DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303) 236-3000 Fax:(303) 236-3100 Industry Information: www.fda.gov/oc/industry	03/03/2014 - 04/11/2014* FEI NUMBER 1713910

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Paul R. Lunsford, Corporate Vice President and General Manager

FIRM NAME	STREET ADDRESS
Edwards Lifesciences, LLC	12050 Lone Peak Pkwy
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Draper, UT 84020-9414	Medical Device Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

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

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

Specifically,

A. Your process validation control of your (b)(4) processing equipment in your Cardiac System's production room with (b)(4) device production lines is inadequate in that you identified 89 processes that require a complete validation which have not been validated as of today (03/12/2014). The (b)(4) device families manufactured on the equipment include: [redacted]

B. Validation of the (b)(4) + (b)(4), according to the Process Performance Qualification, Protocol and Report No. 30228, dated 11/30/2011 and Report No. 30228, Add. 1, dated 4/26/2012, was found to be inadequate due to the following:

1. A lot size of (b)(4) ([redacted]) or (b)(4) ([redacted]) units is not representative of a routine lot at the production build rate at that time, and does not address how it adequately captures manufacturing process variability of multiple shifts/days.
2. In the Addendum for the (b)(4), the Protocol indicates acceptance criteria based on a sample size of (b)(4) (b)(4) however, according to the deviations listed within the report, two tests run during the validation were accepted based on reduced sample sizes. Neither the protocol nor the Process Validation procedure (GSOP7.4.001, Rev. C, dated 06/13/2013) address applying statistical methodology to

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justify omitting failed results or units that were determined to be unfit for testing.

3. Three additional pieces of routine processing equipment (b)(4) (b)(4) were set up for operation on the (b) (4) (b)(4) with no performance qualification data.

C. Validation of the (b) (4) (b)(4) according to the Process Performance Qualification, Protocol and Report No. 41845, Add. 1, dated 3/13/2014, was found to be inadequate due to the following:

1. A lot size of (b)(4) (b) (4) units is not representative of a routine lot at the production build rate at that time, and does not address how it adequately captures manufacturing process variability of multiple shifts/days.
2. In the Addendum for the (b) (4), the Protocol indicates acceptance criteria based on a sample size of (b)(4) (b)(4); however, according to the deviations listed within the report, two tests run during the validation were accepted based on reduced sample sizes. Neither the protocol nor the firm's Process Validation procedure (GSOP7.4.001, Rev. C, dated 06/13/2013) address applying statistical methodology to justify omitting failed results or units that were determined to be unfit for testing.

D. Validation of the BAV Balloon Catheter line (for use with both the RetroFlex3 and the (b) (4) according to the Process Performance Qualification, Protocol and Report No. 27587, dated 12/20/2011, and Report No. 27587, Addendum 1, dated 6/14/2012, were similarly found to be inadequate due to the following:

1. A lot size of (b)(4) is not representative of a routine lot at the production build rate at that time, and does not address how it adequately captures manufacturing process variability of multiple shifts/days.

E. Your firm has yet to validate manufacturing process for all models of Femoral Cannulae (intended for venous drainage during cardiac surgery), to ensure the integrity of the cannulae. For example:

1. (b)(4) of the femoral cannulae is conducted per (b)(4) (Document #70648, Revision F, dated 07/10/12). Your firm utilizes (b)(4) (Equipment #s ERM000245, 000243, and 003627) for (b)(4) (b) tubing to wire reinforced tubing. However, your firm has yet to establish operating parameters for the (b)(4) and operators are allowed to change the temperature for an unspecified number of times. Furthermore, procedure #70648 shows your firm relies solely on operators conducting visual inspection (per Section 8.8) to identify weak bonds. Additional (b)(4) inspection is done (b)(4) (b)(4) but your firm has yet to establish a procedure for this additional (b)(4) inspection.
2. Procedure #70665 ((b)(4) Process, Revision E, dated 06/24/13) outlines the (b)(4) process setup and operation to properly (b)(4) Your firm utilizes (b)(4) machines (Equipment #s ERM000240, and 000244) for this process. However, no records were provided to demonstrate your firm has established operational parameters for the (b)(4) machines. Furthermore, procedure #70665 shows your firm allows operators to increase or decrease the (b)(4) and the (b)(4) to produce acceptable products. The procedure specifically states: (b)(4)

(b)(4) (b)(4) For example, the temperature can be adjusted anywhere between (b)(4) (b)(4) The procedure also shows your operators are allowed to repeat the process (b)(4) (b)(4) "as necessary".

F. Your completed validation of your QuickDraw product/performance validation was inadequate in that a normal production lot is (b)(4) for the QD25 and (b)(4) for the QD22 and your validation lot size was (b)(4) for each of the models (QD22&25). Furthermore your validation protocol does not dictate the size of the lot to be validated.

G. The Packaging Sealing Operation Qualification (#30126, Revision C, dated 10/18/13) was executed to qualify your (b)(4) used to package various finished Cardiac Surgery Systems devices (e.g., venous and arterial cannulae, and catheters). The sealers use (b)(4) to seal the pouches; however, the OQ/PQ #30126 did not establish an acceptable range for (b)(4)

This is a repeat observation from the previous inspection dated 01/22/13 - 02/22/13.

OBSERVATION 2

Procedures for corrective and preventive action have not been adequately established.

Specifically,

A. CAPA #CSS-GEN-000055 (opened on 10/22/12 and closed on 01/10/14) was initiated to address hair particulates found in-house (through the nonconformance process) after the packaging process. Your firm implemented several corrective actions aimed at reducing the amount of particulate on product manufactured by your Cardiac Surgery Systems business unit and also implemented (on 05/13/13) a (b)(4) process; however, this (b)(4) method was not validated for products manufactured by your Cardiac Surgery Systems' products. The Summary of Effectiveness states: "...In review of NCR's [sic] for hair in the pouch with product since 05/13/13 from all manufacturing lines in CSS, there have been four total" (referring to Nonconformances # PRD-0022779, PRD-0022820, PRD-0022898, and PRD-0023296, dated 08/07/13, 08/15/13, 08/28/13, and 10/21/13, respectively). However, the actual number of NCRs for any type of particle (not just hairs), May – October 2013, is actually 46 (see table below).

CSS Particulate NCRs (as of 1-2-2014)

March 2013	4	August 2013	14
April 2013	0	September 2013	6
May 2013	**0**	October 2013	12

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June 2013	1	November 2013	8
July 2013	4	December 2013	1

Your firm concluded that the more stringent inspection criteria resulted "in particulate (including hair) being detected at a much higher rate" and that review of NCRs opened for any form of unacceptable particulate (not just hair) in the CSS cleanroom shows a marked improvement and downward occurrence trend". However, review of the charts included in the Summary of Effectiveness (see table above) shows the number of NCRs for five consecutive months (July, August, September, October, and November) at the same or higher levels than the number of NCRs initiated prior to implementation of corrective actions via CAPA #CSS-GEN-000055 (May 2013).

During the inspection your firm added an "Addendum to Final Closure – Additional Effectiveness Statements" (dated 03/26/14) which states: "The second measure of effectiveness of CAPA-55 is the reduction of the occurrence of external customer complaints due to particulate in our pouched product" and presented a trend chart (excerpt below) showing the number of customer complaints received May 2013 to March 2014 and summarizing "the changes implemented through CAPA-55 were effective in reducing the risk of product with unacceptable levels of particulate being shipped out of the CSS clean room and out of the Draper site".

CSS External Customer Particulate Complaints (as of 3-26-14)

May 2013	1	November 2013	0
June 2013	1	December 2013	1
July 2013	0	January 2014	0
August 2013	2	February 2014	0
September 2013	0	March 2014	0
October 2013	0		

However, review of your complaint database revealed your firm actually received 218 customer complaints (involving 11 out of 20 product families manufactured in the CSS area) for issues related to particulate found on or in the finished devices (complaints dated between May 2013 and March 2014). Seventeen of the 213 complaints (e.g., Complaints # 2014-01270-1, 2014-01225-1, 2014-01075-1, dated 2/6/2014, 2/5/2014, and 1/31/2014, respectively) resulted in Medical Device Reports (MDRs) submitted to the FDA.

Your firm confirmed the presence of particulate upon evaluation of returned products on at least 71 devices; 65 of the Evaluation Summaries show your firm evaluated the returned products using the same (b)(4) (b)(4) and the particulates were found "in less than 30 seconds" (e.g., Complaints # 2014-01270-1, 2014-01225-1, 2014-01075-1, and 2014-00771-1 dated 02/06/14, 02/05/14, 01/31/14, and 01/24/14, respectively).

Furthermore, your firm failed to address a total of 1,561 products (from six different product families) reported to your firm for particulates found in the pouches (e.g., fiber, hair, plastic) which your firm did not document in your

complaint database (see Observation #4A). Your firm also failed to address a total of 1,591 finished devices that were scrapped during manufacturing for particulate issues.

Lastly, your firm initiated another CAPA (#CSS-GEN-0000077, dated 07/24/13) "to address particulate control holistically"; however, the Problem Description section shows the CAPA was initiated to address only four nonconformance reports (PRD #s 0022661, 0020613, 0020842, and 0021027, dated 07/24/13, 07/23/12, 08/28/12, and 10/02/12, respectively), which is not representative of the scope and magnitude of the problem. The CAPA shows you have identified "Proposed" corrective actions, but the investigation section is incomplete in that it does not document how the investigation was conducted or what areas have been evaluated. Your firm has yet to implement effective corrective actions to address this systemic issue of particulates on finished products.

B. Between 02/01/13 and 02/27/14, your firm has received a total of 93 complaints for the IntraClude Aorta Occlusion catheter. Evaluation of returned products revealed that 35 out of 58 products returned (59%) were found to have kinks on the catheter shaft; 10 of the 35 complaints were marked "Occlusion Difficulty" (e.g., Complaints #2013-09537-1, 2013-06029-1, 2013-05854-1, dated 11/4/2013, 7/13/2013, and 7/8/2013, respectively). The risk analysis for the IntraClude (Application FMEA for IntraClude Device, Document #25451, dated 01/15/14) includes:

- Inadequate infusion of cardioplegia could result in a potential harm of cardiac failure if the physician fails to recognize kinking of the catheter ((b)(4)
- Catheter kinks could cause reduction in cardioplegia flow, improper root pressure measurements, and/or balloon inflation difficulty, with a potential harm including delay in cardiac arrest ((b)(4)).

Furthermore, two of the complaints associated with products found with kinks (Complaints #2013-07569-1, and 2013-08225-1, dated 08/30/13, and 09/24/13, respectively) reported patient deaths.
A CSS Clinical Technical Summary for Aortic Occlusion (Document #43269, dated 12/04/13) was written "to provide a rationale for performing a limited complaint investigation and to support complaint closure...applicable to all Complaints involving aortic occlusion difficulties using the IntraClude...". However, this Technical Summary does not address the issue with kinks. Your firm failed to conduct an investigation and implement corrective actions as needed to address the reported kinks of the IntraClude catheters.

C. Your firm performs corrective actions in the Product Risk Assessment (PRA) system, the Nonconformance (NCR) system and the Equipment/Instrument Calibration (OOT) system; the corrective actions taken in these systems do not include conducting verifications of effectiveness to the specific correction to ensure the problem was resolved, reoccurrence was prevented, and the action did not negatively affect the finished device.

Your procedures for Non-Conformance Processing (GSOP8.4.001, Rev. G, Issued 04/02/2012, and Rev. H, Issued 09/13/2012), Product Risk Assessment (GSOP5.1.002, Rev. H, Issued 03/22/2013), Equipment Calibration and

Preventative Maintenance Management, Draper (Doc. # 70777, Rev. D, Issued 09/13/2012, and Rev. E, Issued 11/26/2013), and (b)(4) Out of Tolerance Process (Doc. # 80508, Rev. B, Issued 06/29/2010, and Rev. C, Issued 09/19/2013) do not include instructions for effectiveness checks of corrective actions taken within the individual reports.

For the Cardiac Surgery Systems:

There were no effectiveness checks documented for the following four out of 17 NCRs reviewed:

- NCR-0006032
- NCR-0008218
- NCR-0010266
- NCR-0010379

Nor was there an effectiveness check documented for the following one of 13 OOT reports reviewed:

- OOT0170

For the Transcatheter Heart Valve systems:

There were no effectiveness checks documented for the following fourteen out of seventeen NCRs (PRDs) reviewed (see Observation 6):

- PRD-0022443
- PRD-0024065
- PRD-0023120
- PRD-0022948
- PRD-0022527
- PRD-0023112
- PRD-0022287
- PRD-0023654
- PRD-0023687
- PRD-0023754
- PRD-0023655
- PRD-0022804
- PRD-0021705
- PRD-0024161

There were no effectiveness checks documented for the following six out of nine PRAs reviewed:

- 765
- 778
- 630
- 826
- 822
- 777

There were no effectiveness checks documented for the following two out of eleven OOT reports reviewed:

- OOT0114
- OOT0156

D. Your firm initiated nonconformance #PRD-0022049 (dated 04/18/13) for a lot of (b) (4) Femtrak Venous Femoral cannulae (Lot #59463340) which failed in-process testing due to wire exposed ("not fully encapsulated") in the wire-reinforced tubing received from a vendor (supplier part (b)(4) . As part of the investigation, your firm evaluated supplier parts previously received and inspected (found in the raw material warehouse) and found (b) subassemblies (b)(4) (b)(4) with "excessive bubbles in the wire reinforced tubing". According to the investigation "if enough bubbles were grouped together, the wire within the tubing could be exposed" (documented via nonconformance #PRD-0022053, dated 04/18/13). Supplier Corrective Action Request (SCAR) #000216 (dated 04/24/13) states:

> *...excess bubbles is a typical defect the supplier observes during the manufacturing process. They typically have a high scrap rate for this failure mode, however, they inadvertently* (b)(4) *and these typical scrap parts were forwarded to Edwards.*

These 13 defective lots of wire-reinforced tubing (e.g., Lots #s (b)(4)) were marked as acceptable during incoming inspection. Your firm failed to investigate how/why the (b)(4) defective supplier parts were not identified during incoming inspection.

The investigation conducted through SCAR #000216 shows the nonconformance was due to inadequate production process control because the supplier had not validated the manufacturing process for the wire-reinforced tubing. Your firm has received a total of (b) lots of wire-reinforced tubing from this supplier (since May 2009), which were used in the manufacture of (b)(4) lots of finished devices released for distribution. The risk analysis for the femoral cannulae (Design FMEA for Peripheral Product Family, FMEA #5808, Revisions L, M and N, dated 09/06/13, 01/21/14, and 03/06/14) shows the Severity of potential hazard "[w]ire-reinforcement coil protrudes out of cannula body as "Major" for potential harms: tissue damage and hemolysis. However, your firm failed to assess the risk to patients from potentially defective finished lots of femoral cannulae already distributed and in the field, considering that your firm only found (b)(4) parts in the raw material warehouse, out of a total of (b)(4) parts received, inspected, and released for manufacturing.

Furthermore, it was noted your firm had not adequately qualified the supplier of the wire-reinforce tubing (see Observation #10).

E. Your firm initiated nonconformance #PRD-0020896 (09/14/12) for a (b)(4) introducer (vendor Lo (b)(4) that broke during incoming inspection. The severity for this nonconformance was identified as major because "a failure mode where the dilator breaks within the cannula can potentially cause venous side embolism". This issue was confirmed to be a supplier issue and your firm returned the affected products to the vendor "for their

evaluation"; however, your firm did not follow up with the supplier to ensure corrective actions were implemented as needed.

Your firm subsequently initiated nonconformance #PRD-0021403 (01/08/13) for two finished lots (manufactured with (b)(4) introducer vendor Lot (b)(4) which failed functional testing due to a (b)(4) (b)(4) (Femtrak Venous Cannulae, Lot #s 59381545 and 59400069). Your firm initiated and submitted a Supplier Corrective Action Request (SCAR # 5-130219-1, dated 02/19/13) to the vendor, but failed to investigate why these nonconformances were not identified during incoming inspection of supplier lot (b)(4) SCAR #5-130219-1 shows supplier corrective actions were implemented 03/08/13 but your firm failed to conduct a verification of effectiveness to ensure the actions taken by the supplier were adequate.

During the inspection, your firm completed a "Supplier Corrective Action Request Control Phase", dated 03/25/14, and concluded the SCAR was not effective because additional supplier lots had "failed at Quality Receiving Inspection" and issued yet another SCAR to the supplier (SCAR #000374, dated 03/25/14). The additional failures referenced above were documented via nonconformances # PRD-0022768 (dated 08/05/13) and PRD-0023959 (dated 01/13/14):

> PRD-0022768 shows this failure mode again as a severity of "major", but your firm did not further investigate considering this failure shows the corrective actions implemented by the firm five months earlier were not effective.
> PRD-0023959 shows the affected finished device Lot# 59651877 was manufactured with (b) supplier lots of the introducer (b)(4) ; your firm again failed to investigate why these nonconformances were not identified during incoming inspection.

Your firm identified three additional finished lots of Femtrak Venous Cannulae (Lots #59675074, 59615027, and 59651763, all manufactured with defective supplier lot #s (b)(4) still under your control and held them for investigation (via Product Risk Assessment #PRA0835, dated 02/13/14). Your firm determined those three lots were acceptable because they passed post-sterile testing, and released the three lots for distribution (a total of (b) products). Your firm failed to consider that, based on the aforementioned failures noted, the testing done upon receipt of the raw materials may not necessarily identify all defective products, and also that your firm does not inspect (b)(4) of the products during post-sterile testing. Therefore, there is no assurance that all products released for distribution (as part of these three lots) were conforming.

F. Your firm utilizes the (b)(4) to form the soft tip of the EndoVent Pulmonary catheters (in accordance with the (b)(4) , Document #70751, dated 03/17/11). The risk analysis for the EndoVent (Process FMEA for EndoVent (EV) Pulmonary Catheter, Document #24646, dated 01/29/14) shows the risk of '(b)(4) " as Severity of (b) (4) for potential venous / pulmonary embolism.

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The (b)(4) these (b)(4) were found out-of-tolerance on 02/13/14 (OOT Reports #0202 and #0203) by at least (b)(4) The Root Cause for both failures was documented as (b)(4) (b)(4) The (b)(4) parameter established in procedure #70751 for the (b)(4) process is (b)(4) With the (b)(4) applied the devices were actually processed at (b)(4) Your firm determined the offsets were applied "sometime between the March 2013 and the calibration that was performed in February 2014". During that time period, your firm manufactured (b) lots of EndoVent (a total of (b)(4) devices); all (b) lots were released for distribution. Your firm failed to: 1) conduct a thorough investigation to determine if any other temperature controllers at your firm may also be affected by this personnel practice, and 2) implement corrective action to ensure your firm's personnel do not change equipment temperature offsets.

This is a repeat observation from the previous inspection dated 01/22/13 - 02/22/13.

OBSERVATION 3

Production processes were not monitored to ensure that a device conforms to its specifications.

Specifically, your process monitoring is inadequate in that you have no objective evidence that your devices are manufactured according to your specified and approved processing parameters, for example: (b) (4) line, Balloon Aortic Valvuloplasty (BAV) line, Quickdraw line, Arterial line and specifically the (b)(4) process in your annuloplasty ring manufacturing line:

a)

(b)(4)

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(b)(4)

h)

(b)(4)

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(b)(4)

(b)(4)

(b)(4)

(b) (4)

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OBSERVATION 4

Procedures for receiving, reviewing, and evaluating complaints by a formally designated unit have not been adequately established.

Specifically,

A. From 01/07/2013 to 12/27/2013 you received information from Japan reporting 2,116 incidences documenting rejections of your devices which meet the definition of a complaint as "any electronic communication that alleges deficiencies related to the quality, safety and performance of a device after it is released for distribution" and you did not document any of the 2,116 reported device rejections as complaints. For example of the 2,116 reported rejections there were at total of 1,561 device units documented as having hair, fiber, particles, or plastic in your sterile device pouches to include the following devices: aortic, beating heart, blood management, cardioplegia and venous devices. Furthermore you have no documentation of evaluating these 2,116 rejected device incidences to determine if any are Medical Device Reportable Events.

This is a repeat observation from the previous inspection dated 01/22/13 - 02/22/13.

B. Documentation of the investigation conducted for the following five complaints was incomplete in that the complaints did not include evidence to demonstrate the stated activities were conducted:

- Complaint #2013-02986-1 (initiated 04/10/13 for a defective StraightShot cannula) states "[t]he supplier was contacted to investigate the defect and assess the need for corrective"; however, no evidence was maintained to demonstrate whether the supplier conducted an investigation and implemented corrective actions as needed.
- Complaint #2013-07794-1 (initiated 09/09/13 for a jagged EndoReturn cannula) states "[a] good faith effort was made during the engineering evaluation to evaluate the (b)(4) currently being used on the manufacturing floor at Edwards"; however, no evidence was maintained to demonstrate this evaluation of manufacturing processes was conducted (e.g., who conducted the review, when it was conducted, and what was evaluated).
- Complaint #2013-02378-1 (initiated 03/20/13 for a damaged Arterial Cannula found damaged inside the package) states "Edwards has investigated the way that the these [sic] products are stored and handled by Edwards employees after the final inspection has occurred. There were no places identified where the damage could be caused at"; however, no evidence was maintained to demonstrate this evaluation of manufacturing processes was conducted (e.g., when was the review conducted, what specific areas/procedures were evaluated).
- Complaint #2013-06031-1 (initiated 07/14/13 for an OptiSite (OPTI) Arterial Cannula found severely damaged out of the packaging) states the Manufacturing Engineer and Quality Engineer conducted "a thorough review of the handling and processing of the OPTI products post this inspection...[t]here were no areas identified that would have caused a compression in the cannula such as the one observed"; however, no evidence was maintained to demonstrate this evaluation of manufacturing processes was conducted (e.g., when was the

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review conducted, what specific areas/procedures were evaluated).

- Complaint #2013-10145-1 was initiated 11/21/13 for an IntraClude device balloon burst while in use in the patient. The user requested the firm to analyze the balloon "to make sure no pieces of the balloon were missing"; however, no evidence was maintained to demonstrate that the returned product was evaluated for missing pieces.

C. Complaints #2013-04901-1 and 2013-05347-1 were both initiated (06/06/13 and 06/21/13, respectively) for "flattened" IntraClude intra-aortic occlusion devices. Investigation of returned products confirmed both of the devices were manufactured with the incorrect component; however, the "Manufacturing Defect. Confirmed" box was not marked.

OBSERVATION 5

Products that do not conform to specifications are not adequately controlled.

Specifically,

A. Your control of nonconformances for components/raw materials used in production is inadequate in that when you have raw materials used in production which fail to meet its intended use you do not identify the failed raw material as a nonconformance nor do you track the amount of raw material failures to determine the extent of the problem. For example I observed 8 out of 8 consecutive failures of a (b)(4) raw material used in production, which is critical in that it is used to create the inner diameter of the arterial cannula. In your nonconformance evaluation, which was opened after I observed the 8 out of 8 failures, your investigation states you "searched the arterial product lines from January 2013 to date which did not result in any other NCRs having had the same issue". Nonconforming raw material failures information is valuable to ensure raw materials used in production to manufacture the finished device meets your design transfer criteria and approval and can repeatedly achieve their intended uses.

B. Your identification of nonconformances is inadequate in that you failed to identify a wrong part being manufactured in your arterial cannula line in a timely manner. You processed (b)(4) ER23B device lot before I went to the production line to observe your in-process verification of the (b)(4) which is applied to manufacture the inner lumen of the arterial cannula used in open heart surgery. The line supervisor explained and conducted your (b)(4) and I observed 8 out of 8 consecutive failures to meet your measurement specification. You then placed the lot on nonconformance investigation.

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NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Paul R. Lunsford, Corporate Vice President and General Manager

FIRM NAME	STREET ADDRESS
Edwards Lifesciences, LLC	12050 Lone Peak Pkwy
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Draper, UT 84020-9414	Medical Device Manufacturer

OBSERVATION 6

Procedures have not been adequately established to control product that does not conform to specified requirements.

Specifically, your firm's procedure Non-Conformance Processing (NCR) - AT and THV (SOP3235, Rev. T, dated 10/30/2013) specifies that all investigations, dispositions, and corrective and preventive actions are complete, appropriate, and documented.

- Seven out of 14 closed nonconformance reports (NCRs) reviewed in relation to Transcatheter Heart Valve (THV) products (Sapien and [redacted] (b) (4) product lines) included no documentation of investigation activities.
  - PRD-0022443, occurrence date 1/27/2014, regarding issues [redacted] (b) (4)
  - PRD-0022948, occurrence date 9/4/2013, regarding leak in [redacted] (b) (4) balloon area
  - PRD-0023112, occurrence date 9/26/2013, regarding multiple failures of [redacted] (b) (4)
  - PRD-0021705, occurrence date 2/18/2013, regarding [redacted] (b) (4) missing [redacted] (b) (4)
  - PRD-0022287, occurrence date 5/23/2013, regarding pin hole leak
  - PRD-0023654, occurrence date 11/26/2013, regarding multiple failures in [redacted] (b) (4)
  - PRD-0023687, occurrence date 12/2/2013, regarding Failed [redacted] (b) (4)
- Fourteen out of the 14 closed nonconformance reports reviewed have no documented verification of effectiveness checks of corrective actions (see Observation 2).

In addition to the inadequate documentation observed within the NCR system, 17 NCRs for Product Verification Testing failures were reviewed. Your THV Product Verification Testing Procedure (SOP6336, Rev. C, dated 10/23/2012) states that "[i]f errors occur during testing that are confirmed to be due to operator or equipment error … the erroneous data point may be excluded and (b)(4) to reflect the lower sample size."

The following are NCRs reviewed that did not indicate confirmed operator or equipment error, but were still accepted on excluded (b)(4)

- PRD-0023120, NCR-0009503, received 9/27/2013, regarding a tear in the eSheath (b)(4)
- PRD-0022948, NCR-0009376, received 9/4/2013, regarding (b)(4) test failure of the [redacted] (b) (4))

Furthermore, the following NCRs failed the Product Verification Testing due to an "Erroneously approved PV [Product Verification] sample"; no further investigation or justification for failure was documented:

- PRD-0022287, NCR-0008727, received 5/31/2013, regarding pin hole leak in a [redacted] (b) (4) balloon
- PRD-0023654, NCR-0010118, received 11/26/2013, regarding two units failed (b)(4) testing [redacted] (b) (4)
- PRD-0023655, NCR-0010369, received 11/26/(b)(4) (b)(4) test [redacted] (b) (4)

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OBSERVATION 7

Procedures for acceptance activities have not been adequately established.

Specifically,

A. Your firm manufactures various cannulae, catheters, adapters and suction devices that are coated with a Duraflo heparin solution consisting of [redacted] (b)(4) Duraflo heparin (b)(4) [redacted] The devices are coated with Duraflo solution (b)(4) [redacted] For example, Femoral Cannulae Part #DIIFEMII018A, Lot # 59680241 (released for distribution on 03/11/14) was coated with Duraflo [redacted] (b)(4) [redacted], following the "Heparin Coating/Fill and Drain/All Solvents" procedure (SOP #70634, Revision E).

The labeling that accompanies this Vent Catheter (Instructions for Use, Part #62123, Revision Y, dated 01/21/14) claims:

> *When used on devices for cardiopulmonary surgery, the Duraflo coating improves the blood compatibility of non-biological surfaces in the extracorporeal circuit...Extracorporeal circuit components with a Duraflo coating are intended for use in cardiopulmonary surgery when a heparin coated blood path is desired.*

Your firm conducted a Design of Experiment in August 2013, and concluded that (b)(4) [redacted] (b)(4) [redacted] Your firm (b)(4) [redacted] on April 15, 2013; however, your firm has yet to validate the test method and has not established an acceptable limit for the (b)(4) [redacted] Furthermore, test results obtained since April 2013 show the (b)(4) [redacted] (b)(4) [redacted] Your firm has yet to determine how this (b)(4) [redacted] (b)(4) [redacted] may affect the amount of (b)(4) [redacted]

Lastly, your firm began testing finished devices (in June 2013) to (b)(4) [redacted] (b)(4) [redacted] however, your firm has yet to establish a valid final acceptance criterion for (b)(4) [redacted] (b)(4) [redacted] Design Requirement Documents (DRD) for Duraflo-coated products (e.g., (b)(4) [redacted], Revision H) shows your firm has established the acceptance criterion for the finished devices as: (b)(4) [redacted] The "Technical Summary - Duraflo (b)(4) [redacted] (Document #40362, Revision A, dated 06/10/13) was written to provide justification for this acceptance criterion. Review of this Technical Summary shows your firm incorrectly selected as acceptance criteria the value listed for the (b)(4) [redacted] instead of the value for the

AMENDMENT 1

(b)(4) . No evidence was provided to demonstrate your firm has evaluated and established a valid acceptance criterion for finished, sterilized, cannulae to support the claims made in the Instructions for Use.

Notwithstanding the fact that your firm has not established a valid acceptance criterion for heparin activity, additional validation activities conducted to demonstrate acceptable levels of heparin activity on finished products were found to be deficient as follows:

- A study conducted t(b)(4) (b)(4) (b)(4)) the study compared (b)(4) samples (b)(4) (b)(4) and (b)(4) ' samples (used as test control samples). Th (b)(4) activity for the (b)(4) were found to be below the detection limit of the test method; subsequently, your firm (b)(4) (b)(4) . Your firm failed to demonstrate that all samples exhibite (b)(4) activity.

This is a repeat observation from the previous inspection dated 01/22/13 - 02/22/13.

B. Your firm receives the IntraClude Intra-Aortic Occlusion devices, (b)(4) , from your contract manufacturer. Upon receipt of these devices, your firm reviews the Process Data provided by the contract manufacturer (per procedure #80528, IntraClude Process Data Receiving Inspection, Revision, D, dated 10/16/13). Review of the process data is documented on the IntraClude Component Pre-Sterile Lot Release Testing Form 80548 (e.g., Pre-Sterile Lot Release Testing for Lot #s (b)(4)). This form shows "Sample Size = (b)(4) however, your firm was not able to provide rationale to demonstrate that reviewing the Process Data for five devices (regardless of lot size) constitutes a valid statistical sample to be able to make an inference about the conformance of the entire lot, and your firm does not conduct any functional testing of these devices.

C. Your firm's procedure QA Receiving Inspection (Document 80022, Rev. BD, Issued 2/17/2014) states that employees are to (b)(4) (b)(4) However, upon review of the most recent incoming lots of critical components for the (b)(4) (b)(4) (b)(4) it was observed that (b) (b)(4) received by your firm were out of tolerance and were not identified as a nonconformance during either the preliminary review, or the supervisory review of the lot. The shipment was of the (b)(4) received 1/15/2014 in a lot of (b)(4) , used in the (b)(4) [redacted]

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OBSERVATION 8

Procedures for product handling have not been adequately established.

Specifically, since February 2013, your firm has identified multiple incidences of products manufactured with incorrect components, affecting all three business units at your firm:

Quality Records initiated for issues related to incorrect componenets	Number of records
Nonconformance Reports	50
Cardiac Surgery Systems customer complaints	8
Transcatheter Heart Valve customer complaints	1
Heart Valve Therapy customer complaints	1
CAPA reports	5
Recalls	3

Your firm has yet to implement systemic corrective actions to prevent the manufacture of finished devices with incorrect components. For example, on 03/18/13, your operators discovered that two lots of Dual Stage Venous Cannulae, Part (b)(4) were assembled using the incorrect cannula bodies (with the incorrect diameters). Your firm retrieved non-conforming product from your finished goods inventory, but 154 non-conforming units were distributed to customers. Your firm attributed this mix-up to inadequate line clearance during manufacturing.

The Product Risk Assessment (#0759, dated 09/13/13) shows that corrective action is needed to address this issue and references CAPA #0000057. Review of CAPA #0000057 revealed this CAPA was initiated on 01/23/13, prior to discovery of this Venous Cannulae mix-up and was initiated for multiple documentation errors on (b)(4) CAPA #0000057 does not address actual product mix ups.

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OBSERVATION 9

Procedures for training and identifying training needs have not been adequately established.

Specifically, your firm's Training Policy (GP6.1, Revision A, Issued 1/4/2010) states as the purpose of the document "This Global Policy establishes Edwards Lifesciences Corporate guidelines for Training to ensure that personnel are trained to adequately perform required job functions." It also states under the Training section of the Policy section of the procedure "Managers shall...evaluate the effectiveness of training or actions taken". On 03/04/2014, measuring errors were observed on the EndoReturn (ERB) line during the (b)(4) step for the (b)(4) product due to the incorrect material being used. The issue was documented through nonconformance report # PRD-0024442, dated 03/06/13, which shows the line operator "did not flag the incorrect part number". The training records for the line operator were reviewed. The records indicate training was received on Document number (b)(4) which is the procedure followed for the (b)(4) step where the errors were observed. The training delivery type was "Read and Review" and the Completion Status was marked as "Successful". However, there is no documentation to demonstrate the effectiveness of training has been evaluated.

OBSERVATION 10

Potential suppliers were not evaluated based on their ability to meet specified requirements.

Specifically, in April of 2013, your firm identified multiple lots of wire-reinforced tubing received from a vendor (Supplier Part #(b)(4) with excessive bubbles which could cause the wire within the tubing to be exposed (see Observation #2D). The investigation conducted (through Supplier Corrective Action Request #000216, dated 04/24/13) shows the nonconformance was due to inadequate production process control because the supplier had not validated the manufacturing process for the wire-reinforced tubing. However, review of this supplier's most recent qualification records (dated July 2013) show your firm did not ensure the supplier's manufacturing processes were validated. Furthermore, SCAR #000216 also shows the supplier inadvertently forwarded scrap product to your firm; however, your firm's assessment of the supplier's control of nonconforming products was found to be acceptable.

Furthermore, the risk level determination for this supplier is incorrect in that it is not consistent with the risk of the material provided by the supplier. The current risk analysis for the femoral cannulae (Design FMEA for Peripheral Product Family, FMEA #5808, Revision N, dated 03/06/14) shows the Severity of potential hazard "[w]ire-reinforcement coil protrudes out of cannula body" as (b) (4) for potential harms: tissue damage and hemolysis. However, the current Risk Level Determination for this supplier shows a response of "No" to the question: "Can the component or service's failure reasonably be expected to cause a user/patient unsafe condition...?"; consequently, this supplier was assigned a lower risk level (Risk Level II).

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OBSERVATION 11

Procedures for the control of storage areas and stock rooms have not been adequately established.

Specifically, your handling of components used to supply the arterial line production is not adequate to prevent mix-ups. For example a wrong part number was selected and used to manufacture 59 arterial devices. Your storage area for components for the arterial line is located on the quickdraw line and the (b)(4) [redacted] (b) (4) is removed from the quickdraw supply line and brought, unidentified, to the arterial line. The components should be identified through all areas of production to include from storage to production use.

OBSERVATION 12

Certain measuring equipment is not suitable for its intended purposes.

Specifically, your selection of the(b)(4) on the arterial line for (b)(4) (b)(4) is inadequate for the intended use. The (b)(4) (b)(4) . The acceptance criterion for this (b)(4) I observed the operator measure(b)(4) (b)(4) (b)(4) . This allows for both(b)(4) (b)(4)

OBSERVATION 13

Process control procedures that describe any process controls necessary to ensure conformance to specifications have not been adequately established.

Specifically, your production work instructions are not adequate to control th(b)(4) (b)(4)

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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Observation Annotations

Observation 1:	Under consideration.	Observation 2:	Blank
Observation 3:	Reported corrected, not verified.	Observation 4:	Blank
Observation 5:	Under consideration.	Observation 6:	Under consideration.
Observation 7:	Blank	Observation 8:	Blank
Observation 9:	Blank	Observation 10:	Blank
Observation 11:	Blank	Observation 12:	Reported corrected, not verified.
Observation 13:	Under consideration.		

*** DATES OF INSPECTION:**
03/03/2014(Mon), 03/04/2014(Tue), 03/05/2014(Wed), 03/06/2014(Thu), 03/07/2014(Fri), 03/10/2014(Mon), 03/11/2014(Tue), 03/12/2014(Wed), 03/13/2014(Thu), 03/14/2014(Fri), 03/17/2014(Mon), 03/18/2014(Tue), 03/19/2014(Wed), 03/20/2014(Thu), 04/02/2014(Wed), 04/03/2014(Thu), 04/04/2014(Fri), 04/09/2014(Wed), 04/10/2014(Thu), 04/11/2014(Fri)

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