DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
60 Eighth Street NE Atlanta, GA 30309 (404) 253-1161 Fax:(404) 253-1202 Industry Information: www.fda.gov/oc/industry	07/16/2012 - 07/26/2012
	FEI NUMBER 1048698

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Jamie F. Iudica, Director Plant Operations

FIRM NAME	STREET ADDRESS
Hospira, Inc.	8484 Us 70 Bus Hwy W
CITY, STATE, ZIP CODE, COUNTRY Clayton, NC 27520-9465	TYPE ESTABLISHMENT INSPECTED Pharmaceutical and Medical Device 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

The written stability program for drug products does not include meaningful test methods.

Specifically, stability studies and their results have not been evaluated to determine their suitability and the results of stability studies are not consistently used to establish appropriate storage conditions for finished products.

For example,

A. The data in stability study 438-046-AP-00-R3, "Nitroglycerine in 5% Dextrose Injection: Manufacturing Controls and Stability Data to Support Use of (b) (4) Stopper (b) (4) and (b) (4) Stopper (b) (4) ", approved 1/28/05, showed that inverted storage of some container-closure configurations can reduce the potency of nitroglycerine by up to 2.1%; however, stability samples are not routinely stored in an inverted orientation.

B. The data in stability study 97d-022-AP-95-R6, "Propofol Injectable Emulsion, 10 mg/mL, Vial, List 3919, and Ampul, List 3920: Manufacturing Controls and Stability", dated 10/1/96 did not show any significant decrease in potency or generation of impurities. Data generated during a subsequent 1998 forced degradation study of propofol as reported in document 97d-98-51-R1, "DETERMINATION AND IDENTIFICATION OF PROPOFOL AND RELATED SUBSTANCES IN PROPOFOL INJECTION CONTAINING (b) (4) FORMULATIONS", dated 10/26/98, showed that exposure to light resulted in a significant decrease in potency and a commensurate generation of an unknown impurity. Neither study includes meaningful descriptions of how the materials were stored and exposed to light during the testing process.

OBSERVATION 2

Control procedures are not established which monitor the output and validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

Specifically, the process validation to support the manufacturing process for Propofol is not designed to demonstrate, with a

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SEE REVERSE OF THIS PAGE	Jason F. Chancey, Investigator / Pre-Approval Manager Viviana Matta, Investigator Daphne Santiago, Ph.D, Chemist	07/26/2012

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high degree of assurance, that the active ingredient is homogeneously blended throughout the fill material, and to ensure uniform content in finished products. For example, Protocol # KC-11-081:PQ: Process Validation of List 4699 (b) (4) Batch Size Formulation, 100ml, the sampling methods and sample sizes selected for testing of the final bulk product are not scientifically justified.

OBSERVATION 3

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically, the firm has not sufficiently qualified its manufacturing equipment. For example:

A. The washers for stoppers and bottles ((b) (4) Bottle Washer (b) (4) (b) (4) Stopper Processor (b) (4) and (b) (4) Bottle Washer (b) (4) have not been fully qualified to demonstrate the equipment is suitable for the intended use and operates in an adequate and consistent manner. The performance qualification reports for the washers fail to scientifically justify sampling methods and sample sizes. Additionally, the periodic performance qualification reports fail to analyze samples for the presence of microorganisms and particulate matter.

B. The firm's established procedure for the validation of washers (b) (4) : Washer Validation, effective Mar 16 2012, establishes a general method, irrespective of equipment design or load configuration/size, for the collection of samples and assessment of endotoxin reduction, microbial and particulate loads that is not scientifically justified.

C. The bracketing approach utilized for the performance qualification of the (b) (4) Bottle Washer (b) (4) is not scientifically justified. The approach includes (b) (4) of the minimum container size, (b) (4) of the maximum container size, (b) (4) of the middle container size, and data collected at another facility for the minimum container size which is not representative of the firm's current manufacturing conditions.

OBSERVATION 4

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

Specifically, samples for sterility testing are not necessarily representative of each lot. The sterility testing samples are collected immediately after sterilization and are subject to a special manual quality inspection as opposed to the mechanically assisted or semi-automated quality inspections that the majority of vials are subject to.

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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, a Field Alert Report was not issued within 3 days after Foscarnet (ANDA 77174) lot 87-522-DW yielded out of specific test results for (b) (4) e upon stability testing at the 12 month test point (4/19/11) when stored at 25 °C.

OBSERVATION 6

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

Specifically, multiple defects were observed during an inspection of the pre-treatment water system on 7/17/12 including:

A. A leak was observed at the (b) (4) valve on the carbon filter bed on piping heading towards the storage tank.

B. Leaks were observed at (b) (4)) and (b) (4)) on the water softener skid.

C. A leak was observed along piping exiting the storage tank.

D. Multiple leaks were observed on the reverse osmosis system.

E. A leak was observed at the pH probe (b) (4) on the reverse osmosis skid.

F. A leak was observed at the pump moving water from the reverse osmosis water storage tank to the (b) (4) still.

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