DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	07/30/2012 - 08/24/2012* FEI NUMBER 1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Zena G. Kaufman, Senior Vice President, Global Quality

FIRM NAME	STREET ADDRESS
Hospira, Inc.	3900 Howard Lane
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Austin, TX 78728-6515	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:

The following observations pertain to the firm's manufacture of small and large volume parenterals and/or irrigation products.

Quality System

OBSERVATION 1

An NDA-Field Alert Report was not submitted within three working days of receipt of information concerning significant chemical, physical, or other change or deterioration in a distributed drug product.

Specifically,

a) Initial Field Alert Report (FAR) for NDA 16-366 for 0.9% Sodium Chloride Injection, USP was not filed with the Agency until August 3, 2012. Complaint #949101 was received by your firm on June 13, 2011. The complaint involved 4 bags of lot #05-201-JT of 0.9% Sodium Chloride Injection, USP (100mL) that contained particulates. The complaint sample was analyzed by your laboratory in Lake Forest, IL on 7/26/11. The remaining lot was placed on Quality Hold on August 18, 2011.

b) No Field Alert was filed by your firm for a report of "big black things floating" in a bag of lot #86-008-JT of Lactated Ringers Injection, USP 1000 mL (NDA 17-641). Complaint #970211 was received by your firm on July 5, 2011. The complaint sample was returned to your firm on July 8, 2011 but was not reviewed until June 22, 2012. The complaint investigation determined that the bag was leaking at the interface of the fill tube and the additive port seal. Your firm documented in the complaint record that no Field Alert was to be filed due to the expiration of the product. The product expired on February 1, 2012, which was almost 7 months after the complaint was reported.

c) FAR for NDA 16-366 for 0.9% Sodium Chloride Injection, USP, 1000 mL. The FAR identifies the date

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of 08/03/11 as the date your firm first became aware of the problem and filed the FAR with the Agency on 08/08/11. Hospira became aware of the problem on 06/02/11 for lot 03149JT and the customer sample was returned to this facility on 06/13/11. The sample was sent to the Hospira Particulate Lab on 06/27/11 for analysis and results were communicated to this facility on 08/03/11.

d) FAR for NDA 17-607 for 5% Dextrose & 0.45% Sodium Chloride Injection, USP, VisIV. The FAR identifies the date of 07/28/11 as the date your firm first became aware of the problem and filed the FAR with the Agency on 08/04/11. Your firm became aware of a complaint reporting "black stuff floating in the bag" on 06/14/11 for lot 82212JT. The customer complaint sample was returned to your firm on 06/23/11. Hospira Global Product Safety and Complaints identified this as a "lot trigger event" on 07/28/11. The root cause for the black substance floating in the solution was a container integrity breach of the primary container.

e) FAR for NDA 17-641 for Lactated Ringer's Injection, USP, 1000 mL, Lifecare II Flexible Container, lot 10127-JT. The FAR identifies the date of 03/30/12 as the date your firm first became aware of the problem and filed the FAR with the Agency on 04/04/12. Your firm became aware of a complaint reporting "white plastic particle floating inside. Like a plastic shaving, very small in a primary container". On 03/19/12 Hospira-Austin received the intact customer complaint sample. On 03/30/12, the customer complaint sample was microscopically confirmed to have presence of particulate matter.

OBSERVATION 2

There is a failure to thoroughly review the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

a) Complaint #949101 was received by your firm on June 13, 2011. The complaint involved 4 bags of lot #05-201-JT of 0.9% Sodium Chloride Injection, USP (100mL) that contained particulates. The complaint sample was analyzed by your laboratory in Lake Forest, IL on 7/26/11. There was confirmation that one bag contained polyester fibers, another contained nylon material, another contained cotton and the fourth bag contained a nitrocellulose particle. The remaining bags in inventory were placed on Quality Hold on August 18, 2011. Your firm failed to conduct a thorough investigation to determine the source of the particulates found in these 4 bags and to implement corrective action. Exception Report #47404 was opened on August 16, 2011 to investigate the source of the particulates. The investigation concluded that the source of the particulates could have come from clothing and traces of skin cream or cosmetics. The only corrective action implemented as a result of the investigation was to have employees wear gloves in

production. The investigation did not take into consideration other potential sources of contamination such as the cloths used to wipe filling nozzles during cleaning.

b) Complaint #818590 was received by your firm on February 3, 2011. The complaint stated that there was a black particle floating in a 1000mL bag of lot #94-143-JT of Lactated Ringers Injection, USP. It was reported that almost 900mL of the product was infused in the patient before the particle was discovered. Evaluation of the complaint sample by your laboratory in Lake Forest, IL on June 14, 2012, more than a year after the complaint sample was received by your firm, revealed that the particle was stainless steel. The investigation into the complaint is still open.

c) Complaint #1190431 was received by your firm on February 9, 2012. The complaint stated that particles were noticed in the solution while the product was being infused into a patient. The complaint was for lot #11-012-JT of Lactated Ringers Injection, USP (1000mL). The complainant sent a report from a 3rd party laboratory on February 29, 2012 that was included in the documentation at the Austin facility but was not loaded into the complaint system for review by Global Product Safety and Complaints, who is responsible for closing complaints. The lab report stated that the particulates were consistent with iron oxide corrosion product. The complaint was closed on June 15, 2012 without conducting an investigation to see if the particulates could have originated from your facility. There is no documentation that the report from the 3rd party laboratory was reviewed as part of the investigation by either the Austin site or Global Product Safety.

d) No investigation was conducted or initiated concerning product impact on various lots of product(s) filled on the PartFill line (Bay 4) with "Discoloration found in multiple areas" on the following dates: 07/23/12 (Lot 19-126JT), 07/24 & 25/12 (Lot 19-084JT), 07/29 & 30/12 (Lot 19-080JT), 07/31 & 08/01/12 (Lot 19-129JT), 08/07/12 (Lot 20-004JT), 08/12/12 (Lot 20-132JT), 08/13/12 (Lot 20-027JT), and 08/15/12 (Lot 20-029JT).

e) No investigation was conducted on HEPA filter leaks on the PartFill (Bay 4) line as follows:
   i. On 07/03/12 for HEPA filter ACF51841 (media leak) located directly above the AF1 (automatic filler 1); and ACF51847 (gasket leaks) located directly above the AF2 (automatic filler 2) filling line / placement of ports into bag(s).
   ii. On 07/03/12 for HEPA filters ACF51825 and ACF51839 (media leaks); and ACF51837 (gasket leaks).

   HEPA filters in the AF1 and AF2 areas are tested for leaks annually and were last tested on 07/04/11.

f) Investigations do not determine the root cause when discoloration is found to establish corrective and

preventive action. For examples:

i. On 06/12/12, the fill nozzle collars on both AF1 and AF2 had multiple surface spots on both fillers where discoloration was found. Your firm determined there was no product impact because "Fill nozzles are protected by the collar bar and no discoloration found on them." Collar bars were to be replaced with PMs. On 06/26/12, maintenance records/documentation was not complete and/or lacking for replacement of collar bars. No root cause/conclusion was reached to determine corrective and preventive action regarding the fill nozzle collars on both AF1 and AF2 with multiple surface spots.

ii. On 06/17/12, for "Discoloration Found on multiple spots" on both AF1 and AF2 under the bracket that holds the star wheel to the fillers.

iii. On 07/15/12, for "Discoloration found In multiple spots" on the "Take away conveyer on side and under.

OBSERVATION 3

Procedures describing the handling of all written and oral complaints regarding a drug product are not followed.

Specifically,

As of August 1, 2012, your firm had 413 complaints that have been open for longer than 90 days where the investigation is still considered in progress. At least 11 complaints have been open for longer than 1 year. SOP BQA0014 Complaint Investigations Procedures, all versions effective since 7/31/11, states that "all complaint investigations should target 30 calendar days from date of site awareness date for completion".

OBSERVATION 4

Drug products do not bear an expiration date determined by appropriate stability data to assure they meet applicable standards of identity, strength, quality and purity at the time of use.

Specifically,

Lack of stability data to support expiration dates in that sterility has not been tested at shelf life during the ongoing stability program for the following terminally sterilized products that are parametrically released:

a. Potassium Chloride Injection, 100 mEq/L, 7074-04-99 (18 month)
b. 5% Dextrose Injection, USP, 250 mL, 7100-04-74 (24 month)
c. 0.45% Sodium Chloride Injection, USP, 250 mL, 7132-04-74 (24 month)
d. Mannitol 20% Injection, USP, 500 mL, 7715-04-56 (24 month)

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e. Potassium Chloride in 5% Dextrose and 0.225% Sodium Chloride Injection, USP (20 mEq), 1000 mL, 7901-04-49 (24 month)
f. 5% Dextrose Injection, USP, 150 mL, 7922-04-15 (15 month)
g. 5% Dextrose Injection, USP, 25 mL, 7923-04-30 (24 month)
h. 0.9% Sodium Chloride Injection, USP, 25 mL, 7984-04-30 (18 month)

OBSERVATION 5

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

Specifically,

a) The majority of employees (e.g., laboratory and production) have not participated in at least one current Good Manufacturing Practice (cGMP) course covering Title 21 CFR 210/211 for drug products. For example, (b) (6) (b) (7)(C)
b) Only ten total employees have taken the recently implemented (b) (4) web based Isotrain "GMP Orientation ALL in ONE: Lesson 4", effective on 07/25/12. Three of the ten 10 employees lack certification of the training (e.g (b) (6) (b) (7)(C)
c) Training on SOP BMFG1404 for "General Manufacturing Log Books", dated 06/22/12, consists of self training (i.e., employees reading the SOP) with no assessment of employee understanding of the SOP. Per SOP section 5.5.2 of BMFG1404 "If discoloration or particulate is observed, contact the area supervisor or designee immediately. The area operator will sign and date the Equipment Cleaning Log Book and indicate in the 'Comments' column that discoloration or particulate in the ISO 7/EU-C or ISO 8/EU-D production area was observed and area supervisor or designee was contacted." There is no documentation in the Equipment Cleaning Log Book that the supervisor or designee was contacted regarding discoloration of equipment; however, the supervisor signed off as having reviewed the cleaning log book on 08/09/12 (for entries on 07/23 - 25, 29 - 31 & 08/01 & 07/12), and on 08/19/12 (for entries on 08/12, 13 & 15/12). Sections 5.5.3, 5.5.4, 5.5.4.1, 5.5.4.2, 5.5.5, and 5.5.5.1 of SOP BMFG1404 were not followed.
d) All employees who perform visual inspection activities either on-line (operators) or off-line (MQ Inspectors), are qualified yearly to perform this activity by reviewing a defect library that contains one example of each type of defect and then taking a test to identify the defect. The qualification does not entail reviewing and identifying defects under the same conditions that they perform this function during manufacturing operations (e.g. bags moving on conveyors with specific light sources and backgrounds and position of bags). For examples, employees (b) (6) (b) (7)(C)
e) Microbiologist (b) (6) (b) (7)(C) (hired on 01/11/11 was not trained on 90M-0426 for "Microbial Limits Testing" until

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08/24/12. [redacted] conducted testing on the following raw materials per 90M-0426:

i. Hydroxyethyl Starch for bacteria, yeasts and molds on 06/19/12 for two lots, on 01/12/12 for bacteria only, and on 06/08/11 for bacteria, molds and yeasts for two lots.

ii. Mannitol for bacteria on 05/02/11.

Laboratory System

OBSERVATION 6

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

Specifically, Standard Test Method Document number 90.C-1982 for "Determination and Identification of Amino Acids in Aminosyn Using the ACCQ-TAG Method", dated March 11, 2009, is deficient as follows:

a) The method does not include system suitability of working standards in that the resolution of working standards of late elutes for amino acids are not defined. This caused peak overlaps. Examples where peaks are not fully resolved past approximately 36 minutes of the run for Aminosyn are as follows: Lot #s 17-169-JT acquired on 05/25/2012, 17-115-JT acquired on 05/24/2012, and 14-166-JT acquired on 03/05/2012. Assay results potentially affected by this include: Valine, Methionine, Isoleucine and Leucine.

b) Chromatogram integration is not defined and no Method Change Request has been initiated as of the date of this inspection. As of 08/03/12, your firm did not initiate a Method Change Request to eliminate the choice for peak integration per section XIII, "NOTES TO THE ANALYST" sub section 3B. Chromatogram integration of the test method allows the analyst two choices of integration, namely, valley to valley or drop down baseline. Section 3B reads: "For those Aminosyn products with the glycine / histidine concentration ratio to be about 4 or higher, minimally, glycine and histidine peaks should be integrated by valley to valley if they are not baseline resolved. For others, either valley to valley or drop down baseline integration is allowed". For example, the Laboratory Investigation Single Record Report, PR 57010, concerning Aminosyn (List 4166), Lot 88-154-JT, at the 18-month stability interval failed for amino acid Methionine. The investigation concluded that the analyst chose baseline integration over valley to valley. The method lacks specification for calculation of peak integration.

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OBSERVATION 7

Each batch of drug product required to be free of objectionable microorganisms is not tested through appropriate laboratory testing.

Specifically,

a) No study completed to date to demonstrate the firm is capable of recovering endotoxin with finished product testing of LVPs terminally sterilized. For example, a recovery/extraction study to demonstrate that endotoxins can be recovered from LVP bags using the firm's test procedures (i.e., BBQA0038 and 94.B-014) and a known amount of spiked endoxtoxin. In addition, the firm does not vortex or sonicate LVP products tested for BET for a specified time. On 08/09/12, the analyst gently turned the 3000 mL bags (b) (4) bags) with (b) (4) complete rotations prior to sampling the bags to be tested for BET.

b) Environmental isolates used during growth promotion testing of prepared and purchased media only include gram positive organisms for growth promotion purposes. Environmental isolates do not include gram negative organisms, molds, and yeasts. In addition, environmental, surface, and air samples only identify organisms as GPC, GPR, GNR, and molds/yeasts, etc. when organisms are above alert limits and are not routinely identified to the genus and species.

c) Lack of scientific justification on the placement of surface monitoring settling plates , nonviable particulates, and viable monitoring devices used for environmental monitoring (EM) to provide meaningful information regarding environmental surface and air sampling during filling operations (e.g, in Bays (b) (4) in ISO 7/8 areas. Sample site selection of specific microbial and particulate locations is at the discretion of the Biological Quality management and maps outlined in BBQA0210.

d) The pH meter used for testing prepared media before and after sterilization is not identified on the media prep form for tests performed by the Biological Laboratory.

OBSERVATION 8

The calibration of instruments is not done at suitable intervals in accordance with an established written program.

Specifically, (b) (4) out of a total of (b) (4) Mercury-in-glass thermometers used in the facility have not been calibrated for there intended use. For example:

a. C-8192 and C-8177 thermometers in the Biological Laboratory used for (b) (4) water baths at (b) (4). Both mercury-in-glass thermometers were calibrated at 0°C using the USP ice bath procedure.
b. C - 8093 (Extrusion Line 1, Room 2816) and C-8203 (Extrusion Line 2, Room 2824) both used betwee (b) (4) (b) (4) were calibrated at 0°C.

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Materials System

OBSERVATION 9

Reserve drug product samples are not representative of each lot or batch of drug product.

Specifically, retain samples collected by your firm are not representative of the lot. Samples are routinely collected from the last sterilization load of the lot.

OBSERVATION 10

Each lot in each shipment received was not identified with a distinctive code for each container or grouping of containers for components.

Specifically,

A unique identification number is not assigned to commodities upon receipt for each lot. Rather, the firm maintains the lot number of the sister company (i.e., Buffalo, NY Hospira) as the receiving number. For example:

a. Commodity 750226: Lot 18229FA00 received on 07/27/12 (quantity of (b) (4)) and on 07/28/12 (quantity of (b) (4)); Lot 16221FA00 received on 05/24/12 (b) (4) and on 06/05/12 ((b) (4)); and Lot 16117FA00 received on 05/18/12 ((b) (4)) and on 05/21/12 ((b) (4)).
b. Commodity 750197: Lot 17280FA00 received on 06/15/12 (b) (4)) and on 06/16/12 ((b) (4) Lot 17273FA00 received on 05/24/12 (b) (4) and on 06/05/12 ((b) (4) and Lot 16286FA00 received on 05/10/12 (b) (4) and on 05/16/12 (b) (4)
c. Commodity 905556: Lot 17574FA00 received on 07/28/12 (b) (4) and on 07/31/12 ((b) (4)); Lot 17573FA00 received on 06/07/12 ((b) (4) on 06/11/12 (b) (4) and on 06/15/12 ((b) (4)); and Lot 17572FA00 received on 06/14/12 (b) (4) and on 06/15/12 (b) (4)
d. Isopropyl Alcohol 99% received from the supplier are assigned a lot number by incoming quality (IQ), which is the same lot number assigned for preparation by the firm of Isopropyl Alcohol 70%. For example, lot 17-062-JX-00.

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OBSERVATION 11

Representative samples are not taken of each shipment of each lot of components for testing or examination.

Specifically,

a) Endotoxin testing of PVC film (e.g., R-24 Double Wound 96-2439) following extrusion prior to the slitting and bag fabricator is conducted on a (b) (4) basis and per 94.B-024 uses a minimum of (b) (4) of PVC film from each Extruder (i.e., #s 1 & 2). Test procedure 94.B-024 does not identify where samples are collected from on the master roll per lot within the 24-hour period before the slitting/bag fabrication and reads to collect a PVC film sample representative of the lot (per 24 hours). Your firm collected a sample consisting of two feet from the master roll, which was said to be sampled from the end of the run lot. There is no indication if this is a statistically valid sample representative of the lot over a 24 hour period (e.g. beginning, middle and end of the extrusion process).

b) Each shipment received for commodities (with the same lot number) are not routinely sampled for testing with the receipt of each shipment when received on different dates. For examples, see 10a - c above. In addition, there is no raw data to support placement of commodities on a reduced testing program whereby one lot of commodity per commodity is tested annually for Incoming Quality (e.g., visual, physical, dimensions, and particulates).

c) Testing is not completed on a representative sample that is statistically valid for APIs. For examples:
   i. Dextrose USP Monohydrate: Lot #16011 JR, received on 04/05/12, included (b) (4) containers and one container was tested for ID; Lot 16010JR, received on 04/05/12 included (b) (4) containers and one container was tested for ID; and Lot 09042 JR01, received on 09/23/11 included (b) (4) containers and one container was tested for full monograph testing. The remaining (b) (4) containers were composited (i.e., containers 2-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90, 91-100, and 101-108) and were tested for specific rotation, color and appearance. Dextrose USP Monohydrate API was put on skip attribute/reduced testing in 1995 and said to be tested at your Rocky Mount facility; however, the data used in the qualification for skip attribute/reduced testing could not be located. No other raw data was provided.
   ii. Sodium Chloride, USP: Lot #15024 JR, received on 03/19/12, included (b) (4) containers and one container was tested for full monograph testing.
   iii. Sodium Chloride, USP: Lot 17056 JR, received on 05/24/12, included (b) (4) containers and one container was tested for full monograph testing. (b) (4) containers from the (b) (4) containers were reassigned lot 17057 JR. Lot 17057 JR included testing container 7 and a composite from containers 1-6 for color and appearance. Container 7 was used for full monograph testing excluding ID since this was tested on lot

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17056 JR.

d) Lack of documentation on all lots of 70% IPA prepared from 99% IPA with purified water per BCLN0004 for "Disinfectants Dilutions and Labeling Procedures". In addition, there is no incoming analytical testing of IPA 99% conducted and no analytical testing conducted on prepared 70% IPA (except bioburden). Your firm does not track all lots of 70% IPA prepared (e.g., labels are kept for prepared 70% IPA used in clean room ISO 7 areas for use on operator gloves and/or when used to clean areas in ISO 7 and ISO 8 areas for product contact surfaces (e.g., filling nozzles)). In addition, there is no validation of the C of A received with IPA 99% and no identification exam listed on the C of A.

OBSERVATION 12

Drug product container and closure test procedures are deficient in that closures are not tested for conformance in accordance with appropriate written procedures.

Specifically,

Endotoxin testing for commodity batches received from suppliers is deficient in that receipt of each lot of commodities (e.g. fill port, administration port, and Cobra cover) is not tested for endotoxins. Assessment of the supplier's testing on commodities for endotoxins is conducted on an annual basis for BET, particulates, and bioburden; however, documentation on the initial 3 lots of each commodity said to be used as justification for the firm to go to reduced testing (e.g. split attribute testing on an annual basis) is deficient. For examples, Fill ports #90-5556 per AT-BM-96-25, dated 11/11/96 (no raw data on site), (b) (4) and (b) (4) (b) (4) Commodity (b) (4) does not include negative controls and is not traceable to the LAL lot used. Commodity lot 75-0226 is not traceable to the LAL lot used.

Production System

OBSERVATION 13

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.

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Your firm has not qualified the visual inspection process for large volume parenteral drug products to date.

a) There is no documentation that factors such as line speed, placement of black and white backgrounds and light sources, position of bags on conveyors, and other factors that may affect the ability to inspect bags for defects, including particulates, have been taken into consideration with the current visual inspection process. On Line 2, there are usually 3 fillers running that can each fill (b) (4) bags/minute. There is one operator at the visual inspection station for this line. On Line 4, there are (b) (4) automatic fillers that can fill a maximum of (b) (4) bags/minute, with several manual fillers that can be used. There are (b) (4) operators at the visual inspection station for this line. On Line 5, there are (b) (4) automatic fillers that can fill a maximum of (b) (4) bags/minute each. There is (b) (4) operator at the visual inspection line for each filler.

b) A defect library containing a representative sampling of potential types of particulates that can and/or have been found in your products has not been developed to train your operators and MQ inspectors who perform visual inspection activities.

OBSERVATION 14

Written procedures are not followed that describe the in-process controls, tests, and examinations to be conducted on appropriate samples of in-process materials of each batch.

Specifically,

Your firm takes in-process samples at a frequency and quantity not consistent with procedure BMQA0075, dated July 5, 2012 "Responsibility/Flexible Container Sampling Process (Overwrap - Palletizer Area)" section 1.1 which states "Samples selected should always be representative of the lot. For example, if an equal number of samples are pulled at set intervals, the sample is representative of the lot." and section 1.3 which states "Samples sizes for all pulls should be approximately equal whenever possible." The following are examples of inconsistent sampling with respect to the number of samples pulled per interval:

- During lot # 19-129-JT of 0.9% Sodium Chloride Injection USP (250mL) manufactured in July 2012, your firm sampled from 7/31/12 at 1605 to 8/2/12 at 1300. Samples were pulled at approximately every (b) (4) and there were (b) (4) total groups of samples pulled. The numbers of samples pulled at set intervals range from (b) (4) to (b) (4) bags per interval.
- During lot # 20-029-JT of Metronidazole Injection, USP 500mg (100mL) manufactured in August 2012, your firm sampled from 8/14/12 at 1430 to 8/16/12 at 1225. Samples were pulled at approximately every (b) (4) and there were (b) (4) total groups of samples pulled. The numbers of samples pulled at set intervals range from (b) (4) to (b) (4) bags per interval.
- During lot # 20-004-JT of 0.9% Sodium Chloride Injection, USP (50mL) manufactured in August 2012,

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your firm sampled from 8/7/12 at 2150 to 8/9/12 at 0700. Samples were pulled at approximately every two to two and a half hours and there were (b) (4) total groups of samples pulled. The numbers of samples pulled at set intervals range from (b) (4) to (b) (4) bags per interval.

OBSERVATION 15

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

Specifically,

a. Material Specification 10.75-5261 lists the acceptance requirements for the chemical indicators (steam autoclave indicator tag Class 1) that are used in the sterilization process. One requirement is that the indicators have to meet "ANSI/AAMI/ISO 11140-1 requirements for a Class 1 steam indicator". Standard Test Method 90.0354 Color Change test - Steam Autoclave Indicator Tags, dated 3/30/90, has a procedure for testing the tags that is not that same as the test requirements listed in ISO Standard 11140-1. Lot #s 06285 JX released ***, 19310 JX released ***, and 19340 JX released ***, were not tested per ISO Standard 11140-1.
b. On 08/23/12 while observing Sodium Chloride 0.9% Injection, 50 mL bags, processed on the PartFill line (Bay 4) , lot 20-070JT, the operator placing bags on the line under ISO 8 was observed to touch the opening of the bags with gloved hands at the open ports repeatedly while loading bags on the line for AF2 (AutoFiller 2).

Facilities and Equipment System

OBSERVATION 16

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

Specifically,

a) Lack of quality control during processing of terminally sterilized injectable products as follows:
   i. 70% Isopropyl Alcohol (IPA) sprayed on gloved hands of operators in ISO7 areas for lines 1 - 5 is not filter sterilized and is manufactured from 99% IPA using purified water.
   ii. 70% IPA is used on product contact surfaces (i.e., filling nozzles) as follows: LC1 (Bay 1) and LC2 (Bay 2) daily per BMFG0713; Irrigation (Bay 3) with rotation of operators to wipe manual filling nozzles on a

periodic basis (e.g., approximately every (b) (4) per BMFG0702, section 6.3.1.5; PartFill (Bay 4) on manual fillers when operators rotate every (b) (4) per BMFG0703.

iii. Rotation of operators and wiping of filling nozzles with 70% IPA is not always described in the respective SOPs. Use of purified water to wash/rinse product contact equipment and rinse/wipe down equipment with IPA is described in section 4.1.2 of BFMG1413 for "General Good Employee Plant Practices", dated 10/10/11.

b) (b) (4) Knitted Wipers (Lightweight 100% polyester interlock knit wiper) used for cleaning filling nozzles are not made of non-fiber releasing material. According to the manufacturer's Technical Data the wipes contain readily releasable particles (i.e., $P \geq 0.5$ µm; 3.3 X $10^6/m^2$ and Fibers > 100 µm; 0.620 X $10^3/m^2$).

c) Hand sanitizers located in the gowning room are not tested for microbial content. Hand sanitizers are used on non-sterile gloved hands.

d) On August 7, 2012 it was observed that one end of the Plexiglas that covers the hot stamp area of bag fabrication machine #1 (print station guard) was placed on the floor while the operator made her adjustments to the machine. There is no suitable space on any of the bag fabricators where the cover can be placed and maintained in a clean manner before being placed back onto the machine after adjustments to the label printing have been completed. On August 7, 2012 your firm was fabricating bags for lot #20-123-JT of 0.9% Sodium Chloride Injection, USP (1000mL).

e) After cleaning equipment on August 22, 2012, the hose used to clean equipment in PartFill Filling Bay 4 was observed to be lying on the floor while it was connected to the purified water hand valve (HV4773). The end of the hose on the floor was resting in a pool of water from a backed up drain. After disconnection of the hose from the hand valve, the outside of the hose was sanitized/sprayed with isopropyl alcohol 70% by an operator then hung on the wall. The inside of the hose lying in the water was not sanitized.

OBSERVATION 17

Written records of major equipment maintenance are not included in individual equipment logs.

Specifically,

No maintenance logs maintained by the microbiological laboratory for (b) (4) incubators (b) (4) – 35°C, (b) (4) – 35°C (anaerobic chamber), and (b) (4) – 25° C) and refrigerators (used for storage of media and endotoxin test

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	07/30/2012 - 08/24/2012* FEI NUMBER 1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Zena G. Kaufman, Senior Vice President, Global Quality

FIRM NAME	STREET ADDRESS
Hospira, Inc.	3900 Howard Lane
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Austin, TX 78728-6515	Sterile Drug Manufacturer

kits) showing chronological listing of maintenance/adjustments performed. Adjustments to incubators and refrigerators are currently documented on the Digistrip printout used to monitor incubators and refrigerators.

OBSERVATION 18

Buildings used in the manufacturing, processing, packing, and holding of a drug product are not maintained in a good state of repair.

Specifically,

On August 7, 2012, two live crickets were observed in the corrugate warehouse where shipping boxes are stored and assembled for use in packaging. Doors located in the Northwest part of the warehouse were observed to have light coming from either the bottom or the perimeter of the door. One overhead door in the receiving area was observed to be bent and damaged and not closing flush with the ground. Another overhead door in receiving was observed to not close completely flush with the ground.

OBSERVATION 19

Washing and toilet facilities are not easily accessible to working areas.

Specifically, there is no handwashing sink in the rooms where employees gown up before entering ISO 7/ISO 8 production areas.

*** DATES OF INSPECTION:**
07/30/2012(Mon), 07/31/2012(Tue), 08/01/2012(Wed), 08/02/2012(Thu), 08/03/2012(Fri), 08/06/2012(Mon), 08/07/2012(Tue), 08/08/2012(Wed), 08/09/2012(Thu), 08/10/2012(Fri), 08/13/2012(Mon), 08/14/2012(Tue), 08/20/2012(Mon), 08/21/2012(Tue), 08/22/2012(Wed), 08/23/2012(Thu), 08/24/2012(Fri)

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