

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER 4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax: (214) 253-5314 Industry Information: www.fda.gov/oc/industry	DATE(S) OF INSPECTION 04/04/2011 - 04/27/2011*
	FEI NUMBER 1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
**TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations**

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

**Quality System**

**OBSERVATION 1**

The quality control unit lacks responsibility to approve and reject all procedures or specifications impacting on the identity, strength, quality, and purity of drug products.

Specifically,

- A. The Quality Manual, document #QM-01, dated October 25, 2010, establish the management controls, which "are the tools and systems management uses to continually monitor, assess, and improve the suitability and effectiveness of company operations to ensure effectiveness, efficiency, and regulatory compliance". The Quality Manual lists a number of elements with respect to management controls e.g., Deviation and CAPA Management, Management Reviews, Complaint Management, Material Controls, Production and Process Controls, and Facility, Equipment and Computer Controls. However, the following observations document a lack of adequate oversight by the Quality Unit to approve or reject the products manufactured and processed, as well as, approve or reject the established procedures or specifications impacting the quality of the drug product.
- B. The bag fabrication manufacturing batch record documents within the "Containment Action Plan" pages the "Type of Reject" (e.g., holes, wrinkles, incomplete perimeter and/or mandrel seal to the perimeter seal, missing or improperly placed ports, illegible, missing or misaligned critical print, other defects; Note - this is not an all inclusive list of quality attributes) that are removed during the bag fabrication process. The Quality Unit Director and Manager confirmed that they do not trend the "Type of Reject" that are observed during the containment action plan. In addition;
  - 1. The "Investigation Reports Procedure" document #BQA0034, dated February 4, 2011, "applies to all plant personnel involved in the investigation of nonconformances (events that deviate from specified requirements), the development of corrective and preventive action to address the root or probable cause(s), and implementation of the corrective and preventive action assigned." The procedure established practices

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE Torrance J. Slayton, Investigator JS Thomas J. Arista, Investigator TA Blondell W. Johnson, Investigator JS m BT	DATE ISSUED 04/27/2011

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300.  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: [www.fda.gov/oc/industry](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

**TO:** Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

and procedures that includes for example;

- i. "the criteria used to conduct the historical checks should be broad enough to capture a similar occurrence in order to determine if the event is the same based event type and the cause"
- ii. "the investigation owner and event owner or shall collect and analyze any data required to evaluate whether each of the causes is a root or probable cause";
- iii. "base on root or probable cause(s) identified, Investigation owner shall recommend Corrections / CAPAs, as necessary";

However, the aforementioned observation document a lack of trending with respect to the "Type of Rejects" for the bag fabrication "Containment Action Plan", which precludes the Quality Unit from executing "historical checks", "analyze data required to evaluate whether each of the causes is a root or probable cause", "recommend corrections" and implement an adequate CAPA.

- C. Your SOP BMQA0103, ver. 3/18/11, "Finished Batch Record Package Audit", provides for the review and approval/rejection of a batch by the Quality Unit. However, you firm does not follow this procedure while reviewing batch records. For example, your firm has created "MQ Batch Summary Sheet", an uncontrolled document that is used by the Quality Unit in making batch acceptance decisions. This document has not been reviewed and approved as defined in SOP BADM0001, ver. 3/14/11, "Standard Operating Procedures".
- D. Your Quality Unit does not review or approve maintenance procedures or records. For example,
  - 1. SOP BPTER0004, ver. 11/1/10, "Preventative Maintenance Program", provides for changes to any existing or establishment of a new preventative maintenance (PM) schedule. The changes are implemented without the involvement or approval of the Quality Unit.
  - 2. During the inspection, your firm amended the annual PM schedule for the bag fabrication unit (b) (4) which includes a (b) (4). This change was effected without the approval of the Quality Unit.
- E. Your firm conducts (b) (4) meetings to discuss open complaint reports and open Exception Reports (ER). These meetings are not a part of any approved procedure and no records of the meetings are maintained. For example,
  - 1. SOP BQA0034, ver. 2/4/11, "Investigation Reports Procedure", includes no provision for a (b) (4) meeting. However, your firm conducts a (b) (4) meeting to discuss open ERs and no records of the meetings are generated.
  - 2. SOP BQA0014, ver. 8/19/10, "Handling of Consumer Complaints", includes no provision for a (b) (4) meeting, referred to as Complaint Review Board. However, your firm conducts a (b) (4) meeting where your Quality Engineer is available to assist fellow employees in their evaluations of complaints and no

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator JS  
Thomas J. Arista, Investigator JS  
Blondell W. Johnson, Investigator JS in BS

DATE ISSUED

04/27/2011

**SEE REVERSE  
OF THIS PAGE**

**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		04/04/2011 - 04/27/2011*
		FEI NUMBER
		1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED  
**TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations**

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

records of the meetings are generated.

**OBSERVATION 2**

Drug products failing to meet established quality control criteria are not rejected.

Specifically, your firm routinely "reinspects" (reworks) in-process and finished drug products due to defects discovered in-process or post production (acceptance testing).

- A. SOP BQA0034, ver. 2/14/11 & 6/3/10, "Investigation Reports Procedure", provides guidance for investigations, including the failure of finished drug products. According to your Quality Engineer, the procedure allows for the determination to rework a lot. However, the procedure contains no language to reinspections or the reinspection process and no limit to the number of reinspections that can occur.
- B. SOP BMQA0079, ver. 6/4/10 & 3/25/11, "Finished Product and Commodity Restriction/Rework/Reinspection Report", provides for the reinspection of in-process materials (referred to as on-line rework/reinspection). However, the procedure provides no language to address in what situations reinspections are appropriate or in what manner to make the determination. According to the IC/MQ Manager & Supplier Quality "go back through product and cull out defective product".
- C. BMFG0205, ver. 3/14/11, (b) (4) - Setup and Operation", provides directions for the Production Specialist when an in-process test is failed. Your procedure directs the employee to execute a "Containment Action Plan". The employee is directed to go back to the previous acceptable test results and then work forward according to "stacks" (a system by which you account for your bags). At the point the same defect is noted that resulted in failed test results, that entire stack, and every stack forward, is discarded. According to your production supervisor the primary differences between this rework and the above in-process inspection are:
  - The action can be initiated by the Production Specialist without consulting Quality. There is no procedure in making this determination; it is left to employee discretion.
  - In-process reinspection involves culling units and this action involves discarding entire stacks based on one defective unit.
  - The action is noted within the batch record.

For example, the following in-process and post-process reworks were reviewed:

- 1. 5% Dextrose in Lactated Ringer's, lot #89-095-JT - The batch failed acceptance testing for the (b) (4) P.S.I. test (integrity). The firm identified a pinhole in the PVC bag was created at the "L" in "1000 ml" (labeling) created by a burr on the imprint die plate in die in position (b) (4)

The rework plan was to inspect all filled bags for identification of being produced by die position (b) (4) Of approximately (b) (4) units reworked, approximately (b) (4) units were rejected for displaying die position (b) (4) and

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Torrance J. Slayton, Investigator <i>TS</i>	04/27/2011
	Thomas J. Arista, Investigator <i>TJA</i>	
Blondell W. Johnson, Investigator <i>JS in BJ</i>		

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: [www.fda.gov/oc/industry](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FBI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

**TO:** Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

approximately (b) (4) units were rejected with no assignable cause. Your Quality System Manager stated it was not possible to calculate an expected yield.

2. 0.9% Sodium Chloride Injection, USP, lot #95-070-JT - Two in-process reworks occurred for this lot consisting of:
  - a. Weak bag seam seals were discovered while filling the product. The batch record failed to note when, where, and how the defect was observed. The Manufacturing Quality Auditor that approved the rework could not identify when, where, how the issue was discovered. The rework record specifies "Discard any bags found with weak seals"; however, it fails to specify how to determine which bags have weak seals. (b) (4) infilled bags were examined and (b) (4) bags were discarded. No investigation occurred.
  - b. Leaky bags discovered in packaging lead to the discovery of a pinhole in the PVC bag that was created at the "L" in "1000 ml" (labeling). The pinhole was created by a burr on the imprint die plate in die in position (b) (4). Your firm performed a sub-lot, and all filled bags were isolated in the warehouse and all unfilled bags were reworked to remove bags marked with die position (b) (4). The rework record specifies "Remove all die (b) (4) from carts". (b) (4) infilled bags were examined and (b) (4) bags were discarded. No investigation occurred.

While the above filled bags were isolated in a sub-lot, your firm's records for in-process testing and release testing were acceptable and the filled units were not reworked to remove die position (b) (4) bags. This lot was later recalled due to complaints revealing a number of units on the market were experiencing the characteristic leak.

3. 5% Dextrose and 0.45% Sodium Chloride Injection, USP, lot #02-190-JT - Three in-process and one post-process rework, respectively, consisting of:
  - a. The rework record notes "As a precaution, cart reinspected due to unqualified person in area" and "Inspect lot number from cart". No other details were provided. (b) (4) unfilled bags were examined and (b) (4) bags were discarded. No investigation occurred.
  - b. The rework is identical to the record above, except a different cart number is reported. The record notes "As a precaution, cart reinspected due to unqualified person in area" and "Inspect lot number from cart". No other details were provided. (b) (4) unfilled bags were examined and (b) (4) bags were discarded. No investigation occurred.
  - c. The rework record notes "Perimeter seal leaks" and "Destroy all containers from carts (multiple carts listed)". According to Exception Report, production personnel detected excessive leakers attributed to the perimeter seal that were fabricated on line (b) (4). All unfilled bags from fabricator (b) (4) were destroyed. (b) (4) of (b) (4) bags were discarded. No investigation occurred.
  - d. Your firm determined an issue with leaky bags was related to an improper (b) (4) belt change. Your firm reworked all filled units related to the above mentioned in-process that were produced on fabricator (b) (4) identified

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator TS  
Thomas J. Arista, Investigator TS  
Blondell W. Johnson, Investigator TS for BS

DATE ISSUED

04/27/2011

**SEE REVERSE  
OF THIS PAGE**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: [www.fda.gov/oc/industry](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

**TO:** Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

by die positions (b) (4) bags were reworked and (b) (4) units were rejected due to die position (b) (4) with another (b) (4) rejected for other reasons.

4. 0.9% Sodium Chloride Injection, USP, lot #04-024-JT - On 4/4/11, we observed one unit fail the (b) (4) P.S.I test. Your firm determined a wrinkle at the additive port seal was the cause. As a result, your Production Specialist executed a Containment Action Plan. Your employees went to the previous passing in-process check (b) (4) stacks previous) and worked forward completing a visual exam. Your employees determined (b) (4) stacks of bags were to be discarded. Samples from the non-discarded stacks were tested with passing results. Quality was not involved in the decision, inspection, or verification. No investigation occurred.

Your firm has released approximately (b) (4) lots of finished drug products in the past two years. Approximately (b) (4) of those lots were reworked post-production. According to your Quality Systems Manager, you firm makes no record or log of how often an in-process rework occurs. Additionally, your firm has no record of how frequent a Containment Action Plan is executed.

**OBSERVATION 3**

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

Specifically, your firm has not established an adequate training program for the identification of defects in materials, in-process drug products and containers, and finished drug products. For example,

- A) Your firm utilizes experienced employees (referred to as QFE) to accomplish OJT training, including training in the recognition of product defects. Your firm has established SOP TRMAN003, ver. 8/30/10, "Defect Recognition Manual", which provides the training curriculum for the recognition of defects during production. The procedure requires the employee in training be provided samples of acceptable bags. The training is further delineated into area specific defects related to the particular defects expected to be encountered by the employee, with a requirement to provide the employee in training "...samples/photos of the defects for the appropriate area and explain the defects". According to your Compliance Training Supervisor, QFEs are responsible for maintaining and providing any samples or photos to employee's in training that are necessary for training.

According to your QFE, while completing her duties, she provides OJT to employees in training in the packaging area. She displays and discusses reject samples as she observes them in the normal course of operations. The QFE stated that no standardized defect samples or photos are maintained, no list or log of defects which have been discussed with the employee in training, and no assessment or evaluation by the QFE exists other than marking "yes/no" to the question "Were all reject bags placed in the appropriate bin".

The final categorization of defects is conducted by production employees. These data are used by your firm as the source data for your (b) (4). The (b) (4) data is intended to monitor the performance of the

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator *TS*  
Thomas J. Arista, Investigator *TA*  
Blondell W. Johnson, Investigator *JWJ BT*

DATE ISSUED

04/27/2011

**SEE REVERSE  
OF THIS PAGE**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: [www.fda.gov/oc/industry](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

process. If a (b) (4) limit is exceeded, an evaluation into the excursion commences which could lead to the rejection of the batch. Your quality unit is not involved in production, including the categorization of defects. Without this involvement, you can not assure the quality and reliability of this data and ensure your processes are in a state of control.

- B) Your firm's SOP TRMAN039, ver. 4/15/11, "IQ Technical Manual" provides for the raining of employees involved in the evaluation of commodities at receipt. The procedure provides for OJT; however, fails to provide any examples of acceptable or unacceptable materials or instructions for evaluating materials.

**OBSERVATION 4**

Batch production and control records do not include the results of any investigation made into any unexplained discrepancy, whether or not the batch of drug product had already been distributed.

Specifically, your firm's procedure for conducting investigations is not appropriate. SOP BQA0034, ver. 2/4/11 & 6/3/10 "Investigation Reports Procedure", provides the basis for conducting investigations into non-conformances, including investigations resulting from the receipt of consumer complaints. For example, your procedure fails to delineate instructions to insure all affected lots have been evaluated, fails to ensure the examination of retain samples (when appropriate), fails to evaluate other potentially affected products, fails to specify for adequate effectiveness checks, fails to provide a system to document all complaint evaluations, and fails to provide for a system for the appropriate evaluation of returned complaint samples.

- A. Exception Report (ER) #SOL/AUS-002049 - The ER involves pinhole leaks discovered at the "L" location of the "1000 ml" near the top of the PVC bags for 5% Dextrose in Lactated Ringers, lot #89-095-JT. This ER resulted in a Field Alert dated 6/9/10. You identified (b) (4) potential affected lots, with the oldest, lot #76-205-JT, manufactured April 2009.

1. During the investigation, four complaints (#'s 552010, 576218, 584437 & 602916) involving 5 incidences were received, lot #84-046-JT. Of the four samples returned, all were confirmed as leaking from the same position as lot 89-095-JT. Your firm did not record the date of each complaint sample evaluation. The sample receipt dates were 4/19/10, 5/8/10 and 6/9/10; however, the documentation indicated all samples were evaluated on 6/24/10.

Your Quality Investigator stated that the date listed was the date the Manufacturing Supervisor, which completed the evaluation, signed the Product Complaint Response's. He stated the actual date of evaluation is not documented.

2. The investigation did not identify all potentially affected lots. Your firm can manufacture this product with a maximum of (b) (4) imprint die positions (b) (4) machines (b) (4) positions each). The investigation determined that for lot #89-095-JT, all die positions were used and that the pinhole was created by a burr on the die.

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator JS  
Thomas J. Arista, Investigator  
Blondell W. Johnson, Investigator JS for JS

DATE ISSUED

04/27/2011

**SEE REVERSE  
OF THIS PAGE**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: [www.fda.gov/oc/industry](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

located in position (b) (4)

You records do not provide for the identification of what particular die plate was in position (b) (4). Your investigator identified all lots produced with the die plates for this product. You identified lot #76-205-JT as the lot prior to lot #84-046-JT (the lot with confirmed leakers at the same location as lot 89-095-JT) as the bracketing point to limit the scope of you investigation. However:

- i. Your firm did not determine how many die plates were in inventory and cross-reference to your list of lots produced. According to your records, lot #76-205-JT was manufactured in April 2009. An evaluation of your die plate inventory indicated that your firm was in possession of (b) (4) imprint die at the time of the manufacturing of this lot.
- ii. Your firm failed to ensure that all potentially affected lots were evaluated for potential leaks at the specified position. You further relied on this information to limit you evaluation of other complaints associated with lot # 76-205-JT and forward for this product.

After evaluating and photographing all (b) (4) dies for this product, on 5/26/09, your firm identified and restricted the die plate that caused the pinholes in lot 89-095-JT; however, on 6/2/09 your firm restricted two additional dies and you have no record to document why these dies were restricted and the potential impact on your investigation.

- iii. Your firm did not consider other products manufactured on this bag fabrication equipment, which has been identified as a recurring issue.
3. Your investigation conclusion includes a document titled (b) (4) Problems. The document identifies potential issues with the (b) (4) die press process and solutions identified by applying a "fishbone" analysis. Among the issues listed were missing print due to die damage and time involved in "shimming" the dies. The recommendations include the removal of all shims prior to product changeover, leveling of the ram (die press equipment), and cleaning, grading, and tracking all dies. We observed the implementation of the leveling and die maintenance procedures. Your firm could produce no data to support the conclusions of the (b) (4) document.
4. Your effectiveness check of your CAPA included monitoring the ER data base for (b) (4) days following completion of the CAPA items. You did not consider complaints received for any lots manufactured after lot #89-095-JT. When your Quality Investigator was asked why the complaint data base was not queried, he responded "comes down to investigator style".

During the review of the above mentioned investigation, your Quality Investigator stated that "investigations were more of an art". He also stated that records of conversations, emails, phone calls are not maintained after the completion of an investigation.

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator JS  
Thomas J. Arista, Investigator TJ  
Blondell W. Johnson, Investigator BJS

DATE ISSUED

04/27/2011

SEE REVERSE  
OF THIS PAGE

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

**TO:** Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

B. Exception Report (ER) #SOL/AUS-27213 - The ER involves pinhole leaks discovered at the "L" location of the "1000 ml" near the top of the PVC bags for 0.9% Sodium Chloride Injection, USP, lot #95-070-JT. This ER resulted in a Field Alert dated 1/28/11 and an eventual recall of the lot. You identified (b) (4) potential affected lots, with the oldest lot #94-094-JT, manufactured October 2010.

1. Eight complaints (#s 787614, 794353, 78617, 809945, 81947, 822390, 822683 & 822692) involving 22 incidences, were received for lot #95-070-JT. All samples were confirmed as leaking from the same position as lot as referenced above. Your firm did not record the date of each complaint sample evaluation. The sample receipt dates were 1/11/11, 1/12/11, 1/11/11, 2/22/11, 2/9/11, 3/7/11, 2/28/11, 2/28/11 and 2/28/11, respectively; however, the documentation indicated all samples were evaluated on 4/1/11.

Your Quality Investigator stated that the date listed was the date the Manufacturing Supervisor, which completed the evaluation, signed the Product Complaint Response's. He stated the actual date of evaluation is not documented.

2. Your firm evaluated retain sample(s) as part of your investigation. Your documentation does not include the number of samples to evaluate, the number of samples evaluated, nor the die position indicated on the sample, as specified.

**Facilities and Equipment System**

**OBSERVATION 5**

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

Specifically,

- A. Your firm has failed to properly maintain the (b) (4) press equipment, which is used with imprint die plates to apply product labeling to your PVC bags. Your Maintenance Manager stated that "For press type operations, level is critical". He further stated that during the 2009 annual plant shutdown, the maintenance department leveled all (b) (4) press equipment in response to a "PDCA" document (root cause analysis tool); however, this activity was not part of the annual equipment preventive maintenance program, it was not logged in the maintenance log for the equipment, and no record was created to document what adjustments were required. Further, your firm failed to evaluate any impact of the equipment leveling on the set-up of the equipment, particularly the "shimming" of imprint dies with (b) (4) tape and/or thin sheets of brass material to achieve acceptable copy print (product labeling on PVC bags).

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator *TS*  
Thomas J. Arista, Investigator *TA*  
Blondell W. Johnson, Investigator *TJ BJ*

DATE ISSUED

04/27/2011

**SEE REVERSE  
OF THIS PAGE**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: [www.fda.gov/oc/industry](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

B. Your firm has failed to properly inspect, maintain, and document the imprint die plates (die) used in the application of the product labeling to your LVP bags.

1. Your SOP BMAT0010, ver. 4/4/11, "Assignment, Return, and/or Transfer of Work in Process Materials to a Batch Record", provides instructions for the inspection and cleaning of die prior to use. The procedure provides direction for cleaning the dies and also "Inspect (b) (4) dies for damage before issue to the batch record. Contact the production supervisor if any damage is noted".

On 4/7/11, we observed a Material Handler select, clean and inspect dies to be installed on (b) (4) (b) (4) press equipment for the fabrication of PVC bags. After selecting the dies and cleaning per procedure, the employee proceeded to use a hand-held magnifying glass to visually inspect the surface of the imprint plates and then ran her finger over the face of the imprint plates in order to detect any defects. The employee's actions are not included in your procedures for inspection of dies and the condition of the dies was not documented. The procedure also specifies "For rough surfaces on the imprint plate use polishing stone to smooth out surfaces". Your firm does not document when the polishing stone is used on rough surfaces, such as burrs, and has not evaluated any cumulative effects on the dies as a result of polishing (repairing).

2. Your SOP BMFG0245, ver. 4/4/11, "Quarterly Primary Bag Imprint Plate Preventative Maintenance (PM) Procedures", provides instruction for the (b) (4) PM of imprint die plates (dies). The procedure specifies "Use magnification of camera as a visual aid to identify damage to the die. When magnification camera is out of service, it is acceptable to use a magnifying glass or equivalent as a visual aid to identify damage".

On 4/4/11, we observed the follow devices available to your Material Handlers to examine dies:

- A digital camera (b) (4) magnification (connected to a monitor and computer)
- A (b) (4) diameter mounted magnilight (b) (4) magnification)
- A (b) (4) diameter hand-held magnifying glass (b) (4) magnification)

Your firm has not evaluated the equivalency of the three magnification tools, does not document which tool is used for inspection, and when the digital camera is used, have failed to maintain the data as a digital image, which is the raw data. Damage to dies has been identified by your firm during investigations as a potential cause of pinholes in finished drug products.

3. Your SOP BMAT0010, 4/4/11, "Assignment, Return, and/or Transfer of Work in Process Materials to a Batch Record", is silent to any inspection of dies after use in fabrication. However, on 4/7/11, we observed a Material Handler inspect and store dies after use in fabrication of PVC bags. The Material Handler visually inspected the dies and stored in a locked cage. The employee made no record of the inspection. Your procedures fail to provide for a system to document the inspection of dies after use in production.

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator TS  
Thomas J. Arista, Investigator TA  
Blondell W. Johnson, Investigator JS Jm JS

DATE ISSUED

04/27/2011

SEE REVERSE  
OF THIS PAGE

**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		04/04/2011 - 04/27/2011*
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED		FBI NUMBER
TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations		1628454
FIRM NAME	STREET ADDRESS	
Hospira, Inc	3900 Howard Lane	
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED	
Austin, TX 78728-6515	Sterile drug manufacturer	

**OBSERVATION 6**

Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use.

Specifically,

A. Your firm has not established a specification for imprint die plates (dies) that considers all material properties that may impact upon the quality, strength and purity of the finished drug product. For example, your firm previously used dies constructed of (b) (4) to apply labeling during the fabrication of PVC bags. The die composition was changed in 2004 from (b) (4) construction to (b) (4) with (b) (4) coming into contact with the PVC bags. Your material specification 20.Master-533, "Master Specification No. 533 for Imprint Plates (b) (4) Printing)", provides for dimensional tolerances only. This specification applies to dies constructed of (b) (4) (b) (4) or (b) (4). Your firm has not determined if the material composition of the dies (hardness) impacts upon the integrity of the PVC bag for filling Lifecare line LVPs during fabrication and established appropriate specifications. The labeling (pigment) is applied to the PVC bag (for Lifecare line LVPs) surface by the dies based on contact time, die temperature, and contact pressure.

B. Your firm lacks the data to support the qualification of the (b) (4) imprint press equipment for use with (b) (4) (b) (4) dies. For example, your firm originally qualified the operational capabilities of fabricator line (b) (4) (equipment #ABM10500) (b) (4) imprint press, on 11/20/92 as documented in ECR #AU92181. Included in the evaluation was "bag damage" that could result from the dies contacting the PVC bag surface and affect bag integrity. Your firm qualified the equipment with dies that met specification 20.98-2624, "Imprint plates for List 7953-39, Lactated Ringer's Injection, USP, LC 04 (1000 ml)". The specification was for the material type of (b) (4)

In 2004 your firm changed ownership which required new die plates. In order to meet the time allowed for conversion, your firm changed the composition of all die plates to (b) (4)

Your firm conducted a Periodic Review of fabricator (b) (4) according to SOP BVAL0020, ver. 2/14/11, "Revalidations, Requalifications, and Periodic Reviews". According to the Periodic Review Summary Report, VCR #AU2008-080, approved 11/13/08, your firm reviewed the complaint data, the previous (b) (4) of in-process data, exception reports, operating parameters, software version, incremental and cumulative changes and determined that requalification was not required.

However, your firm has not evaluated any bag integrity effects of (b) (4) die plates in the qualification of your (b) (4) imprint press equipment used to produce LVP bags for Lifecare line.

C. Your firm has failed to operate the PVC bag fabrication equipment in the manner specified. For example, the operational qualification, ECR #AU92181, which provides for the set-up and operation of the hot stamp die press (b) (4). The directions provide no reference to "shimming" (plumbing) the imprint plates with metal shims (thin sheets

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Torrance J. Slayton, Investigator <i>TS</i> Thomas J. Arista, Investigator <i>JA</i> Blondell W. Johnson, Investigator <i>BWJ</i>	04/27/2011



**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

5. The (b) (4) can generate "Roll Defect Reports" that lists and graphically maps the locations of all PVC film (within each PVC roll) that exceeds the high and low alert levels. However, the "Roll Defect Reports" are not generated and the "Roll Defect Reports" data is not reviewed and approved by the Quality Unit;
6. The (b) (4) measurement data (e.g., minimum / maximum and average for the number of scans) can be trended via the "Trend" set-up menu, which will provide a green and red color graphical display (green color is acceptable and red color signifies an out of limit level). However, the PVC extruded process is not trended;
7. During routine PVC extrusion process the (b) (4) will display an out of limit level via a red color graph, which requires the production operator to perform some form of manual adjustments to correct the alarm event. However, there is no record to document the manual adjustments;
8. The (b) (4) consists of a touch screen color monitor that is used to graphically display and monitor the PVC extrusion process. The graphically display consists of, for example, the minimum / maximum thickness of the PVC, the number of total scans (e.g. (b) (4) per PVC roll), start and stop times, and it graphically present the PVC measurement process in real-time conditions. However, the real time data (which can consists of up to (b) (4) scans) is not retained as a permanent record;
9. The (b) (4) can retain up to (b) (4) scans during the PVC film process. After the (b) (4) scan is completed, the preceding data is erased. (Note: please refer to the aforementioned observations noted above);
10. The 6/11/10 (b) (4) Risk Assessment Report, protocol #RA-0228 lists security as one of the critical quality attributes concerns (CQA), i.e., "Access to all (b) (4) program recipe parameters is locked and password protected to prevent unauthorized changes to (b) (4) system settings." Despite the concerns established by the aforementioned CQA the management team confirmed that there is no list to document the individuals who have "Operator Access", "Engineer Access" and/or "Administrator Access";
11. The (b) (4) has the capacity to perform (b) (4) via the (b) (4) set-up menu. However, the (b) (4) evaluation is not performed or currently part of the PVC film manufacturing process.

**OBSERVATION 7**

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically, the "Security Features Required for (b) (4), document #RSOFT005, dated August 6, 2009 establishes the practices and procedures required to implement and maintain security in the (b) (4) applications. However, the standard operating procedure is silent with respect to the security requirements relative to the (b) (4)

(b) (4)

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator JS  
Thomas J. Arista, Investigator TJA  
Blondell W. Johnson, Investigator JS in BT

DATE ISSUED

04/27/2011

SEE REVERSE  
OF THIS PAGE

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: [www.fda.gov/oc/industry](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

**Production System**

**OBSERVATION 8**

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, your firm's process validation for 0.9% Sodium Chloride Injection, USP, 0.45% Sodium Chloride, and Sterile Water for Injection, USP, is based upon the validation rationale/acceptance criteria that includes "All equipment utilized in the process had been documented as qualified to manufacture product within the process ranges..." and "Based on the current validation status associated with the equipment/process, the operating ranges have been appropriately justified..."

However, the following observations document a lack of control with respect to equipment involved in the manufacture of the container used to fill previously mentioned products:

- The (b) (4) which is responsible for assuring the thickness of the PVC film used in the fabrication of LVP bags, and therefore responsible for ensuring container integrity, lacks data to support the qualification and operational parameters
- The (b) (4) die press has not been qualified to imprint labeling on LVP bags via the (b) (4) imprint die plates

**OBSERVATION 9**

Written procedures are not established that describe the examinations to be conducted on appropriate samples of in-process materials of each batch.

Specifically, procedure BMQA0068, ver. 11/22/10, "Sampling Responsibilities in Bag Fabrication", include the execution of the "Tug Test". The Tug Test directs the employee to "Grasp the bag with one hand and firmly grip the additive port housing around the center with pliers, and pull firmly. Repeat the process using the lip of the housing, pull firmly. The port housing should show no evidence of pulling or peeling from the bags around the seal".

On 4/4/11, we observed a production employee execute the Tug Test with a pair of household type needle-nose pliers during production of 0.9% Sodium Chloride Injection, USP, lot #04-024-JT. When the employee was asked how he knew how hard to pull on the port, he replied that he was "looking for separation". Your Quality System Manager confirmed that the procedure was not validated, and not recognized in any standard (e.g. USP).

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator *TS*  
Thomas J. Arista, Investigator *TA*  
Blondell W. Johnson, Investigator *BJ*

DATE ISSUED

04/27/2011

**SEE REVERSE  
OF THIS PAGE**

**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: <a href="http://www.fda.gov/oc/industry">www.fda.gov/oc/industry</a>		04/04/2011 - 04/27/2011*
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED		FBI NUMBER
TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations		1628454
FIRM NAME	STREET ADDRESS	
Hospira, Inc	3900 Howard Lane	
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED	
Austin, TX 78728-6515	Sterile drug manufacturer	

**Packaging and Labeling System**

**OBSERVATION 10**

Each lot of drug product containers is not withheld from use until the lot has been sampled, tested, examined, and released by the quality control unit.

Specifically, your firm evaluates and releases all containers, closures, drug substances, and excipients received from vendors, including components received from other Hospira manufacturing sites, prior to use. Additionally, you firm conducts in-process testing of the bulk drug product, which is not released for filling until acceptance testing is complete. However, a similar level of evaluation is not performed on PVC bags manufactured in-house.

For example, your firm fabricates LVP bags from Polyvinyl Chloride (PVC) film for filling with your drug products. After fabrication, these LVP bags are immediately available for filling, sterilizing and packaging. The quality unit does not review and approve the records for the fabrication of your LVP bags until all drug manufacturing activities (filling/sterilizing, packaging/product acceptance testing) have been completed for the batch.

**Laboratory Control System**

**OBSERVATION 11**

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

Specifically, the Exception Report (ER) Record #31580 was initiated in response to customer complaints 795852 and 837910 (received on 1/10/11 and 2/24/11, respectively) regarding 5% Dextrose Injection, USP, lot #87-214-JT and a complaint of "mold". The ER documents that a "Qualitative Microscopic Evaluation of the discoloration was performed on the ports of all three samples at 10-15x magnification on 3/10/11", which revealed "no filamentous structures consistent with mold". However, the Microbiology Supervisor confirmed that there is no standard operating procedure that addresses a "Qualitative Microscopic Evaluation". In addition;

- A. The "Microbial Isolate Submission for Microbial Identification", document #BBQA0018, dated December 30, 10 establishes the practices and procedures with which samples are submitted and tested for microorganisms. However, the standard procedure is silent with respect to finished product samples returned for microbiological evaluation in response to customer complaints;

<b>SEE REVERSE OF THIS PAGE</b>	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Torrance J. Slayton, Investigator <i>TS</i> Thomas J. Arista, Investigator <i>TA</i> Blondell W. Johnson, Investigator <i>BJ</i>	04/27/2011

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

4040 North Central Expressway, Suite 300  
Dallas, TX 75204  
(214) 253-5200 Fax: (214) 253-5314  
Industry Information: [www.fda.gov/oc/industry](http://www.fda.gov/oc/industry)

DATE(S) OF INSPECTION

04/04/2011 - 04/27/2011\*

FEI NUMBER

1628454

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Arthur J Fiocco, Jr, Corporate Vice President Pharmaceutical Operations

FIRM NAME

Hospira, Inc

STREET ADDRESS

3900 Howard Lane

CITY, STATE, ZIP CODE, COUNTRY

Austin, TX 78728-6515

TYPE ESTABLISHMENT INSPECTED

Sterile drug manufacturer

- B. The "Presumptive Identification to Genus", document #BBQA0183, dated January 01, 2011, establishes "the procedures for the identification to genus of know microorganisms for certification and unknown microorganisms." The standard procedure describes the microbiological method of analysis that is needed to "describe the colonial morphology" and with "lactophenol cotton blue stain" to "examine microscopically to determine the genus of mold and determine the cellular morphology." However, as documented in the preceding observation, the microbiological method of analysis established by this standard procedure was not followed.

**\* DATES OF INSPECTION:**

04/04/2011(Mon), 04/05/2011(Tue), 04/06/2011(Wed), 04/07/2011(Thu), 04/08/2011(Fri), 04/12/2011(Tue), 04/13/2011(Wed), 04/14/2011(Thu), 04/15/2011(Fri), 04/18/2011(Mon), 04/19/2011(Tue), 04/20/2011(Wed), 04/21/2011(Thu), 04/22/2011(Fri), 04/25/2011(Mon), 04/26/2011(Tue), 04/27/2011(Wed)

**SEE REVERSE  
OF THIS PAGE**

EMPLOYEE(S) SIGNATURE

Torrance J. Slayton, Investigator *Torrance J. Slayton*  
Thomas J. Arista, Investigator *Thomas J. Arista*  
Blondell W. Johnson, Investigator *Blondell W. Johnson*

DATE ISSUED

04/27/2011