DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6751 Steger Drive Cincinnati, OH 45237-3097 (513) 679-2700 Fax:(513) 679-2772 Industry Information: www.fda.gov/oc/industry	12/07/2009 - 12/23/2009* FEI NUMBER 3006316363

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: John R. Pratt, General Manager

FIRM NAME	STREET ADDRESS
Amylin Pharmaceuticals Inc	8814 Trade Port Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
West Chester, OH 45071	Pharmaceutical 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:

OBSERVATION 1

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

Specifically,

The firm has yet to complete a media fill that simulates the commercial batch inspection process. From 4/18/2008 to present, ten media fills have been performed. All ten media fills have undergone a manual visual inspection per 2-IPS001. The proposed commercial batches, including the process validation batches, are scheduled to undergo an automated inspection process per 2-INS002 or 2-INS003 which includes the vibrator/shaker table.

OBSERVATION 2

Established laboratory control mechanisms are not documented at the time of performance.

Specifically,

SOP 2-QML-056, "(b) (4) (b) (4) " states that the initial gowning qualification process, which is required to enter the aseptic area where (b) (4) is packaged into sterile vials, will include participation in a training session and technique evaluation. (b) contracted personnel were hired to perform (b) (4) filter testing in the aseptic filling area between 08/25/09 and 08/27/09. Training documents indicate that each of these contractors was trained on the appropriate gowning procedure on 08/24/09, which included an evaluation of the ability of the contractors to perform the gowning. However, the training record for one contractor (b) (6) indicates that he was wearing a cast, and further interview of the trainer revealed that the cast was on his arm. Therefore, it would be impossible for him to adequately demonstrate the gowning procedure.

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Nevertheless, the trainer signed off twice as having evaluated this gowning procedure. Quality control did not appropriately review these training documents nor initiate an investigation into this situation prior to this inspection.

OBSERVATION 3

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

Specifically,

SOP 2-ENG-010, (b) (4) states that when an alarm is triggered, the responding employee should acknowledge the alarm and then follow the proper workflow, including documentation and investigation. There is no SOP which addresses who can disable an alarm, under what circumstance an alarm may be disabled, and who is responsible for determining if an alarm should be disabled. However, at 12:29 AM on 09/23/09, the AIT-21201 alarm was disabled. This alarm detects high levels of Total Organic Carbon in the distribution loop for the hot water-for-injection which is used to manufacture (b) (4) The maintenance log and resulting deviation (PR# 6425) indicates that the facilities department was instructed to disable the alarm by the QA Director.

OBSERVATION 4

In-process materials are not tested for quality and purity and approved or rejected by the quality control unit during the production process.

Specifically,

No investigations were being performed on vials which contained critical defects that were less than 5% [12,500 vials of a 250,000 vial batch]. 5% of the total vials would have to be rejected before an investigation was to be performed. For example, glass particulates located in the vials and cracked vials were not being investigated since they consisted of less than five percent of the overall batch.

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OBSERVATION 5

Laboratory records of methods of testing used do not provide the reference when employing methods in an approved new drug application and the referenced method is not modified.

Specifically,

In review of the firm's standard operating procedure, (b) (4) (b) (4) there is no reference of the USP, Chapter 61 and 62 as the reference method used in the growth promotion of media and to assure sterility of media.

OBSERVATION 6

Written records of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications do not always include the conclusions and follow-up.

Specifically,

A. In review of deviation, Overdue Bacterial read-growth promotion, bulk media fill lot 72013, PR # 8343, the bacteria plate was incubated (b) (4) longer. The deviation was incomplete and did not indicate the incubation of a negative control. No corrective and preventive action generated to assess the significance of the problem.

In review of deviation, Environmental Surface Monitoring Excursion -Action 1421-R-4(14SEP09), PR#8844, (b) (4) of bacteria was isolated from sample site west door in 1421 airlock, MODA # CHP)9821 on September 14, 2009. The bacteria isolated was Staphylococcus epidermis, a human flora. Investigation did not include the environmental monitoring of the operators or the airlock. A corrective and preventive action was not generated and implemented, and the investigation was incomplete due to missing environmental data.

In review of deviation PR# 8283, Isolator Breach Process Simulation Lot #71973, a breach occurred on the left hand glove of suite 2 isolator in the process simulation lot #71973. In review of standard operating procedure, 2-QML-090, Evaluation of Isolator breaches, states how to conduct a breach investigation. The investigation should include the following:

1. Examine the integrity of the isolator

2. Determine breach areas
3. Review Enviromental Data
4. Review isolator operations
5. Review cleaning and decontamination records and procedures
6. Review any deviations or unusual events to the processing of the product.
7. Review operator technique or training records
8. Rreview septic simulation results

These are areas stated in the standard operating procedure to determine the cause of the deviation and included in the deviation report. All areas of investigations were not conducted, and the investigation report is inconclusive. No corrective and preventive action implemented to address the significance of the problem.

B. SOP 2-OUA-011, "(b) (4) _____ (b) (4) _____" states that Quality Systems Management will be responsible for ensuring that Deviations and QSE events are tracked and trended and for verifying CAPA implementation. However, between 04/24/08 and 12/04/09, 140 deviations or QSE events were initiated to report that a differential pressure system (DPS) alarm had been triggered in various rooms of the facility, including those used to manufacture(b) (4) _____ However, quality control was unable to provide documentation that this trend had resulted in the opening of an investigation or a CAPA report.

Furthermore, between 02/15/08 and 10/28/09, 48 deviations or QSE events were initiated to report that calibrations were overdue on various pieces of equipment throughout the facility. However, quality control was unable to provide documentation that this trend had resulted in the opening of an investigation or a CAPA report.

OBSERVATION 7

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

Specifically,

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SOP 2-GEN-011, "Training Procedure," states that it is the responsibility of department management to ensure that employees are only to complete tasks in which they have been trained.

a. Training records reviewed for two of the four vial inspection operators and all three quality analysts revealed inadequate documentation for the employees for evaluation against the training criteria prior to receiving credit and performing the operation.
b. Three of eighteen facilities technicians did not receive training on aseptic technique but were considered by management to be qualified to perform the replacement of sanitized filters in the aseptic generation and distribution systems of water-for-injection used to manufacture (b) (4) Additionally, training records lacked documentation that any of the eighteen facilities technicians had been trained to properly execute this filter replacement procedure.

OBSERVATION 8

Records associated with drug product production and control and within the retention period for such records, were not made readily available for authorized inspection.

Specifically,

SOP 2-FAC-022, "Integrity Testing of Facility Filters," states that the filter integrity test print-out should be attached to the pertaining work order. The GMP facilities engineering department was unable to provide documentation of pre and post use integrity tests for the filters on several pieces of facility equipment which supply water for the manufacture and analysis of (b) (4) batches, including the water-for-injection (WFI) still #1, the WFI storage tank, the laboratory purified water (PW) system and the PW system #1.

OBSERVATION 9

The persons double-checking the cleaning and maintenance are not dating and signing or initialing the equipment cleaning and use log.

Specifically,

The daily, weekly, and monthly cleaning checklists for the filling grade A/B areas do not contain dates,

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initials or signatures verifying that a second operator performed a double check indicating the room was adequately cleaned.

OBSERVATION 10

Written procedures are not followed for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

Specifically,

Calibration weights, (b) (4) sampling head, (b) (4) gloves, and Quality Control Equipment/Bins failed to undergo the required (b) (4) application prior to entry into the Grade A/B filling areas on the following dates:

Calibration weights
8/4/09
11/30/09
12/8/09

(b) (4) sampling head
9/28/09
9/29/09
12/3/09

(b) (4) gloves
10/2/09
10/13/09

Quality Control Equipment/Bins
8/5/09
10/6/09
10/7/09
11/30/09
12/3/09

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*** DATES OF INSPECTION:**
12/07/2009(Mon), 12/08/2009(Tue), 12/09/2009(Wed), 12/10/2009(Thu), 12/11/2009(Fri), 12/14/2009(Mon), 12/15/2009(Tue), 12/16/2009(Wed), 12/17/2009(Thu), 12/21/2009(Mon), 12/22/2009(Tue), 12/23/2009(Wed)

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