DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
m2667n

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

WARNING LETTER

May 27, 1999

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Alice H. Yu, Vice President
Pan Probe Biotech, Inc.
8515 Arjons Drive, Suite A
San Diego, CA 92126

WL 31-9

Dear Ms. Yu:

During an inspection of your facility conducted on April 14 and 19, 1999 our investigator determined that your firm manufactures and distributes a wide variety of in vitro diagnostic products for detection of diseases and drug substance abuse. 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 current good manufacturing practice (CGMP) for medical devices, as set forth in the Quality System Regulations, Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

- Failure to establish and implement a quality policy which bears on the intentions and direction of your organization with respect to quality regarding medical devices [21 CFR 820.20(a)].
- Failure to document the appointment of a management representative for ensuring that the quality system requirements are effectively established and implemented [21 CFR 820.20(b)(3)].
- Failure to establish and implement a quality plan which defines the quality practices, resources, and activities relevant to devices that are designed and manufactured by your firm since the Quality System Regulation became effective [21 CFR 820.20(d)].
- Failure to establish and implement any quality system procedures [21 CFR 820.20(e)].
- Failure to establish and implement any quality audit procedures nor have any audits been conducted to assure that the quality system is in compliance with the established quality system requirements [21 CFR 820.22].

- Failure to establish and implement procedures for identifying employee training needs and ensure that all employees are adequately trained [21 CFR 820.25(b)].

- Failure to establish and implement any procedures to control all documents that are required by the Quality System Regulation [21 CFR 820.40].

- Failure to establish and implement any procedures to ensure that all purchased or otherwise received products and services conform to specified requirements [21 CFR 820.50].

- Failure to establish and implement any procedures to ensure that suppliers were evaluated and selected on the basis of their ability to meet specified requirements [21 CFR 820.50(a)].

- Failure to establish or implement any procedures for the design and development plan of devices [21 CFR 820.30(b)].

- Failure to establish and implement any procedures to control the design process of devices [21 CFR 820.30(a)].

- Failure to maintain any design history files for any devices to demonstrate that the design was developed following an approved design plan [21 CFR 820.30(j)].

- Failure to establish and implement any procedures for identifying product throughout all stages of incoming, production, packaging and distribution [21 CFR 820.86].

- Failure to establish and implement any process control procedures [21 CFR 820.70(a)].

- Production processes are not monitored and controlled to ensure that a device conforms to its specifications [21 CFR 820.70(a)(2)].

- Failure to provide any documented evidence demonstrating that processes and process equipment have been approved [21 CFR 820.70(a)(4)].

- Failure to establish and implement any procedures for controlling environmental conditions [21 CFR 820.70(c)].

- Failure to establish and implement any procedures for addressing the health, cleanliness, personal practices, clothing of employees [21 CFR 820.70(d)].

- Failure to maintain any schedules for adjustment, cleaning or other maintenance of equipment [21 CFR 820.70(g)(1)].

- Failure to establish and implement any procedures to ensure that equipment is routinely calibrated, inspected or checked [21 CFR 820.72(a)].

- Failure to establish and implement any procedures for inspections, tests, or other verification activities for receiving, in-process and finished device acceptance activities CFR 820.80(a)(d)]

- Failure to establish any procedures for labeling and packaging controls [21 CFR 820.120].

- Failure to prepare, obtain approval and maintain any device master records (DMR's) for any devices produced by your firm in accordance with procedures set forth [21 CFR 820.40].

- Failure to establish and implement any procedures to ensure that device history records (DHR's) are maintained for each lot of devices manufactured in accordance with device specifications and production process procedures in the DMR and the Quality System Regulations [21 CFR 820.184].

- Failure to establish and implement any procedures for addressing the identification, documentation, evaluation, segregation, disposition and investigation of nonconforming product [21 CFR 820.90(a)].

- Failure to establish and implement any procedures for implementing corrective and preventive actions addressing analyzing of sources of quality data to identify existing and potential causes of non-conforming product or other quality problems [21 CFR 820.100(a)(1)].

- Failure to establish and implement any procedures for complaint handling to ensure that all complaints are processed in a uniform and timely manner [21 CFR 820.198(a)(1)].

- Failure to maintain any complaint files [21 CFR 820.198(a)].

- Failure to establish and implement any procedures for the evaluation, handling, and reporting events subject to Medical Device Reporting regulation 21 CFR 820.198(a)(3)].

Additionally, your in vitro diagnostic products are adulterated within the meaning of Section 501(f)(1)(B) of the Act in that they are Class III devices under Section 513(f) of the Act and there is no approved application for premarket approval in effect pursuant to Section 515(a), or an approved application for investigational device exemption under Section 520(g).

Additionally, your devices are misbranded within the meaning of Section 502(b) of the Act because the devices in package form fail to bear a label containing the place of business of the manufacturer, packer, or distributor; or an accurate statement of the quantity of contents.

Your in vitro diagnostic products are also misbranded within the meaning of Section 502(o) of the Act in that a notice or other information for the devices was not provided to the FDA as required by Section 510(k) and that the devices were manufactured in an establishment not duly registered under Section 510 of the Act and your in vitro diagnostic products have not been listed with the FDA as required by Section 510(j). Copies of these forms were provided to you at the conclusion of the inspection.

Additionally, you are in violation of Section 802(g) of the Act since you have failed to comply with the requirements outlined in the statute, in that a simple notification was not provided to the Secretary

identifying the devices and the country to which such devices were being exported when the exporter first began to export the devices to a country not listed in Section 802(b)(I)(A)(I) or (ii) of the Act. For example, your in vitro diagnostic devices were exported to China without notification.

The inspection also disclosed that the devices have been exported in violation of Section 801(e)(2) of the Act since you did not receive permission from the FDA to export the devices or failed to comply with the export requirements of Section 802 of the Act. Specifically, you have not demonstrated that the export of the devices was in compliance with the requirements outlined in Section 802(b)(1)(A) of the Act.

According to Section 801(e)(1)(C) and (D) a device intended for export shall not be deemed to be adulterated or misbranded if it is labeled on the outside of the shipping package that it is intended for export, and is not sold or offered for sale in domestic commerce. Our inspection determined that your in vitro diagnostic products packaging does not bear any statement on the outside of the shipping packages that they are intended for export. Our inspection also determined that these products were offered for sale to other companies within the United States.

Requests for Export Permits should be sent to:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance (HFZ-307)
Division of Program Operations
Information Processing and Office, Automation Branch
2098 Gaither Road
Rockville, MD 20850

We acknowledge that you have submitted a written response dated April 21, 1999 concerning the observations noted on the form FDA-483. Whereas, your response provided copies of your proposed established procedures concerning the requirements of the Quality System Regulation, it did not describe any measures undertaken by your company to obtain the necessary premarket clearances necessary to commercially market your devices within the United States or for exportation.

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 requests 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.

Please notify this office in writing, within 15 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 to any underlying systems problems necessary 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 within which the corrections will be completed.

Your reply should addressed to:

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

If you have any questions concerning this matter you may address them to Dannie E. Rowland, Compliance Officer, at this location.

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