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Food and Drug Administration  
555 Winderley Pl., Ste. 200  
Maitland, FL 32751

**FEDERAL EXPRESS**

**WARNING LETTER**

**FLA-01-74**

July 26, 2001

Elliot Block, President and CEO  
TCPI, Inc.  
3333 S.W. 15<sup>th</sup> Street  
Pompano Beach, Florida 33069

Dear Ms. Block:

During an inspection of your establishment located in Pompano Beach, Florida on June 19-22 & 25, 2001, FDA Investigator Michelle S. Dunaway determined that your establishment is a manufacturer and distributor of invitro diagnostic tests, which are medical devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Under the Federal Food, Drug, and Cosmetic Act (the Act), the products that your firm manufactures are considered to be medical devices that are used to diagnose or treat medical conditions or to affect the structure or function of the body. The law requires that manufacturers conform to the Quality System (QS) Regulation for medical devices, as specified in Title 21, Code of Federal Regulations (CFR), Part 820.

The above-stated inspection revealed that the devices 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 Quality System Regulation for medical devices, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Your firm's management with executive responsibility failed to establish an adequate and effective quality system and ensure that it is fully implemented and maintained at all levels of the organization as required by 21 CFR 820.20. For example, no formal management reviews have been conducted (FDA 483, Item #2), only one area has been audited (calibration on 2/7/01) since the schedules have been developed (FDA 483, Item #3), no management representative has been appointed responsible for assessing and directing Quality System requirements (FDA 483, Item #6), no quality policy or plan

was established (FDA 483, Item #20 & 21), and the inadequate establishment of CAPA and Management Controls to ensure the effectiveness and full implementation of the Quality System (FDA 483, Item #1).

Your firm's response dated July 17, 2001 covering FDA 483, Item #s 1, 2, 3, 20 & 21 are inadequate as follows:

- a) FDA 483, Item #1 – Your QOP, General Administration, Doc. No. ADM/0100 fails to establish your firm's policy and objectives for, and commitment to quality. It also fails to address how the policy is distributed to all employees.
  - b) FDA 483, Item #2 – Your response states that there have been frequent informal management reviews conducted, however, there is no documentation to show when they were conducted and what issues were discussed including any resulting actions and conclusions.
  - c) FDA 483, Item #3 - Your response is incomplete because you did not provide any documentation covering what was audited on February 7, 2001. Documentation of planned audits should be provided for our review and will be verified by re-inspection of your facility. Further, your firm's procedure was implemented on November 6, 2000, 3 ½ years after the required implementation date of June 1, 1997.
  - d) FDA 483, Item #6 – Your response appears to be adequate. However, you failed to provide Mr. Moll's qualifications in the areas of QA and the Quality System regulation.
  - e) FDA 483, Item #20 – Your response is inadequate as noted previously for FDA 483, Item #1. Your procedure fails to establish a policy for quality pursuant to 21 CFR 820.20(a). Your QA manager, Manufacturing Manager and Vice President, was not aware of its existence when asked during the inspection. By regulation, a policy is not established until implemented.
  - f) FDA 483, Item #21 – Your response is inadequate as noted previously for FDA 483, Item #s 1 & 20.
2. Your firm failed to establish and maintain written procedures for conducting quality audits as required by 21 CFR 820.22. For example, your procedures are not specific enough to allow the person conducting the audit to adequately implement the requirement (FDA 483, Item #4).

Your firm's response dated July 17, 2001 may be adequate. Your promised response will be reviewed and verified by re-inspection.

3. Your firm failed to establish and have in place resources and personnel to perform all quality assurance activities as required by 21 CFR 820.20(a)(2). For example, complaint handling, nonconformity and CAPA systems have not been maintained since 6/1/01 (FDA 483, Item #5).

Your firm's response dated July 17, 2001 is inadequate because by your own admission you only receive reported complaints on a monthly basis from a contracted 800# call service. You failed to provide the instructions that have been provided to the call service for determining the seriousness of a technical complaint. The fact that none was received is irrelevant to this observation. Your firm was required by regulation to implement this procedure by June 1, 1997.

Your firm's QA manager also admitted that he was not familiar with the QS requirements and advised that he had done nothing regarding complaints, non-conforming product and CAPA since taking over the position. He stated that he spent most of his time performing laboratory analysis because he was the only person responsible for performing all QC/QA activities. Your firm has failed to assign adequate resources to perform all QA activities.

4. Your firm failed to establish and maintain procedures to ensure that all complaints are reviewed and evaluated by a formally designated unit in a timely manner and as required by 21 CFR 820.198. For example, none of the 81 complaints received by the contracted 800# call service were reviewed, evaluated or investigated including 43 reporting no control line for lot #1201001, 1 minute pregnancy wand test kit, and 24 reporting no control line for lot #0112102 for the pregnancy test kit (FDA 483, Item #7) and there are no procedures to determine and identify complaints that represent reportable events pursuant to the Medical Device Reporting requirements (21 CFR Part 803) (FDA 483, Item #9).

Your firm's responses dated July 17, 2001 covering FDA 483, Item #s 7 & 9 are inadequate as follows:

- a) FDA 483, Item #7 is inadequate because by your own statement when a non-control line is experienced the result is invalid. A product that fails to meet specifications is a product nonconformity or quality defect regardless of what caused it. Your failure to investigate, evaluate and take effective preventive and corrective actions is a violation of 21 CFR

820.90 of the Quality System requirements. Your response fails to document or provide any evidence why trending and investigation of these complaints is not required or appropriate. You did not provide any evidence to support your assertion that the lack of a control line on the product would never be caused by a defect or process failure. Your QOP, Customer/Client Complaint Handling Procedure, Doc. No. QAP/0500 is inadequate because it fails to address or incorporate your firm's use of a 800# contracted call service. By not conducting any trending or investigation into these complaints, you have not established that inadequate storage or improper use is the root cause of the reported problem. Further, the procedure's definition of a complaint would apply to the MDC associate reports, however, the procedure was not followed for any complaint received via MCD for the period reviewed during the inspection and does not address any of the operations that MDC reportedly follows nor does it address procedures to follow for complaints received via MDC.

- b) FDA 483, Item #9 is inadequate because your response fails to address the observation. This observation does not refer to a Corrective Action Request; by regulation you are required to have written procedures to review, evaluate and investigate any complaint that represents an event that must be reported to FDA under 21 CFR Part 803 or 804, which is required by 21 CFR 820.198(d). It is not adequate to wait until you receive a complaint to establish written procedures to determine if an event is reportable under the MDR regulation. The procedures were required to be in place by June 1, 1997.
5. Your firm failed to establish and maintain adequate corrective and preventive action procedures as required by 21 CFR 820.100. For example, your procedures fail to address requirements to analyze and document all sources of quality data to identify existing or recurring and potential causes of nonconforming product (FDA 483, Item #12); your procedures fail to address requirements for ensuring that information related to quality problems or nonconformities is disseminated to responsible individuals (FDA 483, Item #14); the corrective action taken as a result of the investigation into the failure of lot T0808001 did not extend to the product in commercial distribution (FDA 483, Item #8); and the CARS report #001 opened on 1/18/01 has not been closed (FDA 483, Item #18).

Your firm's responses dated July 17, 2001 covering FDA 483, Item #s 8, 12,14, & 18 are inadequate as follows:

- a) FDA 483, Item #8 – Your response may be adequate, however, you should be guided by the following: In the case of non-process and process related errors, retesting is suspect. Because the initial tests are genuine, in these circumstances, additional testing alone cannot infuse the product with quality. We acknowledge that some retesting may precede a finding of non-process or process-based errors. Once this determination is made, however, additional retesting for purposes of testing a product into compliance is not acceptable.

A very important rule that governs a retesting program is that a firm should have a predetermined testing procedure and it should consider a point at which testing ends and the product is evaluated. If results are not satisfactory, the product is rejected.

Additionally, the firm should consider all retest results in the context of the overall record of the product. This includes the history of the product, type of test performed, and in-process test results. Failing assay results cannot be disregarded simply on the basis of acceptable results being satisfactory.

Retesting following an out of specification result is only appropriate after the failure investigation is underway and it determines in part that retesting is appropriate. It is appropriate when analyst error is documented or the review of analyst's work is "inconclusive", but it is not appropriate for non-process or process-related errors.

Retesting must be done on the same, not a different sample, may be done on a second portion of a sample that was from the same source as the first sample analyzed, and may be done on a larger sample previously collected for laboratory purposes.

- b) FDA 483, Item #12 – Your firm only reviews complaints received via the contract 800# service on a monthly basis. This procedure fails to ensure that all complaints are processed, evaluated, investigated in a timely manner. Further, your response fails to address the observation because it fails to address other sources of quality such as non-conforming material reports (NCFMR), audits, and CAPA activities.

- c) FDA 483, Item #14 – Your response fails to relate to the regulatory requirement pursuant to 21 CFR 820.100(a)(6). You reference an internal audit procedure, which only applies to CARs initiated as a result of audits and not initiated as a result of receiving information from other sources of quality data.
  - d) FDA 483, Item #18 – Your response fails to address what action was taken, if any, to close CAR 001, opened on 1/18/01 other than promised personnel training and generating a new procedure.
6. Your firm failed to establish and maintain procedures to control product that does not conform to specified requirements and all evaluations and investigations shall be documented as required by 21 CFR 820.90. For example, your written procedures do not identify when investigations will take place and do not include requirements to document the rationale when no investigation is made. The rationale for not investigating NCMR 159 was not documented (FDA 483, Item #13); four nonconforming material reports (NCMR #s118, 152, 156 & 162) were not documented as required by your own written procedures (FDA 483, Item #11); a determination was not made whether CAPA was required (FDA 483, Item #16); subsequent inspection and activities related to rework of NCMR #117 (FDA 483, Item #17) and the disposition of NCMR #156 was not documented (FDA 483, Item #19).

Your firm's responses dated July 17, 2001 covering FDA 483, Item #s 11, 13, 16,17, & 19 are inadequate as follows:

- a) FDA 483, Item #11 – Your response fails to address the steps your firm will take to ensure that your own written procedures are followed pursuant to the regulatory requirements when it is necessary to document a corrective action. For example, you failed to document or provide any evidence that the 4 NCMRs were verified.
- b) FDA 483, Item #13 – Your response fails to address the observation. Your procedures do not identify when investigations are to take place and do not document the rationale when no investigation is made. Your response references your complaint handling procedure but not the procedures that would be followed for non-conforming product.
- c) FDA 483, Item #16 – The exhibit of NCMR 118 provided with your response is the same in all respects as the copy collected by the

investigator during the inspection except that the "Corrective Action Required:" box is checked. When was this change made and where are the records documenting the determination to make the change? Your response regarding NCMR 159 states that no corrective action is required when lot T0808001, which is subject of FDA 483, Item #8 for which you state that test results won't be available until 8/3/2001 and that a recall may be considered. You failed to provide any evidence documenting this determination. Your responses for NCMR 157 and 160 appear adequate.

- d) FDA 483, Item #17 – Your response fails to address the observation. You provide no evidence regarding the labeling of product with the wrong lot number.
  - e) FDA 483, Item #19 – Noted on the FDA 483 as having been corrected and verified.
7. Your firm failed to validate refrigerated storage conditions for retained samples as required by 21 CFR 820.75. For example, there is no documentation that show that test results of retained samples held under refrigeration are equivalent to samples that are held under labeled conditions for storage and use (FDA 483, Item #10).

Your firm's response dated July 17, 2001 covering FDA 483, Item #10 is inadequate because you do not address storage conditions of lots produced before June 25, 2001.

8. Your firm failed to establish and maintain adequate document controls to ensure requested records are readily available for review as required by 21 CFR 820.180. For example, numerous records could not be located during the inspection including, NCMR 20, 21, 29 etc., CAPA report #002, Failure Investigation records and analytical reports related to Event test HCG pregnancy test strips, lot nos. 0224002, 330004, 0503001, etc. (FDA 483, Item #15).

Your firm's response dated July 17, 2001 covering FDA 483, Item #s 15 is inadequate because (a) you fail to address the data from the missing NCMRs, which your procedures require to be input into a histogram for review and evaluation by management pursuant to SOP QAP/0300. Was this ever done? (b) you do not address the missing CAR that is noted on both the NCMR and the CAR logs, and (c) appears to be adequate.

9. Your firm failed to establish and maintain adequate procedures for packaging inspection pursuant to your written procedures as required by 21 CFR 820.72. For example, your procedures require a QA inspector to conduct in-process visual inspections at the rate of 5 kits per hour (FDA 483, Item #22).

Your firm's response dated July 17, 2001 covering FDA 483, Item #s 22 is inadequate because during the inspection your own QA and Manufacturing managers acknowledged that they weren't following this procedure. The procedure also states, that "These inspections are to be performed on an hourly basis until the run is complete." The production record fails to show the results of the in-process visual exams and the times each kit was randomly removed from the line for inspection. From your documentation, we can't verify your statements.

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 Class III devices to which QS regulation 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, injunction, and/or civil penalties. Your responses indicate a basic lack of understanding of the Quality System regulation. We strongly suggest that you contact a consultant to assist you in making effective corrective and preventive action.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of any steps you may have taken to correct the noted violations, including (1) the time frames within which the corrections will be completed if different from those annotated on the FDA 483, (2) any documentation indicating the corrections have been achieved, and (3) 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.

Your response should be sent to Timothy J. Couzins, Compliance Officer, Food and Drug Administration, 555 Winderley Place, Suite 200, Maitland, Florida 32751, (407) 475-4728.

Sincerely,

A handwritten signature in black ink, appearing to read "Emma Singleton". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Emma Singleton  
Director, Florida District