DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

| DISTRICT ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| One Montvale Avenue<br>Stoneham, MA 02180<br>(781) 596-7700 Fax:(781) 596-7896 | 03/09/2005 - 04/07/2005* |
| | FEI NUMBER<br>1219544 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Mark S. Adams, Quality Manager

| FIRM NAME | STREET ADDRESS |
|---|---|
| Boston Scientific Corporation | 480 Pleasant Street |
| CITY, STATE, ZIP CODE, COUNTRY | TYPE ESTABLISHMENT INSPECTED |
| Watertown, MA 02472 | 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.

*The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.*

**DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:**

## OBSERVATION 1

Not all of the actions needed to correct and prevent the recurrence of nonconforming product and other quality problems have been identified.

Specifically, the three non-valved Vaxcel Low Profile Plastic Ports were not included in the recall of the Vaxcel with PASV Valve Low Profile Port affected by the port separation issue, although a similar ultrasonic welding process is used for the non-valved ports. The Recall Letter states that the firm has received reports that the port housing has separated after implantation, and that this, "can result in leakage of infusates and ***have potentially significant adverse health consequences***."

- Both the valved and non-valved port subassemblies consist of a cover, a base and a septum. With the septum installed, the cover and base are ultrasonically welded together. The ultrasonic welding process for the non-valved ports was not validated. The justification was that the process is identical to that used for the valved ports.
- The valved ports have a history of port separation - the cover and base have separated while implanted. Boston Scientific Corporation (BSC) received [redacted] complaints of port separation between August 2004 and February 2005.
- BSC conducted a field action by recalling the valved ports, both hospital inventory as well as implanted units, in March 2005.
- No field actions have been taken on the non-valved ports.

## OBSERVATION 2

The acceptance status of product was not clearly identified throughout installation and servicing of the product.

Specifically, although product was placed on Precautionary Shipping Hold on August 25, 2004, customers were not notified

of the problem of port separation on the Vaxcel Low Profile Ports with PASV technology, until the recall letters were actually sent out to customers on March 11, 2005. The firm's decision to recall was not recommended to the field action committee until 3/3/05. The recall affects both hospital inventory, as well as implanted ports. Customers were not notified separately not to use product in inventory.

**OBSERVATION 3**

A process whose results cannot be fully verified by subsequent inspection and test has not been adequately validated and approved according to established procedures.

Specifically, validation of the ultrasonic weld on the Vaxcel Low Profile Ports, both with and without Pressure Activated Safety Valves (PASV), was inadequate. The ports are subassemblies used in the Vaxcel Implantable Vascular Access System.

For valved ports (those with PASV): Document #90052957 ver. AB, *Plastic PASV Single Lumen Port Ultrasonic Welding Operational and Process Qualification Test Report*, release date 2/19/03, included a [redacted] which was conducted at [redacted]. This did not take into account a safety factor for degradation of the product in the body. There was no tensile test included in the validation. There was no actual or simulated clinical use testing performed. The validation was conducted on units manufactured by R&D personnel rather than production personnel. The validation was conducted on units manufactured prior to incorporating the [redacted] during the welding process. Production units were all manufactured subsequent to incorporating [redacted]. The post-welding inspection procedure, Document 90038661 ver. AC *In-Process Inspection of the Port Welded Assembly*, includes only visual and cosmetic inspections.

The non-valved ports (those without PASV) did not receive an Operational Qualification/Process Qualification (OQ/PQ) test. Change Manager #546297 dated 4/23/03, Described as "OQ/PQ Test Report NV Port Base & Cover" states on page 3 regarding welding of the non-valved ports: "Process is identical to the Std Plastic Port. No further testing required." There is a difference in the valved and non-valved welding process parameters: the port welding procedure for the valved ports (Document #90033786 ver. AE *SL Port Welding Procedure*) includes a [redacted]; the port welding procedure for the non-valved ports (Document #90052347 ver. AB *Mini Port Welding Procedure*) includes a [redacted].

*Annotation: Promised to correct by 6/7/2005 for valved, and 9/30/2005 for non-valved.*

**OBSERVATION 4**

A validated process was not revalidated when changes or process deviations occurred.

Specifically, the ultrasonic weld OQ/PQ test was not done for the valved Vaxcel with PASV Low Profile Ports following the change on 7/10/2003 to sand the port bases. The validation of the change consisted only of verifying that the height of the

base was still within specifications, prior to welding.

*Annotation: Promised to correct by 6/7/2005.*

**OBSERVATION 5**

Procedures were not defined for the control of products that do not conform to specifications.

Specifically,

Procedures are lacking to assure consistency in handling and timing activities from complaint receipt, complaint trending, ship hold, PIR initiation, and field action determination, to actual recall. There were inconsistencies for the 3 recalls on Vaxcel products with subassemblies manufactured at this site:

A. For Product Inquiry Report (PIR), #WAT-2004-01-02, for the recall of the Vaxcel with PASV Titanium 8 Fr Mini Port involving catheter separation and catheter migration:

- Although the preset complaint alert limit [redacted] was exceeded for November 2003, December 2003, and January 2004, as stated on the PIR, the product ship holds were not initiated until 1/30/04 and 2/4/04.
- The Clinical Assessment for Detection (PIR section IIIA) is listed as "High" with a rationale for choice of "The leakage is likely to get noticed during infusion of the fluids."
- The Clinical Assessment for Severity is listed as 4-Critical, and the separate box is checked under total score for "Any Severity Factor (Severity 4 or above = Unacceptable Risk)"
- The Recommendation for Field Action for recall was signed as approved by the Business Group VP of Quality on 2/13/04, and by the Field Action Committee (FAC) Chairperson on 2/13/04 (3 months after identifying the trend, and 1-2 weeks after the ship holds).

B. For PIR #WAT-2004-09-01, for the recall of the Vaxcel with PASV PICC - Single Lumen 4-3 involving catheter fractures and catheter migration:

- Although the complaint rates listed on the PIR for July, August and September 2004, each exceeded th[redacted] preset upper control limit (UCL), the product ship hold was not initiated until 10/1/04.
- The complaint rate for August 2004 is shown as [redacted] based on [redacted] complaints [redacted] with a note that although [redacted] additional complaints were phoned in for that month, the events happened in January 2004-July 2004.
- The Clinical Assessment for Detection (PIR section IIIA) is listed as "Low" with a rationale for choice of "Separation of the catheter distal to the suture wing may not be easily detectable and therefore may not prevent the leakage of infusion fluids or catheter migration."
- The Clinical Assessment for Severity is listed as 4-Critical, and the separate box is checked under total score for "Any Severity Factor (Severity 4 or above = Unacceptable Risk)"
- The Recommendation for Field Action for recall was signed as approved by the Business Group VP of Quality on 10/28/04, and by the FAC Chairperson on 12/1/04 (5 months after identifying the trend, and 2 months after

the ship hold).

C. For PIR #WAT-2004-08-01, for the recall of the Vaxcel Low Profile w/ PASV Ports involving port separation, there are two revisions of the PIR. Revision AA is dated 9/17/04. Revision AB is dated 2/23/04, however should have been dated 2/23/05:

- The complaint rate for August 2004 listed on the local trend report is [redacted], and a product ship hold was initiated on 8/25/04.
- The complaint rate for August 2004 shown on the PIR rev. AA, section [redacted]
- The complaint rate for February shown on the PIR rev. AB, section II[redacted]% based o[redacted] complaints. BSC actually received [redacted] complaints of port separation between August 2004 and February 2005: 8/19/04, 9/2/04, 10/19/04, 11/16/04, and 2/9/05. The Quality Manager said that only [redacted] of these complaints were confirmed.
- The local trend report shows complaint rates of:
  [redacted]% for September 2004 based o[redacted] complaint and [redacted] shipments;
  [redacted] for October 2004 based o[redacted] complaints and [redacted] shipments;
  [redacted] for November 2004 based on [redacted] complaint and [redacted] shipments;
  [redacted] for December 2004 based o[redacted] complaints a[redacted] shipment;
  [redacted] for January 2005 based on [redacted] complaints and [redacted] ipments; and
  [redacted]% for February 2005 based on [redacted] complaint an[redacted] shipment.
- On Rev. AA, the Clinical Assessment for Severity is listed as 4-Critical, however the separate box is *not* checked under total score for "Any Severity Factor (Severity 4 or above = Unacceptable Risk)"
- On Rev. AB, the Clinical Assessment for Severity is listed as 4-Critical, however the separate box is *not* checked under total score for "Any Severity Factor (Severity 4 or above = Unacceptable Risk)"
- On Rev. AA, the Recommendation for NO Field Action (PIR section V) is approved by the Business Group VP of Quality on 9/27/04, and by the FAC Chairperson on 9/29/04.
- On Rev. AB, the Recommendation for Field Action for recall is approved by the Business Group VP for Quality on 3/4/05, and by the FAC Chairperson on 3/3/05 (5 ½ months after the ship hold).

The PIR procedure (90030420 *Corporate SOP Product Inquiry Procedure*) says to include the rate of complaints per month, but does not explain how to determine the rate of complaints (i.e. the number of complaints received that months vs. the number of events that occurred that month).

The complaint trending procedure (S808543-00 rev. AC *Complaint Trending*) identifies a complaint rate pre-set upper control limit (UCL) o[redacted] as well as a statistical UCL. The procedure states that a Complaint Trending Report will be generated each month for specific products including, but not limited to, the products for which Complaint Evaluation is conducted at the facility. Although the port separation issue is being investigated at the Watertown, MA facility, the Quality Manager stated that this procedure is local to the Watertown, MA facility, and does not apply to the Vaxcel ports since the official complaint trending site for the ports is the Glens Falls, NY facility. He said he chooses to track this data for the Vaxcel ports for his own information.

The Glens Falls procedures (QA-004.EB *Product Complaint and MDR Processing*; and QA-094.C *Determination of Control/Action Limits*) describe statistical UCLs, but not th[redacted]% preset UCL.

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Neither the PIR procedure nor the complaint trending procedure states whether to include all complaints received in a particular month, or only those that have been "confirmed". The trend report for Watertown appears to include all complaints received in a particular month. The complaint rate for August 2004 listed on PIR #WAT-2004-09-01 appears to include only the complaints where the event happened in the month of August 2004. The complaint rate listed on PIR #WAT-2004-08-01 rev. AB appears to include only the "confirmed" complaints for the trend reported.

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*Annotation: Under consideration.*

## OBSERVATION 6

The organization structure is not adequate to assure that quality system requirements are fully met.

Specifically, the responsibilities for a particular product family are shared among various facilities. Process requirements are not necessarily the same from one facility to another, or from local procedures to the corporate procedures.

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*Annotation: Under consideration.*

## OBSERVATION 7

Procedures that describe the review and disposition process for nonconforming product were not implemented.

Specifically, Shipping Holds for 2 instances were incorrectly classified as Business Holds rather than Precautionary Holds. Both involved products with subassemblies manufactured at this facility, which ultimately resulted in product recalls. The Product Shipping Hold and Release procedures #S842160-00, (both revs AF & AG), state that "Business Holds" may not be "as a result of performance related issues."

A. The shipping hold for the Vaxcel with PASV 4-3 Fr Single Lumen Peripherally Inserted Central Catheter (PICC) was initiated on 10/1/04 as a "Business Hold" for all lots of the following 4 Material Numbers: M001454500, M001454510, M001454520, and M001454540. The reason for the hold is not filled out on the Notification of Shipping Hold form. The firm's 3/10/05 memo states that the firm became aware of a number of complaints of catheter fractures at the suture wing connection, some of which resulted in catheter migration. A recall was initiated on 12/3/04, as stated in the same memo.

B. The shipping hold for the Vaxcel with PASV 8Fr Mini Titanium Port was initiated on 2/4/04 as a "Business Hold" for 9 lots of Material Number M001453620, and 2 lots of Material Number M001452380. The reason for the hold is "Design-Related". This followed the 1/30/04 Shipping Hold for Material Number M001452150 which was classified as a "Precautionary Hold". The firm's 3/10/05 memo states that the firm became aware of a number of complaints for catheter separation from the port connector, some of which resulted in catheter migration.

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*Annotation: Under consideration.*

## OBSERVATION 8

The device history record does not demonstrate the device is manufactured in accordance with the device master record.

Specifically, 43 of 55 shop floor paperwork (SFP) records reviewed were missing elements. These SFP records included welded port subassemblies, molded port bases and molded port covers.

A. Nine (9) SFPs were missing one or more of the following fields of data on the Injection Molding Process Log Sheet: cushion data, rear zone, middle zone, mold temperature, and/or back pressure. The [redacted] temperature (rear and middle zone recordings) and [redacted] temperature are considered "critical process parameters (Inputs)" according to the firm's memorandum dated 3/28/03. Two (2) of these 9 SFPs were missing critical parameters: lot 5566779 (non-valved port base - missing Rear Zone data and Middle Zone data); and lot 5470571 (valved port base - missing the [redacted] Temperature).

B. Three (3) SFP records were lacking the Injection Molding Process Log Sheet altogether.

C. 38 SFPs were lacking time and/or initials on the Injection Molding Process Log Sheet.

D. Five (5) SFPs were missing the shift and/or date of the technical set up on the Injection Molding Process Log Sheet.

E. One (1) SFP was missing the lot number.

F. Three SFP records containing hand-written corrections to the pre-printed order quantity, did not have dates next to the initials for the corrections. SOP S800149-01, rev. AF, *In-Process Handling of Product for Inspection*, requires that, "any changes to pre-printed information are to consist of, item crossed out, new item written in, initialed and dated by proper signatory."

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*Annotation: Promised to correct within 30 days.*

## OBSERVATION 9

Procedures for acceptance or rejection of incoming product were not defined, documented, and implemented.

Specifically,

A. Seven of nine incoming material inspection records showed acceptance stickers with "Accept Dates" prior to the actual accept date listed on the documents.

| SEE REVERSE OF THIS PAGE | | DATE ISSUED |
|---|---|---|
| | Elizabeth B [illegible] Carla Ca[illegible] | 04/07/2005 |

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B. Eight of nine incoming material inspection records were missing the accept date next to the inspector's handwritten initials. SOP 9610001-01 rev AY, *Incoming Material Inspection*, requires the date in addition to the inspector's initials.

*Annotation: Reported corrected, not verified.*

*** DATES OF INSPECTION:**
03/09/2005(Wed), 03/10/2005(Thu), 03/11/2005(Fri), 03/15/2005(Tue), 03/18/2005(Fri), 03/22/2005(Tue), 03/29/2005(Tue), 04/05/2005(Tue), 04/07/2005(Thu)

**FDA EMPLOYEES' NAMES, TITLES, AND SIGNATURES:**

Elizabeth B. Griffin, Engineer/Investigator

Carla C. Cummins, Investigator

Darin S. Wiegers, Investigator

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DATE ISSUED
04/07/2005