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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Atlanta District Office
HFI-35

60 8th Street, N.E.
Atlanta, Georgia 30309

(FSV)
11/3

October 23, 1997

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

E. Nigel Harris, MD
President
Louisville APL Diagnostics, Inc.
Suite 1528
455 South Fourth Avenue
Louisville, Kentucky 40202

WARNING LETTER

Dear Dr. Harris:

An inspection of your firm located in Doraville, Georgia, was conducted between September 26 and October 3, 1997. Our investigator found that you are manufacturing and distributing the APhL ELISA Test Kit. This product is a device as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The investigator documented several significant deviations from the Good Manufacturing Practice for Medical Devices (GMPs) as set forth in Title 21 of the Code of Federal Regulations (21 CFR), Part 820. These observations would also be violations of the Quality System Regulation, 21 CFR Part 820, which became effective June 1, 1997. These deviations cause the device you manufacture and distribute to be adulterated within the meaning of Section 501(h) of the Act.

You have failed to validate the heat sealing equipment utilized on the antigen test strip packaging. You could not provide documented evidence which established a high degree of assurance that the sealing equipment and process in use are effective and could consistently produce a product meeting its predetermined specifications and quality attributes. You had failed to formally establish acceptable limits for the three variable parameters in use on the [redacted] sealer which would provide an appropriate seal. This sealing process is significant in that our investigator was told that the microwell plates are sensitive to light and moisture. You could provide no documentation as to the testing or calibration of this instrument after it was relocated from the Kentucky facility. You could provide no documentation that any package integrity testing had ever been performed on sealed pouches at this location.

You have failed to validate the software in use [redacted] to calculate GPL and MPL unit values. These test values are used in the release of finished product. This specific application has never been validated for this intended use by your firm or the software supplier. You could provide no documentation that the results produced are comparable to the data obtained previously by manual calculations. There is no assurance that absorbance values are properly converted to MPL and GPL units to meet final product specifications.

You could not provide adequate documentation to assure that your product will maintain its functionality throughout its labeled expiration date of nine months. The available stability data consisted of random unsorted raw data lacking any approved protocol, acceptance criteria, or final evaluation of the data. Stability testing was discontinued in March 1996 and there was no current procedures requiring additional studies. Additional stability studies are needed if there is any significant change which may affect stability in the manufacturing process, equipment, or components. The relocation of the manufacturing operations to the current facility could qualify as a significant change.

You had failed to evaluate the current product packaging and shipping procedures to determine if they adversely affect product performance. You could provide no documentation that current shipping methods could maintain the specified storage conditions for your product.

Your quality assurance program failed to respond to device quality problems identified as a result of consumer complaints and retained product testing. Your quality assurance program is responsible for identifying, recommending, and providing solutions for quality assurance problems and verifying the implementation of such solutions. On three separate occasions, product malfunction complaints were confirmed from testing of retained product. In each of these instances, no investigation was performed to identify the possible cause or extent of the problem. The only action taken by your firm was product replacement. The above discussed shipping studies and stability studies could be useful in the evaluation of these types of product functionality complaints.

You could provide no statistical rationale for the sampling plan currently in use for the testing and release of finished product kits. No explanation could be provided for the current sampling level of [redacted] kits per lot.

You could not provide adequate assurance that all production and quality assurance testing equipment was suitable for its intended purposes and capable of producing valid results. No documentation was available to indicate that the [redacted] pH Instrument, [redacted] Scale, or [redacted] Monitors had ever been calibrated. There were no established procedures in place addressing the routine calibration of this equipment or establishing a calibration schedule. A review of the available calibration data for the [redacted] Pipette found that it failed to verify the accuracy and precision of each channel. The ability of each channel to consistently deliver a specified volume of liquid was not evaluated. This instrument is used in the release of finished product.

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. At the close

of the inspection, the Inspectional Observations (FDA 483) was issued to and discussed with Dr. Silvia Pierangeli, Technical Director. A copy of the FDA 483 is enclosed for your review. The specific violations noted in this letter and in the FDA 483 could be symptomatic of serious underlying problems in your firm's quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions. We are aware that the Cincinnati District Office issued a Warning Letter to you in March 1996 We are concerned that although those specific deviations were corrected, significant problems continue to exist at your firm.

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 submission of devices to which the GMP deficiencies are reasonably related will be cleared until these 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 actions being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) 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.

We are in receipt of the October 11 response from your firm to the FDA 483. That response is currently under review. You may reference the October 11 letter in your Warning Letter response, if you feel that it adequately addresses any of the issues raised in this letter. Your response should be sent to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead.

Sincerely yours,

Ballard H. Graham, Director
Atlanta District

Enclosure

cc: Dr. Silvia Pierangeli
Louisville APL Diagnostics
3988 Flowers Road, Suite 620
Doraville, Georgia 30360