483 response

MERIDIAN
MEDICAL TECHNOLOGIES™
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Meridian Medical Technologies, Inc.™
1945 Craig Road
St. Louis, MO 63146

March 5, 2012

Mr. John W. Thorsky
District Director
United States Food and Drug Administration
11630 West 80th Street
Lenexa, Kansas 66214

RE: Meridian Medical Technologies, Inc. Response to FDA483 issued February 13, 2012

Dear Mr. Thorsky:

Attached please find our response to the Form FDA483 for the January 30-February 13, 2012 inspection at Meridian Medical Technologies, St. Louis, MO.

We appreciate the opportunity to respond to each observation. For clarity, each observation is listed in order presented on the Form FDA483, followed immediately by our response in italic. Where applicable, we made systemic changes to prevent recurrence of the observations.

We are committed to compliance with the GMP's and to meeting all regulatory requirements. If you have any questions or require information pertaining to our response please do not hesitate to contact me at 314-682-3094.

Sincerely

Clint R. Lawson

Clint R. Lawson
Senior Director, Quality
Meridian Medical Technologies, Inc.
A Pfizer Company
1945 Craig Road
St Louis, Missouri 63146
314-682-3094

Meridian Medical Technologies is committed to ensuring that all staff are properly trained, all procedures & processes are understood & followed and activities are accurately documented at time of performance in order to ensure the integrity of our processes and products. We therefore provide the following specific actions in response to observations reported in the February 13, 2012 FDA 483.

OBSERVATION 1

Written production and process control procedures are not followed in the execution and process control functions and documented at the time of performance.

Specifically,

A. Supervisor (b) (6) reported times recorded for specific steps in the batch record are not the actual times steps started and stopped but rather theoretical times. For example, step (b) (4) for the filling batch record of AtroPen lot #1PT716 on (b) (4) is documented with a start time of (b) (4) and stop time of (b) (4) However, (b) (6) stated the start time is recorded and the stop time is immediately written for when the step should theoretically end. In step (b) (4) this is (b) (4) minutes later. It is not recorded when the step actually ended.

B. During the filling of lot #1PT716 of AtroPen on (b) (4) operator (b) (6) exited the aseptic area at (b) (4) and did not return that day. Operator (b) (6) signed off that they verified step (b) (4) and performed step (b) (4) of the batch record, both of which occurred after (b) (4) Step (b) (4) could not have been performed until at least (b) (4) minutes after the (b) (6) exited for the day. Supervisor (b) (6) reported the batch record would have been prefilled out by (b) (6) before (b) (6) exited the aseptic area.

Response:

Meridian has taken several corrective actions to help ensure that such incidents do not recur.

The AtroPen filling batch record has been revised to clarify the documentation requirements for recording the start and actual stop for the saturation step. The original record contained a field to record a "start time" and a field to record a "stop time". The revised record contains a field to record a "start time", a field to record the " (b) (4) (b) (4) *" and a field to record the "actual stop time". Operator and Verification sign offs for each of the steps are required. Training on the changes to the batch record has been performed. Among other things, the training reinforces that batch records must reflect actual start and actual stop times and not theoretical times.*

Meridian is committed to ensuring accurate and complete documentation. When issues such as stated in observation 1B are discovered, disciplinary action is taken with the employee and appropriate re-training conducted. In this instance, employee (b) (6) was disciplined for improper batch record documentation.

Moreover, all relevant employees were made aware of documentation issues described in Observations 1 A & 1 B during department wide training which occurred on (b) (4) *and* (b) (4) *In this training session, Proper Batch Record Documentation (SOP MQA-QLA-00603) was reviewed with emphasis placed on recording information contemporaneously and that failure to follow this procedure would lead to disciplinary action up to and including termination.*

Please note that, based on management personnel interviews of employees from Meridian's Component Preparation, Formulation, Filling, Inspection, Labeling and Packaging departments, we believe that the issues identified in Observations 1 A & B represent an isolated exception to our practices. Nevertheless, to further improve Meridian's documentation practices, all manufacturing batch records which contain start and stop times will be updated to more clearly delineate the recording of "actual start" and "actual stop" times in the specific field describing the action to be taken. Completion dates have been prioritized by product line based on the frequency of manufacturing: (1)

(b) (4)

With regards to the particular batch in question and the documentation of the (b) (4) *time, Meridian notes that the employee* (b) (6) *who performed the* (b) (4) *equipment, which delineated the completion of the* (b) (4) *period, entered the aseptic area at* (b) (4) *on* (b) (4) *as documented on the aseptic area entry log. As this time was after the* (b) (4) *minute* (b) (4) *period, it was concluded that the minimum time was met for the batch. With regards to the batch record step signed off by operator* (b) (6) *signifying the completion of previous steps completed after* (b) (6) *had left the area, the only other action performed was the verification of initiation of Environmental Particle sampling. This process was started at* (b) (4) *as was printed by the monitoring instrument. Based on the minimum* (b) (4) *time being met and the instrument printed start time for the Environmental monitoring, Meridian has concluded that there was no negative impact to AtroPen lot 1PT716.*

C. The "performed by/date" was not recorded for the inspection of the gasket on the active air sampling forms for (b) (4) and (b) (4) on (b) (4) at the time of performance.

Response:

The technician that inspected the gasket on the active air sampling forms did not include the "performed by/date" on Form FRM-LAB-381 - Level I - Active Air Sample Data on (b) (4) *. This error was detected by the FDA investigator on 1-31-12. A deviation report (NOE 12-01-017-SL) was issued on 1/31/12 and the corrective action has been*

completed. The EC technician who committed the error received awareness training. As a part of the corrective action in order to improve right first time performance FRM-LAB-381 was revised to make it easier to follow.

There was no effect on the batch where this issue occurred based upon the following. This gasket is used to seal the connection between the (b) (4) *line on the* (b) (4) *filling machine and the hose barb adaptor needed to connect the* (b) (4) *tubing to the active air monitoring unit. This is cleaned* (b) (4) *and only the* (b) (4) *tubing and monitoring unit is* (b) (4) *The previous use of the* (b) (4) *filler in clean room* (b) (4) *was on* (b) (4) *The use of room* (b) (4) *after the occurrence on* (b) (4) *was on* (b) (4) *The gasket was present on both the* (b) (4) *and* (b) (4) *fills. This demonstrates that the* (b) (4) *gaskets were present on both tubing connections during the fill on* (b) (4)

This item is closed

D. Batch 1M1726 – Multichambered Autoinjector 2.1 mg Atropine/0.7mL dose 600mg Pralidoxime Chloride/2.0 mL Dose states to pull a sample of (b) (4) basic units and check for proper plunger placement per SOP-PRO-FIL-00109-SL. If the plunger depth is out of range, the batch record allows for a retest. If the retest is out of range, an operator would segregate to the last good test and perform 100% inspection. Only the final result of the rework inspection is documented on the observation sheet and not the raw data obtained from the 100% inspection. This rework is not reviewed or approved by the Quality Unit.

Response:

As explained in more detail below, we have modified procedures to require that such rework is reviewed and approved by the Quality Unit.

More specifically, segregation of product and performing additional testing are required when a plunger depth is verified to be out of range during inprocess monitoring, per the filling batch record instructions. The testing of the plunger depth on the segregated units is to ensure that units with plunger depths outside the established operational range are removed prior to shipping the product to the Packaging & Inspection department for the final 100% inspection and further processing. This product is collected into and transported in bags. The bag quantities in the batch record were changed to reflect the final number of good units in each bag after the 100% inspection was performed but the individual results were not recorded.

To more specifically address this Observation, a documentation form has been created, FRM-PRO-049, for recording the individual results and rejected quantities. The final page of the form has a reconciliation for total units inspected, number of units rejected and acceptable units. The form requires a review signature from Production and QA before returning the good units back to the batch and before making corrections in the batch record. Batch record instructions for documenting the plunger depths every (b) (4) (b) (4) *have been revised to reference FRM-PRO-049 for documenting the individual*

test results and Quality Assurance approval to proceed after the plunger depth verification has been completed.

This item is closed

E. Batch 1M1726 - Multichambered Autoinjector 2.1 mg Atropine/0.7mL dose 600mg Pralidoxime Chloride/2.0 mL Dose states in step (b) (4) *"***Prior to inspecting each bag/container, verify the count of each container using a weight counting scale per SOP-MAN-PKG-00103-SL. Notify SPM if weight count quantity varies morn than -/+ (b) (4)% of the transfer sheet quantity***"*. The weights from this verification are not documented.

Response:

The Master Batch Record for the Multichambered Autoinjector will be revised to change the language currently in step (b) (4) to the following:

> *Prior to inspecting each bag/container, verify the count of each container using Form FRM-MDP-008 per SOP-MDP-GEN-00006-SL. Notify SPM of any count quantity variance. NOTE: If a count discrepancy occurs, use Discrepancy Reconciliation Form (FRM-MDP-007).*

Form FRM-MDP-008 has already been revised to require recording of the quantity for each bag/container.

These changes will ensure that the quantities of product in each container are recorded as raw data which will add up to the final overall count.

Estimated completion date: March 23, 2012

F. SOP-MDP-GEN-00013-SL – In-process Product Transfer procedure was not followed during the transfer of Atropine, batch 1M1726. The Product Transfer Form for 1M1726 states that (b) (4) tubs were transferred to Westport on (b) (4), but the Carrier signed off on the transfer on (b) (4).

Response

To address this observation, the transfer form "Transfer Form from Brentwood to Westport" (FRM-MDP-008), was modified to clarify and record the in-process packed date and the actual transferred date.

Lot 1M1726 was packed on (b) (4) by Manufacturing at the Brentwood Sterile Product Support site, and transferred to the Packaging & Inspection department on (b) (4) by a warehouse driver. During the (b) (4) the lot was held in a controlled temperature warehouse as required for this product's storage. Procedure "In-Process Product Transfer" SOP-MDP-GEN-00013-SL Version 4.0 (current version

at that time) did not require transfer of the lot on the (b) (4) *as when the lot was packed and was stored in accord with Meridian procedures. Manufacturing notifies the warehouse driver when the lot is ready to be transferred and the driver signs the applicable transfer form as the carrier for the receipt of the product.*

Meridian believes that the process can be improved with the Form modification requiring documentation of the actual date transferred. Nevertheless, Meridian has confirmed that the quality of the lot at issue in this Observation was not negatively impacted by use of the transfer procedure that was in place at the time of transfer. Form FRM-MDO-008 was modified to clarify the packaged date to be transferred and the actual transfer date.

This item is closed

G. The annual review of product reserves for AtroPens were not approved by the statistical quality control supervisor or designee by the (b) (4) reserve report due date, (b) (4) listed in SOP-QLC-SQC-00384-SL. The listed lot numbers were approved by the statistical quality control supervisor or designee on 6-27-2011.

- AtroPen, 2 mg, Lot Number: 954408
- AtroPen, 2 mg, Lot Number: 954821
- AtroPen, 2 mg, Lot Number: 954409
- AtroPen, 1.0 mg, Lot Number: 95L847
- AtroPen, 0.5 mg, Lot Number: 75M749
- AtroPen, 1.0 mg, Lot Number: 05L214

Response:
All reports show that the review/inspection of the retain samples was completed by the due date and no product issues were found during those reviews. However, the supervisor did not sign final approval of the test reports within the month because the procedure was not clear that signature was required in order to consider the review complete.

A change was made to procedure SOP-QLC-SQC-00384-SL to require that the SQC Supervisor or Designee must sign the form as reviewed in order to consider the annual reserve review to be complete.

This item is closed

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not written and followed.

Specifically,

A. "SOP-PRO-FIL-00001-SL General Aseptic Procedure" was not followed. The (b) (4) s a component of the finished product. During aseptic assembly of (b) (4) lot # (b) (4) in room # (b) (4) on (b) (4) the following was observed:

1) Operator (b) (7) (C) was observed to pick (b) (4) Sheath components off the assembling turret and toss them back in the (b) (4) Sheath bowl. Section (b) (4) of the procedure states "***To clear a component, use sterile forceps to remove the item(s) from the area***".
2) Operator (b) (7) (C) was observed to shake a bag of (b) (4) and allow the bag to touch the inside of the (b) (4) bowl while adding (b) (4) . Section (b) (4) of the procedure states "***When adding components, one smooth motion is used to pour components into the bowl***".
3) Operator (b) (7) (C) was observed to make unnecessary hand movements and reach over the assembling turret area. Section (b) (4) of the procedure states "***Personnel will eliminate ** unnecessary hand or arm movements***".

Response:

Aseptic technique is evaluated as part of the (b) (4) qualification requirements and is part of a routine sampling and surveillances program performed by the Quality Assurance department. Operators demonstrate as part of the (b) (4) Aseptic Qualification program proper techniques and these are observed by Quality Assurance colleagues. Meridian Medical Technologies includes detailed training through procedures, videos, individual training courses and monitors performance through gowning surveillances and batch monitoring. Instruction is given to specifically detail the requirement to preclude disruption of air flows or "first air" requirements. Operators (b) (6) and (b) (6) had received the proper training but their actions as documented in these observations were not in accordance with that training. Therefore, disciplinary action was given to operators (b) (6) and (b) (6) for not following procedure requirements in the Aseptic Processing Area and retrained on SOP-PRO-FIL-00001-SL, "General Aseptic Procedure".

In order to determine whether there had been any product impact relating to work performed by these two operators, Meridian evaluated environmental monitoring trends for operators (b) (6) and (b) (6) from 2/2011 to 2/2012. Monitoring data representing (b) (4) plates sampled on (b) (6) and (b) (4) plates sampled on (b) (6) were reviewed and no growth was detected on plates for either operator. As a result of this monitoring data, Meridian has concluded that the behavior of these operators did not have an impact on aseptic processing.

Quality Assurance and SPM Management monitor aseptic behavior per SOP-MQA-QLA-00600-SL, "Quality Assurance Batch Record and Product Disposition" and document results on FRM-QLA-222, "Quality Batch Record and Aseptic Technique Review". This form is used to document observations and to identify and correct performance concerns and document findings for evaluating techniques outside of the (b) (4) aseptic

qualification program. MMT expects all employees that work in aseptic areas to comply with aseptic processing techniques and if personnel are not in compliance, personnel will not be allowed to enter the APA without additional training and subsequent evaluation. If after additional training and coaching a repeat observation is observed by Quality Assurance or SPM Management, the event will be documented through appropriate disciplinary action and the person's performance will be evaluated to determine if the person should be disqualified from the clean room.

All clean room qualified operators have been trained on SOP-PRO-FIL-00001-SL as additional follow up to this observation. SPM Management performed training for the observations and discussed the compliance expectations and the auditing procedure for aseptic behaviors in the clean room as part of the response to this observation.

A review of environmental data from Room (b) (4) and Operators (b) (6) & (b) (6) for (b) (4) lot # (b) (4) on (b) (4) showed no microbiological growth on surfaces or air, therefore the product was not adversely affected by the activities reported in this observation.

This item is closed.

B. On (b) (4), "SOP-PRO-FIL-00001-SL General Aseptic Procedure" was not followed. Supervisor (b) (6) was present in the class 100 area and performing batch record step (b) (4) and weight checks during the filling of AtroPen lot #1PT716, but did not sign the filling operation sign in sheet. Section (b) (4) of the procedure states "***Any person entering a class 100 area while production is in progress must sign the batch record***" and section (b) (4) of the filling batch record states "***All PA personnel entering this filling area must sign the appropriate table below***".

Response:

Per SOP-PRO-FIL-00001-SL, section (b) (4) states that "Only personnel related to the aseptic activity should enter class 100 areas. Any person entering a class 100 area while production is in progress must sign the batch record and be plated at (b) (4) for the lot. The following exceptions apply: Support personnel do not need to be plated for each specific class 100 area they enter. Only (b) (4) plates documented as working under all lots will be required for the following personnel: Supervisors, EC Monitoring Personnel and MQA. Supervisor (b) (6) did not sign the batch record log for the lot however was plated at (b) (4) on (b) (4) meeting the general requirement for being plated at (b) (4) for entering the class 100 area.

To improve on the current practice, SOP-PRO-FIL-0001-SL, "General Aseptic Procedure", has been revised to state under section (b) (4), to state that "Support personnel do not need to be plated for each specific class 100 area they enter unless they perform a batch processing step for that operation. If a batch record step is performed by a supervisor, they must sign the batch record entry log and be plated specifically for that operation".

This item is closed

C. SOP-PRO-FIL-00001-SL Aseptic Processing Area Gowning was not followed in that:

1) On 2/3/2012 two of the (b) (4) individuals observed aseptically gowning placed their foot on the bench while putting their boots on. After 8:50am on 2/3/2012 an additional two of (b) (4) individuals were observed to also don sterile boots by placing them on the bench and then proceed to enter the Aseptic Processing Area. Under (b) (4) of the procedure it states "***don boots one at a time over the shoe covers, allowing only the boots to touch the floor on the other side of the bench.***"
2) One employee was observed to don the sterile coveralls and then reach across the boot cart allowing the coveralls to rub against the cart while retrieving boots.

Response:

1) The operators observed placing their boots on the step over bench did not strictly follow the written instruction as described SOP-PRO-FIL-00002-SL, "Aseptic Processing Area Gowning". We believe that this was caused by inconsistency between the written instruction and the video training provided for operators. Specifically, while the SOP instructs the operator to only allow for their boots to touch the floor on the other side of the bench, Meridian's clean room training video (watched as part of their gowning training requirements) depicts operators placing boots on the bench top to aid in the gowning technique. In response to this observation, SOP-PRO-FIL-00002-SL, "Aseptic Processing Area Gowning" was revised to allow for the sterile boot to touch the bench top. The requirement remains that after donning and securing the boot, sitting or standing, the sterile boot can only touch the sterile side of the bench.

A trend of the Environmental Monitoring plating of the stainless steel bench in room (b) (4) shows acceptable results with no alert or action levels for this location from 2/2011 to 2/2012. These trends support the change made to SOP-PRO-FIL-00002-SL to allow using the bench top to fasten the boot or sitting on the bench as option for securing the boot. Donning of the boots while sitting or standing helps take into consideration how to safely don the boot and helps minimize contact with the outside of the boot prior to stepping over to the aseptic side of the bench.

2) The Operator observed to don the sterile coveralls and then reach across the boot cart allowing the coveralls to rub against the cart while retrieving boots was identified as Filling Technician (b) (6) Operator (b) (6) was retrained on SOP-PRO-FIL-00001-SL, "General Aseptic Procedure" and SOP-PRO-FIL-00002-SL, "Aseptic Processing Area Gowning" and the training video "Dressing for the Clean Room ". Operator (b) (6) also performed a gowning cycle in response to this observation and was watched by SPM Management and a QC/EC representative for proper technique. Gowning results for (b) (6) were evaluated for the last year to review the employee's gowning history with acceptable results obtained from February 2011 to February 2012.

To help avoid potential contact with the cart storing the boots in gowning room (b) (4), the cart was immediately replaced with a clean room cart which has shelves only 18" deep. This shallower depth cart will reduce the possibility that a gown will contact the cart during the gowning procedure.

Refresher training on SOP-PRO-FIL-00002-SL is required as additional follow up to this observation for all aseptic operator personnel. SPM Management performed training for the observations and discussed the compliance expectations and the auditing form, FRM-QLA-222, that will routinely observe aseptic technique and gowning into the clean room as part of the monitoring.

Environmental Data from 2/3/12 was reviewed. There were no alert/action levels excursions or negative trends for air, surfaces, personnel, differential pressure, temperature, humidity and non viable particulates for 2/3/12 therefore the observations noted had no negative effect on the product.

This item is closed

D. During the cleaning / sanitization in Room (b) (4) on 2/2/2012 one individual was observed cleaning from the ceiling to and including the return air vent and the second employee was observed cleaning the floor. Neither individual cleaned the "Cove Base", the portion between the return air vent and the floor.

Response:
The room that was observed was room (b) (4) from room (b) (4) The sanitizers procedurally use dedicated mops for the walls and floors inside the Aseptic Processing Area. The (b) (4) cove is part of the floor. However, to clarify the requirement for cleaning the cove base, a specific instruction to clean this area was added to form FRM-PRO-124, "Cleaning – Sanitizing Schedule –APA". Training for the sanitizers was performed on (b) (4) (b) (4) to inform them about the observation and the expectation for the cleaning this area.

The routine and (b) (4) monitoring results for room (b) (4) were evaluated from 2/2011 to 2/2012 and no growth was detected on any of the plating results.

This item is closed

E. The microbial alert and action levels established to initiate investigations of environmental monitoring results are not based on historical environmental monitoring sampling data.

Response:
Current alert and action levels were established based on the USP <1116> Microbiological Control and Monitoring of Aseptic Processing Environments.

Although the alert and action limits are not regularly exceeded, Meridian has systems in place to track room growth and to track trends. Per procedure SOP-LAB-ENV-00805-SL (Environmental Sampling of the Sterile Manufacturing Area), (b) (4) Environmental reports are generated to track and monitor the (APA) Aseptic Processing Area. Part of this report reviews each APA room to watch for trends by percentage of growth. The report also reviews the overall plate growth percentage to see if any shift is occurring. The data for each APA room is also attached to the environmental (b) (4) report to see if there is a shift in the individual environmental data. Overall, this data indicates the growth levels in our APA are low and the APA is in a state of control.

A statistical analysis of the Environmental Data from February 2011 to February 2012 will be performed to evaluate the Class 100, 10,000 and 100,000 areas. This data will be utilized to establish new alert and action limits for these areas. Based on the data, the appropriate Forms and SOP's will be revised to reflect the new limits. In addition, procedure SOP-LAB-ENV-00800-SL "Environmental Monitoring and Control Program" will be revised to add an annual environmental trend evaluation to consider any revision to the limits.

Estimated Completion Date: (b) (4)

F. Media Fill OP-11-808 is inadequate to qualify personnel in that it does not adequately document the process manipulations that simulate the routine filling operations and exposure that the product itself would undergo. According to Attachment 5.12A: List of Filling Events, several operators ((b) (6) and (b) (6)) were qualified during media fill OP-11-808 without performing any filling events.

Response

Per procedures SOP-LAB-ENV-00810-SL and SOP-PRO-FIL-00104-SL to maintain gowning and aseptic processing qualification, Meridian personnel have to participate in a media fill, and go through aseptic technique re-certification (b) (4). During media fills employees perform the same routine activities as the ones performed in regular aseptic processing activities. This information is captured on media fill event log and on the personnel environmental plates obtained (b) (4) by the Quality group. On commercial aseptic processing activities, a list of routine aseptic activities is issued with each batch record to Manufacturing as a remainder of what routine activities that operators are allowed to perform (FRM-PRO-403).

On media fill QP11-808, Manufacturing Supervisor ((b) (7) (C) participated as an observer, and his presence was recorded several times in the event log. He also was plated (b) (6) times. During routine aseptic processing activities, observing and documenting are one of the main roles of a Manufacturing Supervisor. Environmental Technician ((b) (6)) and the other (b) (4)Operators (b) (6) were plated for several routine activities, but they were not documented on the event log as performing the same routine activities they would perform on a regular product fill.

As a corrective action, a similar list of routine aseptic activities currently used for commercial lots will be used by Quality during media fills to observe each employee depending of their job function. All the routine activities will have to be performed and verified by Quality during the media fill as part of the requirements for a person's (b) (4) *re-qualification.*

The media fill protocol list of interventions will be revised to group the intervention examples in Routine Events and Non-Routine Events to harmonize with the groupings identified on FRM-PRO-403 and the new form (FRM-PRO-050).

The media fill protocols and procedures SOP-QLA-VAL-00020-SL "Media Challenge of Aseptic Processes" and SOP-TRN-GEN-00049-SL "Training requirement" will be revised to reference the new form (FRM-PRO-050), and to add this new (b) (4) *requirement.*

Estimated Completion Date: (b) (4)

OBSERVATION 3

Established laboratory control mechanisms are not followed.

Specifically,

The identity of the incubator used to store environmental monitoring plates is not recorded. There are (b) (4) incubators at (b) (4) °C and (b) (4) at (b) (4) °C for environmental monitoring samples. Records do not indicate which incubator was used for environmental monitoring plates. Therefore, quality personnel reviewing results can not verify the correct temperature conditions were used.

The times environmental monitoring microbial plates are placed into the incubator is not recorded. Therefore quality personnel reviewing results can not verify the plates were incubated for the specified period of time.

Response:

FRM-LAB-380 and other similar type forms were evaluated. FRM-LAB-380 was revised to add the Incubator identification number to the form to track which incubator was utilized. In addition, the forms listed below were also revised to add the Incubator identification number to the form.

FRM-LAB-180 - Personnel Monitoring
FRM-LAB-182 - Surveillance Report Form
FRM-LAB-183 - Random Surveillance Report
FRM-LAB-380 - General Aseptic Processing Area

FRM-LAB-381 - Level [redacted] Active Air Sample Data
FRM-LAB-382 - General Level [redacted] Areas
FRM-LAB-383 - (b) (4) Sample Sites for Aseptic Processing Area

To better clarify the timing of the plates being placed in the incubator, the following two procedures were revised to address that plates are incubated the same date of the sampling. Sampling date is currently captured on all the above forms.
SOP-LAB-ENV-00003-SL - Incubation and Counting of Microbial Plate Samples
SOP-LAB-ENV-00805-SL - Environmental Sampling of the Sterile Manufacturing Area

Although the test form did not include the incubator number at the time of the inspection, MMT maintains procedures and documentation that enable the Quality group to confirm that correct incubator conditions were used. Environmental Monitoring Technicians follow Form FRM-LAB-380 - General Aseptic Processing Area and SOP-LAB-ENV-00003-SL (Incubation and Counting of Microbial Plate Samples) and place the plates in the [redacted] C incubator on the same date as the sampling. After the (b) (4) days of incubation at [redacted] C, the plates are removed and read for growth. The appropriate data is recorded on FRM-LAB-380 under column labeled "Interim Read [redacted] C" along with the initials of the person reading the plates and date of the reading. The plates then are moved on the same day to the [redacted] C incubator as specified in the form FRM-LAB-380 and SOP-LAB-ENV-00003-SL. The plates are then read after a minimum of (b) (4) total days with data recorded on FRM-LAB-380 under column labeled "Final Read [redacted] C" along with the initials of the person reading the plates and date of the reading. As a result Quality has documentation to establish the dates the samples were in each temperature condition. All incubators are continually monitored and any temperature excursion would be documented in the deviation report, which would also document which plates were in the affected incubator. Therefore, any temperature deviation will be detected and evaluated immediately.

This item is closed

OBSERVATION 4

Written procedures are not followed for the handling of components.

Specifically, batch records call for the washing of needles per SOP-PRO-CLP-00050-SL – Preparation of (b) (4) Needles. The firm does not document to assure the validated soak time is met during the preparation of the needles.

Response:
The batch records ([redacted] Atropen and Morphine) that document the cleaning of the needles will be revised to include documenting the actual start and actual stop times in the batch record.

Estimated Completion Date: (b) (4)