COPY

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612 (949) 608-2900 Fax:(949) 608-4417 Industry Information: www.fda.gov/oc/industry	01/25/2010 - 02/12/2010* FEI NUMBER 2082946

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Robert J. Hull, General Manager

FIRM NAME	STREET ADDRESS
Gilead Sciences Inc	650 Cliffside Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
San Dimas, CA 91773-2957	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 I OBSERVED:

FACILITIES AND EQUIPMENT SYSTEM

OBSERVATION 1

Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to aseptic processing of drug products.

Specifically, the firm's initial qualification of Aseptic Processing Areas (APAs) 1077/1077B and 1079 performed 6/20/08 through 8/19/08 following replacement of HEPA filters in 1077/1077B and room modifications to 1078 and 1079 in support of the installation of the (b) (RAB) filling line is deficient. Filling room 1079 did not meet the performance qualification acceptance criteria of Operational ISO 5 Classification for Non-viable Particles. The qualification of 1079 was approved on 9/17/08 as Operational ISO 6 classification. Partially stoppered vials of AmBisome 50 mg/vial (liposomal formulation of amphotericin B) are conveyed through 1079 to the lyophilizer accumulation table in 1077. Eighty-one (81) lots of AmBisome were filled in 1079 and released from 8/21/08 through 4/3/09 until modifications and requalification of the room was performed 3/17/09 through 3/24/09 re-classifying 1079 as Operational ISO 5; twenty of those lots were distributed in the US market.

OBSERVATION 2

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically, the firm's environmental monitoring practices used to assess the environmental quality within the aseptic filling areas are not adequate:

a. The firm's procedure SDSOP-0776, Environmental Monitoring of Product Fill, Revision 26 states that for pre-fill monitoring of APA 1077/1077B and 1079 multiple random samples per room for airborne microbial testing by RCS and non-viable particles (NVP) are to be monitored. There is no documentation at the time of sampling where within the room the samples have been taken so that any alert or action levels documented can be adequately assessed.

b. There is no data to support that the (b) (4) filling equipment locations selected for post-fill monitoring of surface microbial contamination (RODAC) are appropriate in assessing the filling equipment surfaces. There is no monitoring of filling needles that directly contact product and enter vials or of the needle manifold surface that

slides directly over open vials during filling.

c. The firm's procedure SDSOP-0417, Environmental Monitoring for the Controlled Manufacturing Areas, Revision 57 does not specify the location of random sites for the environmental monitoring of airborne microbials using an RCS, non-viable particles using a laser particle counter or equipment surface locations using RODAC.

d. There is no data to support that the location of active air sample sites in aseptic processing areas used for continuous non-viable particle monitoring of 1079, 1077 and 1077B during the filling operations are adequate in assessing non-viable particles in the environment where partially stoppered vials are present.

OBSERVATION 3

Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

Specifically, HEPA filter performance is not evaluated or monitored for uniformity of velocity across the filter face and relative to adjacent filters within APA 1079 (outside of the RAB) or in APA 1077/1077B to facilitate detection of adverse airflow patterns and the need for maintenance or replacement of the filters.

OBSERVATION 4

Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically, there is no data to support the monthly clean out of place (COP) cleaning frequency for non-product contact belts and filler parts in the ISO Class 5 and 6 areas. Cleaning validation and verification studies are not performed for non-product contact parts.

OBSERVATION 5

Buildings used in the holding of a drug product are not maintained in a good state of repair.

Specifically, the following conditions were noted during a walkthrough of the facility:

a. On 01/28/10, a leak in the reverse osmosis water system was noted at the reject valve leading to the second pass of the RO. A bucket was placed under the leaking valve with a plastic type wrapper placed on top of the leak to prevent water spray. The initial leak was noted during a routine equipment check on 1/22/10.

b. On 01/25/10, a roof leak was noted in the 542 warehouse aisle (b) (4) A review of work orders found two additional leaks in the roof above aisle (b) (4) in warehouse 542 had occurred previously dated July 14, 2008 and August 25, 2008.

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PRODUCTION SYSTEM

OBSERVATION 6

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

Specifically, on 1/27/10 the following employee aseptic techniques were observed in aseptic processing areas during the filling operations for AmBisome, Lot #042004A that were not in accordance with the firm's procedure *SDSOP-0416, Controlled Area Aseptic Gowning, Qualification, Aseptic Technique, and Monitoring, Revision 52*:

a. A filling operator in APA 1079 was observed monitoring the sterile fill and intervening in the RAB without executing slow and deliberate movements. The filling operator was observed making excessive body and hand movements; having animated conversions; and touching a supply cart with his gloved hands.

b. An operator was observed exiting APA 1077 (ISO Class 5) to retrieve sterile forceps to remove a downed vial from the accumulation table while loading the autoloader for transport to the Lyophilizer, there was no container with IPA and sterile forceps observed at the accumulation table work location in 1077.

OBSERVATION 7

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include adequate validation of the sterilization process.

Specifically, the firm's aseptic filling process simulation runs (media fills) designed to validate the aseptic filling of AmBisome in 20cc molded vials & 20 mm lyo stoppers utilizing the (b) (4) vial filling and stoppering machine in APA 1079 and lyophilizer in 1077/1077B are deficient in that:

a. Modifications to the (b) (4) vial filler and restricted access barrier (RAB) were made after qualification and media fills on 7/31/08, 8/2/08 and 8/4/08 were performed and approved without requalification and successful media fills until December 2008. Changes to air velocities and balancing of HEPA filters inside the RAB of the (b) (4) vial filler were made after performing the media fills and were then set back to the condition (state closest) to that at the time of the media fill on 8/4/08.

b. During the media fill performed in March 2009, modifications to th (b) (4) vial filler and air flow within the RAB were performed between media fill # (b) (4) nd media fill # (b) (4)

LABORATORY CONTROL SYSTEM

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OBSERVATION 8

Laboratory controls do not include the establishment of scientifically sound and appropriate sampling plans and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically, during the firm's investigation into the recoveries of *Chaetomium globosum* mold species from the pre-fill microbial surface monitoring for AmBisome Lot 042962A on the out-feed conveyor (within the RABS) in APA 1079 on 7/26/09 and four settling plates from APA 1077 during the fill of AmBisome Lot 042963A on 7/28/09 (SD-ISS-CAPA-0616 and SD-ISS-CAPA-01625), increased surface microbial and airborne monitoring was performed to detect mold contamination in the APA manufacturing environment. The increased monitoring settling plates and RCS strips used TSA media, incubated at (b)(4) C for only (b)( ) days rather than a selective method for the recovery of mold isolates.

OBSERVATION 9

Acceptance criteria for the sampling and testing conducted by the quality control unit is not adequate to assure that batches of drug products meet each appropriate specification and appropriate statistical quality control criteria as a condition for their approval and release.

Specifically, the firm's special instructions SD-ISS-SI-00459 lacks an acceptance criteria for the 100% visual inspection of Viread bulk tablet process validation lots J190511 and J190521. Three lots were contract manufactured, two of which were shipped to San Dimas for final packaging. Due to an issue identified with the validation lots, Lots J190511A and J190521A were reclaimed for 100% visual inspection to cull out tablet defects. There is no data to support that all defects identified during 100% visual inspection are properly identified and that the visual defects have no impact on the validation performed at the contract manufacturer.

QUALITY SYSTEM

OBSERVATION 10

Written procedures are not followed for evaluations conducted at least annually to review records associated with a representative number of batches, whether approved or rejected.

Specifically, the firm's 2009 Annual Quality Reviews for DaunoXome (April 7, 2008 to April 6, 2009) and AmBisome (October 31, 2008 to October 30, 2009) were not completed until the date of this inspection, approximately 8 and 2 months (respectively) past the target completion date of 60 days following the end of the review period specified in the firm's written procedure, *GSSOP-0024.01, Annual Quality Review (AQR)*.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Carla J. Lundi, Investigator	02/12/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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*** DATES OF INSPECTION:**
01/25/2010(Mon), 01/26/2010(Tue), 01/27/2010(Wed), 01/28/2010(Thu), 01/29/2010(Fri), 02/02/2010(Tue), 02/03/2010(Wed), 02/04/2010(Thu), 02/05/2010(Fri), 02/08/2010(Mon), 02/10/2010(Wed), 02/12/2010(Fri)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Carla J. Lundi, Investigator 	02/12/2010

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 USC374(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."

2/12/10