DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
8050 Marshall Drive, Suite 205 Lenexa, KS 66214 (913) 495-5115 Industry Information: www.fda.gov/oc/industry	9/25/13-10/9/13
	FEI NUMBER 1937280

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Kevin M. Jenkins, Vice President Pharmaceutical Operations-Quality

FIRM NAME	STREET ADDRESS
Meridian Medical Technologies A Pfizer Company	1945 Craig Road
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Saint Louis, MO 63146-4105	Sterile Drug Manufacturer

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DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

Observations cover inspections of the firm from 25Sept2013 – 09Oct2013 at the following addresses:

Meridian Medical Technologies, Inc.
1945 Craig Rd
Saint Louis, MO 63146-4105
FEI- 1937280

Meridian Medical Technologies, Inc.
1444 Strassner Rd.
St. Louis, MO 63144
FEI - 3010091964

cGMP Deviations:

1. Failure to validate a process for remediation of ATNAA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection) auto-injectors.

Specifically,

a. Process Validation 13-134, using Lot 2M1501, was executed without an approved process validation protocol. Lot 2M1501 was remediated from 4-7Jun2013 as an "at risk process" prior to approval of Process Validation 13-133, using Lot 2M1431, which was determined a failure and rejected on 21Jun2013. The Process Validation Protocol for 13-134 was signed and approved on 6Jun2013. The protocol for Process Validation using Lot 2M1501 was initiated prior to verification of standard operating procedures (7Jun2013), process (critical) instrumentation calibration (7Jun2013), process parameters (7Jun2013), and training (10Jun2013). Process Validation 13-134 utilized the same protocol as the failed Process Validation 13-133 and proceeded with no investigation to determine the root cause of the failure (accountability and documentation) and no changes or corrective actions were implemented. Subsequently, eight out of (b) (4) lots remediated in St.Louis have investigation reports for accountability issues.

b. You failed to revalidate your process when you made changes to your remediation program after 23Jul2013 including: changing your check weighing scales (from (b) (4) to (b) (4)); changing your flow

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	Michele Perry-Williams Kathleen B Swart	Michele Perry-Williams, Investigator Kathleen B Swart, Investigator Sherry G. Bass, Supervisory Investigator Dawn C. Olenjack, Investigator Erma E. Mbuli, Investigator	10/9/2013

process eliminating counting operations (both a (b) (4) and (b) (4); and (b) (4) the number of units in the counting bins (from (b) (4)) to (b) (4)) to improve reconciliation. These changes were implemented as corrective actions to correct systemic accountability issues originating from failed process validation lot # 2M1431.

ISSUES WITH PROCESS VALIDATION IS A REPEAT OBSERVATION FROM THE 20Mar-29Apr2013 EI.

2. Insufficient qualification in the remediation of ATNAA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection) autoinjectors. Without successful IQ, OQ, and PQ, you still proceeded to Process Validation.

Specifically,
a. Qualification Protocol, QP 13-610, Addendum to the Installation and Operation Qualification (IQ/OQ) of the (b) (4) ler with (b) (4) scale set-up) was performed on 19May2013 and signed and approved on 20May2013. Scale (b) (4) (b) (4) was not tested due to being tagged "out of service" and the qualification was conducted on the other scales. Scale (b) (4) was sent for repair on 19May2013, returned and approved for use on 20May2013. (b) (4) (b) (4), Scale , used for all remediation weight checks for all lots, was not assessed for Installation Qualification or Operation Qualification activities.

b. Performance Qualification Protocol QP-13-121, approved 14Apr2013, and completed and final summary approval on 29Apr2013, had an unexplained accountability discrepancy of one ATNAA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection) unit. The PQ used lot 2M1644, a lot that was QA approved for release, but never distributed. The accountability could not be reconciled, no investigation was initiated, and the PQ was approved to proceed to process validation.

ISSUES WITH IQ/OQ/PQ ARE REPEAT OBSERVATIONS FROM THE 20Mar-29Apr2013 EI.

3. The quality control unit lacks authority to review production records to assure that no errors have occurred and fully investigate errors that have occurred.

Specifically,

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You failed to implement adequate corrective and preventive actions as your product continues to have accountability issues after you implemented the following changes to your process: changed (b)(4) of your counting scales (b) (4) asset numbers (b) (4) and (b) (4)); changed your flow process eliminating counting operations (both a counting scale and counting bin step); and (b) (4) the number of units in the counting bins (from (b)(4)) to (b) (4)) to improve reconciliation. This is evidenced through your continued accountability failures with ATTNA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection) lot numbers 1M1132 and 1M1780 which were processed after 23Jul2013 when the previously mentioned changes were implemented.

THIS IS A REPEAT OBSERVATION FROM THE 24Jan-4Apr 2013 EI AND THE 20Mar-29Apr2013 EI.

4. Written production and process control procedures are not followed in the execution of production and process control functions.

Specifically,
a. You failed to follow your SOP, "Proper Documentation", QLA-MQA-00603, dated 29May2013, when you did not record reconciliation discrepancy information on Batch Production Records for the following ATNAA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection) batches:

1. Lot 2M1431: the operator failed to record the count on the batch record when there was a discrepancy between the physical count and the count received from the counting scale.

2. Lot 2M1029: you failed to document a reconciliation discrepancy in the Batch Record.

3. Lot 2M1019: you failed to document a reconciliation discrepancy in the Batch Record.

b. In addition, you failed to follow your SOP, "Proper Documentation", QLA-MQA-00603, dated 29May2013 when you did not record information contemporaneously for the following lots of ATNAA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection) batches:

1. Lot 2M1020: the Supervisor failed to include the entry for the quantity of unpouched units located on pallet (b)(4), at the time the task occurred, and later included the omitted information incorrectly.

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2. Lot 2M1431: the following information is missing from the batch record (including but not limited to): pg. 6, missing the Supervisors signature and date in two locations for employees (b) (6) and (b) (6) ; pg. 10, missing verification signatures for no. 2b. and the Verified By/Date signature for Defect Tally Table –Unpackaging; pg. 11, missing the Performed and Verified By signatures for the incoming pan count on half pallet 1B; pg 13, no. 8, is missing "Verified By" initials and "Verified By/Date:" signature for the "Defect Tally Table"; pg. 20, is missing the "Verified By" initials for step no. 16; pg. 45, is missing the "Verified By" initials for step no. 4; and pg. 47, is missing the "Performed By" initials for no. 13; is missing the "Verified By" initials for numbers 12 and 13; missing the "Defect Tally" "Verified By/Date" initials.

c. You failed to use your change control management system before implementing changes when you replaced (b) (4) of your Counting Scales (from (b) (4) to (b) (4)) during the ATNAA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection) remediation process, which were identified as critical pieces of equipment in your Process Validations 13-133 and 13-134.

THIS IS A REPEAT OBSERVATION FROM THE 24Jan-4Mar2013 EI.

5. Written production and process control procedures are not followed in the execution of production and process control functions.

Inventory Control System (b) (4) is not reliable or accurate:

Specifically,
Your Inventory Control System (b) (4) is not reliable or accurate in that it does not always reflect the true status of your drug products, for example:

- ATNAA lot (1M1843) was physically/labeled as quarantined and in (b) (4) it was on hold
- ATNAA lot (2M1018) was physically/labeled on hold but in (b) (4) was in quarantine status

THIS IS A REPEAT OBSERVATION FROM THE 24Jan-4Mar2013 EI. ISSUES WITH (b) (4) ARE ALSO

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DOCUMENTED IN THE 483 FOR THE 20Mar-29Apr2013 EI.

The Following Additional Contract Non-Conformances Were Observed:

1. You failed to follow the ISO 2859-1/ANSI/ASQ Z1.4 Standard.

Specifically,
In your contract modification dated/signed 19Sept2013, it reads "(b) (4) (b) (4) (b) (4) (b) (4)." In your MPID contract dated 14Jan2013 section 3.2.2 it reads, "(b) (4)" However, you do not follow ISO 2859-1/ANSI/ASQ Z1.4 because you do not use it in the way it is intended which would require implementing the switching rules. ISO 2859-1, Section 12.6.1, "Use of individual plans", reads, "Occasionally, specific individual plans are selected from this part of ISO 2859 and used without the switching rules. For example, a purchaser may be using the plans for verification purposes only. This is not the intended application of the system given in this part of ISO 2859 and its use in this way shall not be referred to as "inspection in compliance with ISO 2859-1"".

When switching rules are implemented, ISO 2859-1, section 9.3, "Switching rules and procedures", reads "When normal inspection is being carried out, tightened inspection shall be implemented as soon as two out of five (or fewer than five) consecutive lots have been non-acceptable on original inspection". Section 9.4 continues, "If the cumulative number of lots not accepted in a sequence of consecutive lots on original tightened inspection reaches 5, the acceptance procedure of this part of ISO 2859 shall not be resumed until action has been taken by the supplier to improve the quality of the submitted product or service".

In addition, (b) (4) lots were remediated in St. Louis and Kalamazoo, and sampling was placed on hold after you found ATNAA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection) units with low fills during your sample of (b) (4) instead of (b) (4) as required by your modified contract. The contract reads, "(b) (4)

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(b) (4)

2. You failed to collect your AQL Samples randomly.

Specifically,
Your AQL samples were not collected at random from the beginning, middle, and end of each remediated lot of ATNAA (Atropine 2.1mg/0.7mL and Pralidoxime Chloride 600 mg/2 mL Injection). The modified contract section 2c reads in part, '(b) (4)'. ISO 2859-1 reads in section 8.1: "The items selected for the sample shall be drawn from the lot by simple random sampling".

In addition, your SOP, SOP-QLC-SQC-00360 "ATNAA FILL VOLUME WEIGHT CHECK", (Version 3, effective 14Jul2013) reads "Randomly sample (minimum of beginning, middle, end) determined amount of ATNAA auto-injectors from the remediated (acceptable) units generated from the remediation of the lots of interest. Use Form FRM-LAB-161 to record removal of samples from batch."

According to your Senior Supervisor of Quality, Sample Submission Forms (Form FRM-LAB-161), and Tally Sheets, samples are either pulled during the remediation process whenever the Sample Submission Form is received by quality, at which time the sampler will pull (b) (4) from the end of the line, or the sample will be pulled from the top box of a pallet, sometimes from multiple pallets. For example:
- Samples for ATNAA lot 2M1524 were pulled from the top box of (b) (4) different pallets
- Samples for ATNAA lot 2M1501 were pulled from the top box (b) (4) different pallets
- Samples for ATNAA lot 1M1843 were pulled during the remediation process on (b) (4) at the following times: (b) (4) units at (b) (4), (b) (4) units at (b) (4), and (b) (4) units at (b) (4). The remediation process for lot 1M1843 started on (b) (4) at (b) (4) and ended on (b) (4) at (b) (4).

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