effectively established and maintained.

14. Failure to establish any procedures to ensure that all purchased or otherwise received product and services conform to specified requirements. For example, there is no specified requirements for the contract services of the company which services and maintains the deionized water system used by the company for production of their devices.

15. Failure to establish any procedures for identifying product during all stages of receipt, production, or distribution. For example, incoming components and inprocess devices are not identified.

16. Failure to establish any procedures to control labeling activities.

17. Failure to establish procedures for the control of storage and stock rooms for products to prevent mixups, damage, deterioration, contamination, or other adverse effects.

18. Failure to establish a quality system record.

19. Failure to establish any MDR procedures.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the form FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violation identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal Agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no request for Certificates For Products For Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunctions, and/or civil penalties.

Because of the serious nature of these violations and our concerns regarding the safety and efficacy of your devices and methods used in, or the facilities or controls used for manufacturing, packing, and storage of your in vitro diagnostic products, our office wishes to meet with you at the earliest possible date to discuss your corrective measures. Please contact

FDA Compliance Officer Dannie E. Rowland at (714) 798-7649 in order that the necessary arrangements can be made for the meeting.

Additionally, please prepare a written response within (5) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections. You may bring your written response with you to the meeting.

Your reply should be addressed to:

Dannie E. Rowland
Compliance Officer
U.S. Food and Drug Administration
19900 MacArthur Boulevard, Suite 300
Irvine, California 92715-2445

Sincerely,



Elaine C. Messa
District Director

cc: State Department of Public Health
Environmental Health Services
Attn: Chief Food and Drug Branch
601 North 7th Street, MS-357
P.O. Box 942732
Sacramento, CA 94234-7320