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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3128

March 13, 2007

Ref: 2007-DAL-WL-11

WARNING LETTER

CERTIFIED MAIL
RETURNED RECEIPT REQUESTED

Mr. Miles D. White
Chairman of the Board and Chief Executive Officer
Abbott Laboratories, Inc.
100 Abbott Park Road
Abbott Park, Illinois 60064

Dear Mr. White:

During an inspection of your firm (Abbott Diagnostics Division – Dallas ADD) located at 1921 Hurd Drive, Irving, Texas 75038, from October 30 through November 17, 2006, the United States Food and Drug Administration (FDA) determined that your firm manufactures, distributes, and installs automated clinical chemistry and immunoassay analyzers for the diagnosis of diseases. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 321(h)), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or are intended to affect the structure or function of the body.

This inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act, 21 U.S.C. § 351(h), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820. Your devices are also misbranded under section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), because your firm submitted several late MDR reports.

We received your firm's responses, dated December 14, 2006, January 15, and February 14, 2007, responding to our investigators' observations noted on the Form FDA 483, List of Inspectional Observations, which was issued to your firm (copy enclosed) on November 17, 2006. At your firm's request, on January 25,

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2007, representatives of the FDA's Dallas District Office held a meeting with the management team from the Dallas ADD and Chicago Corporate Office to discuss your firm's quality system improvements. Your firm responded that its corrective actions are ongoing and that your firm will implement a more robust, comprehensive corrective action plan to correct compliance and quality issues globally across your product lines and update the FDA of the progress of your firm's corrective actions in subsequent progress reports. Although the Agency recognizes your firm's commitment to improving product quality and compliance with the Quality System Regulation, the Agency is not satisfied with the pace and the results of your firm's past corrective actions as they have not been effectively, timely, and globally implemented for your entire family of analyzers. The current inspection documented repeat inspectional observations in your firm's CAPA System, Production and Process Control System, and MDR reporting. Your firm responded that it is still collecting and analyzing various quality sources and conducting engineering studies to determine potential root causes of the failures of the pressure monitors and pumps in the i2000, i2000SR, and ci8200 analyzers in order to implement effective corrective actions. Abbott Laboratories must timely and effectively implement permanent and substantial actions to correct systemic noncompliant issues at its Irving, Texas manufacturing site. Your firm's responses are incomplete until your firm adequately corrects recurring inspectional observations, specific issues cited in this warning letter, and various quality issues in all of your analyzers in a systemic manner; submits the progress reports your firm promised; and meets the Agency's requirements that call for the audits and certifications by an outside expert consultant and the certifications by your firm's Chief Executive Officer in the specific timeframes outlined in this warning letter. FDA follow-up inspections will be required to assure that corrections are adequate.

These violations include, but are not limited to, the following:

Quality System Violations

1. Failure of the management with executive responsibility to ensure that an adequate and effective quality system has been fully implemented and maintained at all levels of the organization, as required by 21 C.F.R. § 820.20. For example, your firm's management has not effectively implemented adequate and global corrective actions in a timely manner to correct quality issues across your analyzer product lines. The FDA's current inspection involved the issuance of an 11-item FDA-483 to your firm. Your firm made incomplete corrections as some of the current inspectional observations were repeat observations from the previous inspections of 2003 and 2004.

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2. Failure to establish and maintain adequate management review procedures and conduct adequate management reviews to meet the requirements of the Quality System Regulation and the manufacturer's established quality policy and objectives, as required by 21 C.F.R. § 820.22(c). Your firm's management failed to review all quality sources and take appropriate corrective actions to address various quality issues or document their adequate justification for not taking corrective actions. For example, your Dallas ADD's site management used a "dollar value" as the alert level for part replacements as a measure of malfunctions of the analyzers upon installation at their user sites to determine whether or not to further evaluate, conduct investigations, or take actions to address potential quality issues with your analyzers. If the cost of the replacement parts or "bad installs" did not exceed a "dollar" alert level, there was no investigation conducted. See your firm's Quality Metrics Report "The Installation and Performance Metrics for the c8000, i2000, i2000SR analyzers" that characterized that a number of the analyzers were found DOA (dead on arrival) upon installation in each month from 10/2004 through 9/2006.
3. Failure to establish and maintain procedures for the analysis of all sources of quality data to identify existing and potential causes of nonconforming product or other quality problems, as required by 21 C.F.R. § 820.100(a)(1), and failure to document the results of corrective action activities, as required by 21 C.F.R. § 820.100(b). For example, your firm failed to collectively analyze all sources of quality data (e.g. defective parts rejected during incoming and factory testing, defective parts rejected during initial installation of the analyzers at user sites, and defective parts replaced during service calls of the analyzers) to identify potential quality issues and their root causes at the component level or the analyzer level, and document the results of your analysis. Your firm's responses stated that your firm had not analyzed service calls for parts being replaced in the past. To remedy this situation, among the issues explained in your responses, you stated that your firm will analyze critical components at a minimum of [REDACTED] every [REDACTED] collect failed part returns for further evaluation, and conduct investigations into the causes of failed parts during field services of your analyzers. Your firm's responses are not adequate as your firm should conduct analyses of all quality data on a more frequent basis to timely identify quality issues and their root causes, and therefore, implement timely corrective actions. Regardless of the assigned classification for each analyzer component (e.g. critical, major, and minor parts), your firm must take appropriate actions to improve product quality (reliability) as each defective part could cause your analyzer to stop working and result in the delay of testing patient samples, transmitting patient test results to their physicians, or could cause aberrant test results.

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4. Failure to identify the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems, as required by 21 C.F.R. § 820.100(a)(3). For example, at the time of the inspection, your firm had not initiated and implemented adequate actions to address potential quality issues with your analyzers despite the fact that from November 2004 through October 2006, your firm received 612 worldwide complaints of pressure monitor failures, factory nonconforming reports documenting 313 pressure monitors and 306 pumps that failed factory testing, 58 out-of-box failures of the pressure monitors upon installation of analyzers at user sites, field service calls to replace these components and other components, and the DD005 Metrics Report identifying that the pressure monitors and pumps were two of the top ten defective parts. Your firm's responses concluded that your firm is still conducting additional investigations and/or analysis in order to understand the causes of the part failures.
5. Failure to establish and maintain procedures for verifying and validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished devices, as required by 21 C.F.R. § 820.100(a)(4). Your firm's DD005 Metrics Report entitled "i2000SR Arrive Alive," dated April 2005, documented that the pressure monitors were susceptible to freezing when exposed to cold temperatures and that a correction would be implemented with Software Version [REDACTED]. This information was not elaborated further in the subsequent September 2006, DD005 Metrics Report or was not included in your firm's responses to verify the effectiveness of this software change. Additionally, your responses indicated that the majority of the factory failures of the pressure monitors [REDACTED]%) were due to "erratic/no results" and the other failures [REDACTED]%) were due to "aspiration errors" and that your firm did not investigate each failure individually. Regarding the pumps, your firm's responses confirmed that the majority of their factory failures and field replacements were due to motor step loss errors but that their failure causes were not well understood. In short, your firm's action which was to simply replace malfunctioned pressure monitors and pumps, or any other defective components during factory testing, site installation, and subsequent service calls of analyzers, is not an effective solution, and cannot be effectively verified nor validated without investigating all possible hardware and software fault conditions occurring during factory testing and field clinical use of the analyzers.
6. Failure to establish and maintain adequate procedures for finished device acceptance to ensure that each production run, lot, or batch of finished devices meets acceptance criteria prior to releasing the devices for distribution, as required by 21 C.F.R. § 820.80(d). Your factory testing failed

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to adequately detect and reject defective device components, including the pressure monitors and pumps, and nonconforming device functions prior to releasing the analyzers for site installation. According to your firm's DD005 Metrics Report for the period of November 2004 through October 2006, many analyzers were characterized as "bad installs" at the user sites and their components had to be replaced. For example, this report stated that in April 2005, out of the [REDACTED] installations of the i2000SR analyzers, [REDACTED] analyzers were "Dead On Arrival" and that the "Arrive Alive" percentage was 76%.

7. Failure to establish and maintain adequate procedures to ensure that all purchased or otherwise received product and services conform to specified requirements, and to include evaluation of suppliers, contractors, and consultants, as required by 21 C.F.R. § 820.50. For example, your firm rejected defective components during incoming and finished device testing, documented nonconforming material reports for rejected components, and then sent supplier corrective action reports to your suppliers to notify them of quality issues. However, your firm failed to collectively use these sources of information to re-evaluate the overall quality rating of your suppliers as required by your procedures. Additionally, despite the fact that your firm documented negative quality data for the pressure monitors and pumps, your firm has not adequately evaluated the ability of the two suppliers to meet your firm's requirements.
8. Failure to establish and maintain adequate procedures for acceptance or rejection of incoming product, and for documenting the results of acceptance or rejection, as required by 21 C.F.R. § 820.80(b). For example, your Inspection Quality Assurance (IQA) unit did not follow your firm's inspection procedures in that your IQA staff used incorrect sampling plans, released components that failed acceptance criteria for production without documenting adequate justification, and did not completely document the types of inspection and secondary checks by peer review.
9. Failure to establish and maintain adequate procedures for review and disposition of nonconforming product, and for documenting adequate justification for use of nonconforming product, as required by 21 C.F.R. § 820.90(b)(2). Your firm allowed the production use of components that did not meet your approved specifications. Your firm simply documented "the impact assessment rating is low per procedure S05.015" without providing adequate narrative details to justify the risk for using nonconforming product. For example, defective pumps were returned to your supplier for reprocessing or repair and sent back to your firm for use. During your factory testing, the motors of the reprocessed pumps were found to be ceased. Your firm nether

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adequately documented any adverse effect of the [REDACTED] of the reagents in the pumps when these pumps were replaced during field service calls and returned to their supplier for reprocessing nor evaluated the reliability of reprocessed pumps for reuses. See Supplier Corrective Action Report (SCAR) and Exception Report (ER) Report 168285.

Medical Device Reporting (MDR) Violation

The inspection also revealed that your devices are also misbranded under Section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed to furnish any material or information respecting the devices that is required by or under Section 519 of the Act, 21 U.S.C. § 360i, and 21 C.F.R. Part 803 – Medical Device Reporting (MDR) regulation. For example, your firm submitted to FDA several MDR reports that exceeded the 30-day timeframe of becoming aware of medical adverse events.

Audit Certifications

We are requesting that you submit to this office on the schedule below, certification by an outside expert consultant that he/she has conducted an audit of your establishment's manufacturing and quality assurance systems relative to the requirements of the device's QS regulation (21 C.F.R. Part 820) and the MDR regulations (21 C.F.R. Part 803). You should also submit a copy of the consultant's report, and certification by the establishment's Chief Executive Officer (if other than yourself) that he or she has reviewed the consultant's report and that the establishment has initiated or completed all corrections called for in the report. The initial certifications of audit and corrections and subsequent certifications of updated audits and corrections should be submitted to this office by the following dates:

- Initial certifications by consultant and the establishment's Chief Executive Officer are due on August 15, 2007, approximately six months after issuance of this warning letter.
- Next certifications by consultant and the establishment's Chief Executive Officer are due in May of 2008 and 2009. FDA may conduct follow-up inspections any time between August 2007 and May 2009.

Response to the Warning Letter

You should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action being

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initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties. Also, 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, premarket approval applications for Class III devices to which the QS regulation deviations are reasonably related will not be approved until the violations have been corrected. Requests for Certificates to Foreign Governments will not be granted until the violations related to the subject devices have been corrected.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include documentation of the corrective action you have taken. If your planned corrections will occur over time, please include a timetable for implementation of these corrections. If the 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 response should be sent to Thao Ta, Compliance Officer, DAL-DO, Food and Drug Administration, HFR-SW140, 4040 N. Central Expressway, Suite 300, Dallas, TX 75240. If you have any questions about the contents of this letter, please contact Mr. Ta at 214-253-5217.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. 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 problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to correct the violations and to bring your products into compliance.

Sincerely,


Michael A. Chappel
Dallas District Director

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cc:

Mr. Jeff Binder, Division President
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