DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
8050 Marshall Drive, Suite 205 Lenexa, KS 66214 (913) 495-5100 Fax:(913) 495-5115 Industry Information: www.fda.gov/oc/industry	03/20/2013 - 04/29/2013* FEI NUMBER 1937280

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Stephen C. Natsch, Vice President and General Manager

FIRM NAME	STREET ADDRESS
Meridian Medical Technologies, Inc.	1945 Craig Rd
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Saint Louis, MO 63146-4105	Sterile Drug Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

Observations cover inspections of the firm from 20Mar2013 - 29Apr2013 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

Meridian Medical Technologies, Inc.
2555 Hermelin Dr
Brentwood, MO 63144-2504
FEI - 1950222

OBSERVATION 1

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,

1. The Quality Unit failed to adequately review the Installation and Operation Qualification report (OP 13-610), dated (b) (4), for the (b) (4) Balances. Balances failed the acceptance criterion for accuracy ((b) (4) g weight should read (b) (4) g). In addition, The Quality Unit failed to adequately review Personnel Qualification report (QP13-110), dated 14Apr2013, for the remediation of ATNAA multi-chamber auto-injectors for accurate reconciliation and protocol adherence. The Quality Unit approved both reports as successful when, in fact, these protocols failed acceptance criteria.

2. The Quality Unit failed to assure all employees involved in the remediation of ATNAA were adequately trained before beginning tasks associated with the new remediation process.

3. The Quality Unit failed to submit an NDA-Field Alert Report within three working days of receipt of information concerning a failure of one or more distributed batches of a drug to meet the established specifications for ATNAA during

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	Anthony R. Bucks, Investigator Michele Perry Williams, Investigator Kathleen B. Swat, Investigator	04/29/2013

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three different occurrences:

- Missing Pralidoxime Chloride was identified in ATNAA (Atropine and Pralidoxime Chloride Injection) lot 2M1645 on 08Feb2013 and again in lot 2M1644 on 26Feb2013 but was not reported to the agency until 15Mar2013.
- Missing Atropine was identified in (Atropine and Pralidoxime Chloride Injection) lot 1M1591 on 11Sep2011 but was not reported to the agency.
- During your investigation of ATNAA lot 2M1645 for a faulty safety pin in the power pak, it was discovered lot 2M1536, which had been distributed, contained the same power pak component lot number. Subsequently, (b) (4) lots of Atropine/Pralidoxime Chloride Injection products were quarantined on 31Jan2013 including lot 2M1536. No Field Alert Report was submitted for ATNAA Lot 2M1536.

4. The Quality Unit failed to identify the root cause after completing investigations of deviations. Specific examples include, but are not limited to:

- NOE #: 06-02-006-SL, investigation for missing atropine in ATNAA lot 6M1086B, documented the root cause as "lack of attention by the inspectors" for failing to remove unfilled units rather than a failure of the equipment to fill all units.
- NOE #: 11-09-023-SL, investigation for missing atropine in ATNAA lot 1M1591, documented the root cause as "inspectors and the final inspectors failed to note the missing medication in the atropen chamber during their inspections", rather than a failure of the equipment to fill all units.

5. While testing ATNAA lot 1M1591, your firm found a defect (missing Atropine), and failed to reject the entire batch; only half of the batch was rejected and subsequently reworked, as documented in NOE-11-09-023-SL.

6. The Quality Unit failed to expand investigations to other lots of drug product which may be affected by the same root cause, for example:

As documented in NOE-11-09-023-SL, while testing ATNAA (Atropine and Pralidoxime Chloride Injection) lot 1M1591, your firm found two defects (missing Atropine) after it had undergone a 100% visual inspection specifically designed to detect missing drug product. At that time your firm became aware the 100% visual inspection was not effective for its intended purpose. While ATNAA lot 1M1591 was reworked, you failed to document or extend the investigation to other lots of ATNAA or other products which utilize the 100% visual inspection as the only means of detecting missing drug. In addition, your investigation failed to include an evaluation of the effectiveness of the 100% visual inspection to detect other defects.

7. The Quality Unit failed to be apprised of, evaluate or approve the movement of all drug product reserve samples on 7-8Mar2013 and 26Mar2013 from your Westport facility to the "Base" and back to Westport.

8. The Quality Unit failed to evaluate whether the amount of (b) (4) for (b) (4) studies was appropriate for its intended use.

9. Your Quality Unit failed to perform an investigation after you identified (b) (4) units of DuoDote Injectable Product, Lot no. 2AE781 product was packaged incorrectly between 2/15/13 and 2/25/13.

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OBSERVATION 2

Employees engaged in the manufacture, processing, packing, and holding of a drug product lack the training required to perform their assigned functions.

Specifically,

1. Qualification Protocol QP13-110 (dated 06Apr2013) was performed for the remediation process involving ATNAA (Atropine and Pralidoxime Chloride Injection). In addition to the technician executing the protocol and the verifier for the performance, seven members of management, representing Validation, Engineering, Quality Engineering, Statistical Quality Control, Packaging and Inspection, Regulatory Affairs and Quality Assurance reviewed and approved the protocol report. Upon review of the protocol report by FDA investigators it was revealed that while the protocol was deemed a success by the firm, the acceptance criterion of 100% accountability had not been met (unaccounted units). This discrepancy was not detected through the routine batch review, nor was it found during the review and approval of the final qualification report by your firm's management who are responsible for reviewing the report.

2. Qualification Protocol QP13-110 and Process Validation Protocols QP13-111 and QP13-114 for ATNAA and DuoDote failed due to unaccounted-for units. Members of Quality and Production Management explained the failure of technicians to achieve 100% reconciliation of units was caused by confusion (batch records were confusing to the technicians) however your firm provided records documenting technicians' training on the remediation process and batch records.

OBSERVATION 3

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications prior to release.

Specifically,

The 100% visual inspection used by your firm for products, including but not limited to ATNAA/DuoDote (Atropine and Pralidoxime Chloride Injection) Morphine, Alsuma, NGA EpiPen / NGA EpiPen Jr. (Epinephrine) and (b) (4), fails to identify critical defects. Defects which were not detected during the 100% visual inspection (but reported and documented in your firm's customer complaints from 01Jan2011 to 19Apr2013) are listed below:

Product	Complaint	# of Complaints	# Batches Produced
Morphine			(b) (4)
	Labeling Unclear/Missing	1	
	Missing Component	2	

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Alsuma			(b) (4)
	Angled/Crooked Needle	2	
	Failure to Activate	6	
	Failure to Deliver Drug	6	
NGA EpiPen Sr.			(b) (4)
	Angled/Crooked Needle	16	
	Empty Cartridge	5	
	Failure to Activate	126	
	Foreign Matter in Tube	2	
	Labeling Unclear/Missing	8	
	Loose Safe Pin	6	
	Missing Component	20	
	Spontaneous Activation	93	
NGA EpiPen Jr			(b) (4)
	Angled/Crooked Needle	8	
	Empty Cartridge	1	
	Failure to Activate	19	
	Foreign Matter in Tube	2	
	Loose Safe Pin	1	
	Missing Component	9	
	Spontaneous Activation	47	
(b) (4)			(b) (4)
	Low Fill Volume	3	
	Missing Component	3	
	Missing Lot Number /Exp. Date	1	
(b) (4)			(b) (4)
	Defective (Slow Dose)	48	
	Foreign Matter in Tube	24	
	Labeling Unclear/Missing	3	
	Low Fill Volume	7	

OBSERVATION 4

Drug products failing to meet established standards are not rejected.

Specifically,

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As documented in NOE-11-09-023-SL, while testing ATNAA lot 1M1591, your firm found a defect (missing Atropine), and failed to reject the entire batch; only half of the batch was rejected and subsequently reworked. You also found another assembled unit which had missing Atropine product from one of the multi-chamber units which was found during the "Additional" (rework) Assembly/Final Inspection process performed on this lot on (b) (4).

OBSERVATION 5

An NDA-Field Alert Report was not submitted within three working days of receipt of information concerning a failure of one or more distributed batches of a drug to meet the specifications established for it in the application.

Specifically,

1. Your firm became aware the 100% visual inspection of DuoDote (Atropine and Pralidoxime Chloride Injection) for missing Pralidoxime was inadequate (b) (4) for lot 2M1645 and again on 26Feb2013 for lot 2M1644, but you did not notify the agency about the missing Pralidoxime until 15Mar2013.

2. Your firm became aware during the 100% visual inspection of Atropine and Pralidoxime Chloride Injection (lot 1M1591) for missing Atropine was inadequate (b) (4) but did not notify the agency.

3. Your firm became aware of a faulty safe pin in the safety pin cap for ATNAA on (b) (4) when an auto-injector spontaneously activated after assembly on lot 2M1645. You identified (b) (4) lots of powerpaks which were used in (b) (4) ots of Atropine/Pralidoxime Chloride Injection products. The (b) (4) ots were quarantined on 31Jan2013. Lot 2M1536, one of the lots in question, had been distributed on 27Dec2012. No field alert report was submitted.

Note: This is a repeat observation from the 1/2013 inspection.

OBSERVATION 6

The accuracy, sensitivity, and reproducibility of test methods have not been established.

Specifically,

Qualification Protocol QP13-610 (dated 07Apr2013) for ATNAA and DuoDote remediation was performed as your "Installation & Operation Qualification (IQ/OQ) of the (b) (4) (b) (4). You failed to document the actual reason for the scale fluctuation. (b) (6) Validation Engineer II and (b) (6) Project Engineer stated these variations were due to air flow and you documented, "Due to slight fluctuation in scale reading at time of recording some weights were recorded twice to be within (b) (4) g."

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In addition, your raw data documents values outside of your (b) (4) g established tolerance; reproducibility has not been established.

OBSERVATION 7

Investigations of a failure of a batch or any of its components to meet any of its specifications did not extend to other drug products that may have been associated with the specific failure or discrepancy.

Specifically,

As documented in NOE-11-09-023-SL, while testing ATNAA (Atropine and Pralidoxime Chloride Injection) lot 1M1591 your firm found two auto-injectors missing Atropine after it had undergone a 100% visual inspection specifically designed to detect missing drug product. At that time your firm became aware the 100% visual inspection was not effective for its intended purpose. While ATNAA lot 1M1591 was reworked, you failed to document or expand the investigation to other lots of ATNAA or other products [including, but not limited to Alsuma (sumatriptan), Diazepam, Pralidoxime, (b) (4) and (b) (4) which utilize the 100% visual inspection as the only means of detecting missing drug. In addition, your investigation failed to include an evaluation of the effectiveness of the 100% visual inspection to detect other defects.

OBSERVATION 8

Representative samples are not taken of each shipment of each lot of components, drug product containers, and closures for testing or examination.

Specifically,

Your component consolidation program in which you combine multiple lots under one MMT number (per SOP-QLC-SQC-00187 ver. 3.0 "Supplier Lot Consolidation" and SOP-QLC-SQC-01103 ver. 7.0 "Sampling at Incoming Inspection") does not ensure all lots of incoming components are sampled and tested. This program is utilized for incoming components used in drug products including, but not limited to, ATNAA, Diazepam, Pralidoxime Chloride (Combopen) and EpiPen.

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OBSERVATION 9

The written stability program for drug products does not include test intervals based on statistical criteria for each attribute examined to assure valid estimates of stability.

Specifically,

Although your firm has conducted (b) (4) studies for ATNAA and DuoDote (Atropine and Pralidoxime Chloride Injection) at (b) (4), you have not evaluated the "worst case" for the total amount of (b) (4) over the life of the product. While you refer to ICH (International Conference on Harmonisation) guidelines for (b) (4), (b) (4) is the minimum (b) (4) required by ICH. Your firm has not established if (b) (4) (b) (4) was appropriate or if more (b) (4) was required.

OBSERVATION 10

Reserve drug product samples are not retained and stored under conditions consistent with product labeling.

Specifically,

On 3/7-8/13, reserve samples [ATNAA (Atropine and Pralidoxime Chloride Injection), DuoDote (Atropine and Pralidoxime Chloride Injection), MARK I (Atropine and Pralidoxime Chloride Injection), Atropen (Atropine) and Epipen (Epinephrine)] were moved from Westport to the Base facility without a protocol for moving material or an authorization/approval from QA. Reserve samples are not inventoried in your (b) (4) system and you have no system in place to track or account for your reserve samples. There is no documented qualification of the Base facility to store the reserve samples. In addition, SOP LOG-WHS-00115-SL "Transportation of Product, Components and Materials Between Manufacturing Facilities" (ver. 14) was not followed in the movement of the reserve samples. The SOP states, "ONLY (b) (4) ARE ALLOWED TO BE TRANSFERRED (b) (4) AT ANY ONE TIME." The reserve samples were moved in 3 shipments consisting of 12, 9, 12 pallets each.

In addition, you fail to document the number of reserve samples taken from each lot of components approved on your lot consolidation list which are used to manufacture your sterile drug products.

*** DATES OF INSPECTION:**
03/20/2013(Wed), 03/21/2013(Thu), 03/22/2013(Fri), 03/25/2013(Mon), 03/26/2013(Tue), 03/27/2013(Wed), 03/28/2013(Thu), 03/29/2013(Fri), 04/01/2013(Mon), 04/02/2013(Tue), 04/03/2013(Wed), 04/04/2013(Thu), 04/05/2013(Fri), 04/09/2013(Tue), 04/10/2013(Wed), 04/12/2013(Fri), 04/15/2013(Mon), 04/16/2013(Tue), 04/17/2013(Wed), 04/19/2013(Fri), 04/22/2013(Mon), 04/23/2013(Tue), 04/24/2013(Wed), 04/26/2013(Fri), 04/29/2013(Mon)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."