FOI 6/98

Tetrionics Inc.
Madison, WI 53711
ID 12/17/97 CRC

Summary of Findings

This inspection of a prospective manufacturer of was conducted as a follow-up to an earlier FDA inspection of 7/97. The finished produc

This firm will synthesize and supply th During the 7/97 inspection, several inspectional observations were noted and discussed with the firm. Immediate corrections were promised by the firm and the purpose of this follow-up was to determine if suitable corrective actions have indeed been enacted.

Credentials were shown and FDA482 issued to Mr.Herbert E. Paaren, Vice President of the corporation. Mr. Peter O. Johnson, President of the corporation is not present at the firm on a daily basis and was not present during this inspection. According, to Mr. Paaren, he himself is actually the person most responsible for day to day operations. He added that there have been no changes to the firm's ownership, responsible parties or corporate standing since the last inspection. Also present during this inspection were Christopher M. Henrich, QC, and Katherine J. Beardsley, Director of Regulatory Affairs. All three of these individuals answered questions and supplied document copies as requested.

This inspection was limited in scope and covered only the firm's correction of the previous FDA483 items.

#1. There is no documentation showing the procedures for the finishe product have been validated.

The firm has corrected the above situation in the following manner. Immediately following the inspection they made contact with th who was contracting the work. They discussed the amount of activity would be required to perform in order to validate the system and allow for mini validations before or during each set of tests and lab determined that they could not perform these tasks. After this, the firm decided that other tests were available to them including the two that they settled upon for release testing. The firm now performs several tests in addition to appearance including The firm no longer employ to perform testing on a routine basis.

The firm has purchased instruments to enable them to perform these tests in house. These are on line and these tests have been performed retrospectively on all finished batches of finished product (using retain samples). These instruments include

, installed by installed by

The firm has updated thei_ _ _ _ and has reportedly submitted the above changes to FDA CDER. I reviewed the and it appears satisfactory.

The firm has constructed adequate SOP's to cover these changes and for performing suitable validation of the systems. This appears to have been successfully completed.

#2. Identification tests conducted on many incoming components are general in nature and non-specific to a component.

The firm no longer employs the use of testing. The firm has purchased two instruments that are now used to determine identity of incoming raw materials. These, as described in #1 are a The firm has created a change form and updated its SOP regarding it specifications, whereby it dropped the requirement fo , which it agreed was not a real good indicator and now do either or both of the above, per the schedule. Attached as Exhibit #1 is a copy of that section of the change request and SOP that describes the new changes.

The firm initially compared its and is in the process of putting together its ow The only item that has no published is the finished product. Since the early batches have been tested by other means and accepted as the standard, they are using the . as a standard. In any case, the firm is constructing t using all for comparison.

Th that compares the to all available that product), chooses the highest degree of match and compares against that standard. In addition, it rates the degree of certainty of match using a numeric scale. The firm does not currently rely on this feature, choosing instead to review the , generally by , however they are attempting to validate the Their current SOP states the test should match th and should generally appear similar to the standard. It appears the firm has corrected this area of concern.

#3. No testing is done on , nor is any C of A received f : before release and use. This component is used t product in the container during packaging.

The firm has requested and has received a Cof A covering the l[illegible] hat they have currently in use. In addition, they have constructed a series of ID tests to be done in house prior to approval of the product for use, including [illegible] All raw materials are now received under Cof A.

#4 [illegible] component has been released without meeting [illegible] or without documentation (deviation report) allowing for release and use.

The firm determined before the inspection that [illegible] they had listed in their SOP was not suitable for this material. A retrieve of historical data indicated that none of the [illegible]atches in this parameter, [illegible] The firm has since created deviation reports to cover these situations and has changed the specification to delete this test and add a test b [illegible]Jince that time, the firm has purchased the equipment and retrospectively tested samples from each of the [illegible] and has found them suitable for use. It appears the firm has corrected this deficiency.

#5. Calibration weights used to calibrate in-house scales / balances are not documented as traceable to NIST standards nor have they been recalibrated at the required time interval.

The set of calibration weights were returned [illegible] who certified them against NIST traceable standards. The firm now has written certification of the testing and the individual results of testing. All of the weights passed the certification. This deficiency has been corrected.

I made a brief walk thru inspection of the rest of the facility and found no obvious problems. No objectionable conditions were noted and it appears that the firm has adequately corrected / addressed the problems reported during the earlier inspection.

Attachments
Exhibit #1....Change form and a portion of SOP showing addition of additional ID tests.

Charles R Cote

Charles R Cote, RIC
Madison, WI RP

IND 21,129
cc: MAD-RP
HFD-324

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Minneapolis District
240 Hennepin Avenue
Minneapolis, MN 55401
Telephone: 612-334-4100

FOI 6/98

Date: January 22, 1998

Peter O. Johnson, Sr.
President & CEO
Tetrionics, Inc.
University Research Park
505 Science Drive
Madison, WI 53711

Dear Mr. Johnson:

A Good Manufacturing Practice (GMP) inspection was conducted at your bulk pharmaceutical facility on December 17, 1997 as follow-up to an inspection performed on July 29-30, 1997. The inspection included review of your firm's corrective action implemented for GMP deficiencies uncovered during the previous inspection and review of the The inspection reviewed your firm's ability to manufacture and test bulk

GMP deficiencies uncovered during the previous inspection were found to be corrected during the most recent inspection. Your approach to implement corrective action is viewed highly by the Agency. An was submitted to the Agency and is under review by the Center For Drug Evaluation and Research.

We understand that you have ar on site and that your firm no longer perform for identification of th We also understand that your firm will no longer use the as a contract laboratory for testing on a routine basis.

It is your responsibility to ensure that all of the requirements of the Federal Food, Drug and Cosmetic Act and regulations promulgated thereunder are being met. Based upon the inspectional findings and filing of your , the applicatio
was recommended for approval at the District level on January 22, 1998. Final authority for approval of this application lies with our review division in the Center For Drug Evaluation and Research.

Sincerely yours,

James I. Roberts
Acting District Director
Minneapolis District

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