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HAND DELIVERY

November 7, 2012

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Alonza E. Cruse
District Director
U.S. Food and Drug Administration
Los Angeles District Office
19701 Fairchild
Irvine, CA 92612

Re: St. Jude Medical IESD - Sylmar Response to October 17, 2012 (FDA-483) Inspectional Observations

Dear Mr. Cruse,

St. Jude Medical Implantable Electronic Systems Division (IESD[1]) is providing this response to the FDA Form 483 inspectional observations issued to the Sylmar, California facility by U.S. Food and Drug Administration investigator Commander Sean Creighton, Consumer Safety Officer.

We recognize and take seriously the observations in the FDA-483, and are committed to taking all actions necessary to address them as part of our effort to continuously strengthen our quality system.

We provide here our initial response collated in three binders. In Appendix 1, "Response to FDA-483" we describe our completed and planned actions to the listed observations. To facilitate review, the FDA-483 observations are denoted by italicized font. Appendix 2 lists associated objective evidence attached to the response. We plan to submit our next update to FDA on or before December 7, 2012 and then each month thereafter, until the time when quarterly updates may become more appropriate.

To ensure our response to the FDA inspection is both responsive to the specific issue noted and addresses the processes and people we deploy to produce products and services, we are embarking on the following activities beyond addressing specific observations noted in the FDA-483:

1) Provide additional learning activities to ensure enhancement of our staff's knowledge regarding the quality system elements.

2) Identify and implement improvements to ensure robust processes for the Design and Development of our products and processes.

3) Identify and implement improvements to our CAPA and Risk Management processes to enhance monitoring and control of our overall quality system.

[1] Implantable Electronic Systems Division "IESD" was formally known as the Cardiac Rhythm Management Division or "CRMD".

We consider the information contained in this letter and its attachments as confidential and proprietary commercial information and not subject to disclosure under the Freedom of Information Act. Accordingly, we have designated this letter and its attachments as confidential and proprietary and exempt from disclosure under FOIA exemption (b)(4).

Should you have any questions, please do not hesitate to contact me.

Respectfully,

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Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 1

Process Validation

Your process validation protocol covering (b) (4) different machines performing (b) (4) of (b) (4) and (b) (4) was inadequate in that:

a. the protocol covers (b) (4) machines installed from 1999-2011 and does not evaluate the potential differences in the machines.

Response:

Background:	Examples of the validation documentation we had in place at the time of the inspection for Model (b) (4) and Model (b) (4) have been provided (See Attachments 1.1 and 1.2, respectively). We maintain validation documentation for each of the (b) (4) workstations. In addition to the (b) (4) process validations and (b) (4) inspection we also perform process monitoring of each (b) (4) process used in Leads Manufacturing. Per the Quality Control Requirement section in each (b) (4) schedule, a sample of each weld assembly per its specifi (b) (4) chedule is (b) (4) (b) (4) to failure at the (b) (4) of each production shift. The results are recorded on (b) (4) Test Record Sheet Form 9190889 Rev. AD. A copy of the form is provided (See Attachment 1.3). Should a failure be encountered, MO-0105, Section 7.8, defines the steps that should be followed. (See Attachment 1.4, excerpt of complete document)
Completed Actions:	1) There are (b) (4) workstations used across all lead families ((b) (4) (b) (4), of which (b) workstations are (b) (4) and (b) are (b) (4) We identified the differences between the (b) (4) workstation models and evaluated their criticality to affect the (b) (4) process. The differences were reviewed and determined to be non-critical to the (b) (4) process. See "(b) (4) Workstation Assessment". (Attachment 1.5) 2) The procedure, "Process Validation" SOP4.2.1, Rev. U, was revised to include improved documentation per Section 6.1.6.1 to list factors critical to process validation. (See Attachment 1.6). a. Note: The validation activities will be conducted on an individual equipment and process basis. This will include assessing, as part of the validation planning activity, the critical process variables for the process undergoing validation to assure the appropriate equipment qualification and process qualifications are conducted. This is intended to prevent overlooking potential equipment and process variables that may be unique and critical to the overall process validation. 3) Training of the Quality personnel who conduct process validation activities was completed on November 2, 2012. (See Attachment 1.7).

Planned Actions:	Remediation activities include the following: • By November 30, 2012 we will conduct a gap analysis between the updated procedure "Process Validation" SOP4.2.1, Rev. U and the validation documentation associated with the equipment for the (b) (4) machines to identify gaps. • We will plan and take action to close any identified gaps. If the risk analysis of any of the gaps results in an unacceptable condition, the equipment will be taken out of service and a further determination of necessary product remedial actions will be completed.

b. you create multiple different holders to hold the leads during (b) (4) *and did not specify how you would install and verify the holders as part of the validation.*

Response:

Completed Actions:	1) A review of the qualification of all the holders supporting leads production was conducted. We confirmed the holders were approved for use by using a first article inspection. (See Attachment 1.8 "(b) (4) Holder FAI Summary" and an example of one FAI report) 2) The (b) (4) including instructions for installing holders and training for the installation of holders, was completed. See "Training of Operations Staff for Installation of Holders" (Attachment 1.9). 3) A memorandum "Detectability of Holder Installation Issues" discusses how holder installation errors and tool wear are detectable via our (b) verification of the (b) (4) (See Attachment 1.10) 4) The procedure, "Process Validation" SOP4.2.1, Rev. U, was revised to include improved documentation of how tools (e.g., holders) are addressed as part of the validation activities in Section 6.1.9. (See Attachment 1.6) 5) Additional Training of the Quality personnel who conduct process validation activities was completed on November 2, 2012. (See Attachment 1.7)
Planned Actions:	Remediation activities include the following: • By December 15, 2012, we will conduct a gap analysis between the updated procedure "Process Validation" SOP4.2.1, Rev. U and the documentation for the tools (e.g., holders) associated with the validation documentation of the (b) (4) schedules. • We will plan and take action to address any identified gaps. • If a gap were to be identified, a risk analysis shall be conducted to determine if further process or product remedial actions are required.

c. Your statistical rationale for your sample size for your "parametric method" sample size selection is unclear

d. you specify 95% of the population shall exceed specifications as your predetermined acceptance criteria.

Response:

Background:	These two observational issues are associated with the clarity of the use and positioning of the word "minimum" rather than the statistical sampling and resulting analysis used within the record "*Generic Plan for the Validation of* (b) (4) *(PVP107-90)*", Rev. 05. Within the aforementioned record, the following is stated: *1.* To address 1c: Section 8.1, Sample Preparation – Parametric Method (analysis of variable data), states that a minimum of (b) samples shall be (b) (4) The Acceptance Criteria within the same record in Section 8.1, states the following: *"A statistical analysis shall be performed that demonstrates that a minimum of 95% confidence that 95% of the population shall exceed specification."* *2.* To address 1d: In Section 8.0, Validation Protocol, Subsection 8.2, Sample Preparation – Non Parametric Method, Acceptance Criteria, the following is stated: *"The* (b) (4) *results shall provide 95% confidence that 95% of the production population shall have* (b) (4) *that exceed the required minimum in the applicable* (b) *schedule.*
Planned Actions:	The following clarifications will be made: **(1c)** To improve clarity of the statistical rationale used, a specific Sample Size section will be included in validation planning to state the following: *"The validation results shall provide a minimum of 95% confidence level that a minimum of 95% reliability level shall meet or exceed specifications",* and **(1d)** to clarify the acceptance criteria in the Acceptance Criteria section to: *"All of the* (b) (4) *samples shall meet or exceed the specification and that the calculated lower tolerance limit based on the statistical rationale for the chosen sample size meets or exceeds the specification."* The above clarifications will be incorporated as part of planned activities identified in Observation 1b.

e. in your process validation of (b) (4) *I was unable to verify the results of your 3 cross-sectioned samples*

Response:

Background:	In PVR-107-90-123, '(b) (4) using (b) (4) (b) (4) the three cross-section sample pictures were not physically retained with the report. It is important to highlight, however, that the report did summarize and document the acceptable analysis of results from the three pictures. The cross-section sample picture analysis record was retrieved and provided during the FDA inspection, although the picture analysis record did not specifically reference (b) (4)
Completed Actions:	Since the inspection, we have revalidated the process documented in (b) (4) (b) (4) using (b) (4) (b) (4) The three cross-section analysis reports are retained in the appendix of the report. (See Attachment 1.11) The procedure, "Process Validation" SOP4.2.1, Rev. U, was revised to clarify attachments or supporting data shall be retained with the process validation report in Section 6.3. (See Attachment 1.6) Training of Quality personnel performing process validation was completed on November 2, 2012. (See Attachment 1.7)

f. you do not measure the pressure and flow of the (b) (4) *that is delivered to your* (b) (4) *at the end points of use, which specifies a maximum of* (b) *and a* (b) (4) *per* (b) (4) *recommended consumption flow*

Response:

Background:	The (b) (4) is used as a (b) (4) of the (b) area during (b) (4) to prevent discoloration of the (b) Discoloration is detectable when the (b) (4) is (b) (4) inspected using (b) (4) Each (b) (4) schedule requires the operator to conduct (b) (4) inspection for (b) discoloration. See "Technical Memo Describing the Correlation of (b) (4) Flow Rate to (b) Discoloration" (Attachment 1.12).
Planned Actions:	We will install pressure and flow meters for the (b) (4) on the (b) (4) machines. Documentation of the installation activities shall include assuring the satisfactory installation, establishing appropriate preventive maintenance and calibration activities, and establishing the necessary monitoring and control procedural instructions have been defined for the utility measurements. We are waiting for delivery of these instruments due to the lead time. With the next update on December 7, 2012, we will provide a completion date for installation and subsequent training for operations staff regarding use and monitoring of instruments.

Observation 2

Design Verification:

A. Your design verification activities were inadequate in that you failed to validate 3 test methods you created in-house to verify your design inputs during your design verification, for example:

Response:

Completed Actions:	We have drafted the procedure "Test Method Validation" SOP 60046416, Rev. A for test method validation. (See Attachment 2.1) A preliminary review of the three test methods has been completed by engineers who will be performing the test method validation and each has concluded that the methods are able to be validated. A memo on the ability to validate the three tests has been completed. (See Attachment 2.2)
Planned Actions:	Remediation of the test method validations will be completed as follows: 1) Procedure release and training of users (Expected completion: November 30, 2012) 2) Develop inventory of test methods used during development of Durata (Expected completion: November 30, 2012) 3) Determine if each test method requires validation per revised procedure (Expected completion: November 30, 2012) 4) Prioritization of test methods requiring validation will be based upon the following: (Expected completion: December 14, 2012) • Determine the effect the design input tested by the method under consideration, has on the quality, functionality and extent of use of the product. • Conduct test method validation* • Should a test method validation fail, an evaluation will occur to determine the cause and assess if it has an impact on design verification, including assessment of any retesting to be performed. Additionally the cause of the validation failure will be investigated, corrected, and then validation will be attempted again. This process will be followed until test method validation is successful. 5) A plan will be developed to address Test Method validations for other product lines. (Expected completion: November 30, 2012) *Details related to the validation activities associated with the three specific test methods are included in sections a, b, and c.

Appendix -1
Response to FDA-483 dated November 7, 2012

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a. Durata input specified for verification testing: (b) (4) *of the* (b) (4) *tip shall be* (b) (4) *Non-validated test method:* (b) (4)

Response:

Background:	This test method determines (b) (4) by measuring the (b) (4) of the (b) (4) of the lead. The test mimics compressive loads due to (b) (4) contraction and uses the (b) (4) and tip surface area to calculate tip (b) (4) This method defines the process for test equipment and setup, test sample preparation, run conditions and acceptance criteria.
Completed Actions:	The (b) (4) Tips Test Method is defined in Test Method ES1178, Rev. G (See Attachment 2.3) and was approved for use March 3, 2012. As part of our review of the aforementioned test method, we have determined that validation is required per our newly drafted test procedure "Test Method Validation" SOP 60046416 Rev. A.
Planned Actions:	1) Validation of the test method has been initiated. (Expected completion: February 28, 2013) 2) Should a test method validation fail, an evaluation will occur to determine the cause and assess if it has an impact on design verification, including assessment of any retesting to be performed. Additionally the cause of the validation failure will be investigated, corrected, and then validation will be attempted again. This process will be followed until test method validation is successful.

b. Durata design input specified for verification testing: (b) (4) *shall not change by more than* (b) *%. Non-validated test method:* (b) (4) *test.*

b(i). You are currently conducting design verification testing using the (b) (4) *test method testing* (b) (4) *leads (model number#* (b) (4) *and IDE#* (b) (4) (b) (4) *(model #* (b) *and model #* (b) *.*

Response:

Background	This test method determines (b) (4) fatigue performance up to a predetermined number of cycles. The test mimics (b) and (b) (4) motion at the (b) (4) of the lead while running at an accelerated speed. This method defines the process for equipment, setup, maintenance, sample preparation, duration and data logging.
Completed Actions:	To address these two observations (2Ab and 2Ab(i)), the (b) (4) (b) (4) Test Method is defined in Test Method 60028637, Rev. D, (See Attachment 2.4) and was approved for use on June 26, 2012. As part of our review of the test method, we have determined that validation is required per our newly drafted test procedure.
Planned Actions:	1) Validation of the test method has been initiated. (Expected completion: May 31, 2013) 2) Should a test method validation fail, an evaluation will occur to determine the cause and assess if it has an impact on design verification, including assessment of any

	retesting to be performed. Additionally the cause of the validation failure will be investigated, corrected, and then validation will be attempted again. This process will be followed until test method validation is successful.

c. Durata design input specified for verification testing: (2 items tested) in (b) (4) *condition shall be maximum* (b) (4) *and in* (b) *condition minimum* (b) (4) *Non-validated test method:* (b) (4) (b) (4)

Response:

Background:	This test method, (b) (4) Test Procedure, ES1240, Rev. D, (See Attachment 2.5) released May 5, 2009, is a (b) (4) pull-test procedure which measures the (b) force of a (b) (4) on a lead body with and without (b) (4) The method provides definition for test sample soak conditions, (b) (4) (b) (4) locations, and force gauge measurements. An acceptance criterion is provided, allowing verification of the maximum (b) force of an (b) (4) in the wet and dry condition, and verification of the minimum (b) force of a (b) (4) in the wet condition.
Planned Actions:	1) We are reviewing the test method to determine extent of validation activities required per "Test Method Validation" SOP 60046416, Rev. A (Expected completion: November 30, 2012) 2) If required, we will validate according to the result of the assessment. 3) Should a test method validation fail, an evaluation will occur to determine the cause and its impact on product safety and effectiveness. Additionally the cause of the validation failure will be investigated, corrected, and then validation will be attempted again. This process will be followed until test method validation is successful.

B. You failed to follow your written test procedure during design verification testing of your (b) (4) *test, which ensures the* (b) (4) *is not greater than* (b) (4) *to prevent a potential* (b) (4) *Your procedures require each lead to be tested 5 times and the mean of the 5 tests is considered your test result. During your design verification you only tested each lead one time to determine your design verification results as opposed to determining the mean of 5 tests per lead.*

Response:

Background:	In the testing of Durata product model number, 7120, approved on June 27, 2007, per the qualification test report QTR 2117 Rev. 001 (See Attachment 2.6), the technician conducting the test did not follow the test procedure as defined. Rather, one (b) (4) measurement was made and recorded per lead as opposed to calculating the average of five successive (b) (4) measurements per lead as defined in Test Method ES1178, Rev. D in effect at the time of the testing (See Attachment 2.3 for Test Method ES1178, Rev. G, Sec. 5.0 for this requirement which had not changed from Rev. D to Rev. G.). Note: While this test involves measuring (b) (4) we refer to this test as (b) (4) in our documentation and throughout this response.

Appendix -1
Response to FDA-483 dated November 7, 2012

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Completed Actions:	Training to Test Method ES1178, Rev. G to ensure completeness of adherence to defined activities and associated review activities was completed October 29, 2012. (See Attachment 2.7).
Planned Actions:	We will complete the following activities: 1) Validate Test Method ES1178. (Expected completion: February 28, 2013) 2) Repeat testing for Durata leads to assure the product tested continues to conform to specifications. (Expected completion: March 31, 2013) 3) Provide training for the development and review of protocol requirements and acceptance criteria. (pre and post execution) (action also in response to observation 6B(b)) (Expected completion: December 31, 2012)

C. You conducted your Durata (b) (4) *design verification to verify the "* (b) (4) (b) (4) *on 06/07/07 which was prior to your approval of your Durata lead inputs revision #004, Document number 60010874 which occurred on 07/16/07.*

Response

Background:	An initial version of design inputs "Lead Product Specification: Model 7120 and 7121 (b) (4) (b) (4) " 60010874 Rev. P01) was completed on June 30, 2006 which occurred prior to Design Verification. Because the specific requirement for (b) (4) did not change throughout the development of the Durata lead, verification testing prior to approval of the design inputs did not have an effect on the design input specification, it remained the same. The final referenced version of the design inputs for "Lead Product Specification: Model 7120 and 7121 (b) (4) (b) (4) Leads" 60010874, Rev. 004, in the design verification test report was finalized after the testing was completed.
Planned Actions:	We will revise "Global Product Development Protocol" SOP 2.1, Rev. R to require that the design inputs are completed prior to design verification. Additionally the procedure will similarly be revised to require the design verification be completed prior to design validation as identified in Observation 2D. Each of these distinct phases will be gated and deemed completed based upon a final phase review. Training will be completed for appropriate personnel on the revised procedures. (Expected completion: November 30, 2012) Remediation activities shall include a systematic review of completion dates of key phases in design history files for products currently manufactured and distributed in the US as listed below. Gaps identified will be prioritized and subject to remediation as follows: (Expected completion: June 30, 2013) 1) A summary document that outlines the gate completion dates for design inputs, design outputs, design verification, design validation, and design transfer will be added to each design history file

	2) Determination if any of these gate completions preceded the completion of the prior gate a. If so, an assessment will be completed to determine if there is any impact to design verification. b. If gaps are identified, a plan will be developed to address the gap identified 3) A summary report will be completed describing any remediation activities that have occurred on each product family.

D. Your (b) (4) design verification activity to verify the design input of (b) (4) was conducted on 06/07/07 which was after you implanted (b) leads into canines as part of your design validation.

Response:

Background:	The (b) (4) study (design validation) used for the validation testing was a (b) month study with a total of (b) (4) canines being implanted. (b) of the canines in the (b) study were implanted prior to the (b) (4) testing (design verification) being completed. The (b) (4) test evaluates the leads (b) (4) potential. Although the evaluation of (b) (4) was performed at the end of the study, the validation activity was initiated prior to verification completion.
Planned Actions:	1) This action will be covered as part of the previous observation described in Planned Actions (2C – Design Verification) given that the corrective action and remediation efforts are identical. Going forward, design inputs will be completed prior to authorizing design verification. Similarly, design verification will be completed before authorizing design validation. 2) The procedure revisions are expected to be completed by November 30, 2012. 3) Training to the revised procedures will be completed by November 30, 2012. 4) The remediation activities are expected to be completed by June 30, 2013.

Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 3

Design Validation:

A. Your Durata risk analyses (2007) identified canine testing as a mitigation addressing (b) (4) (b) (4) *In the mitigation you reference study* (b) (4) *as your design verification and it was inadequate in that:*
a. It did not include predetermined acceptance criteria corresponding to (b) (4)
b. A review of your approval of the verification found 4 of the total population of 30 canines implanted to support a sample size of 21 canines tested had (b) (4) (b) (4)
c. you failed to evaluate one of the study results which stated, (b) (4) (b) (4)

Response:

Background:	Observation 3A states that the mitigation study referenced in the Durata Risk Analyses (2007) was inadequate to address (b) (4) The reference to study (b) (4) in the documentation was incorrect. The correct reference is to (b) (4) which was performed specifically to evaluate the Durata lead performance on measures such as (b) (4) (b) (4) lists assessment of overall lead stability during the course of the study along with histopathological analysis of surrounding heart tissue in the study objectives that are designed to assess (b) (4) (b) (4) and other risks. (b) (4) concluded with no observations of (b) (4) (b) (4) The following documents are included as attachments: • (b) (4) The remaining observations similarly relate to the incorrect reference to Study (b) (4) and are explained below.

	Observation 3A, a. states that there were no predetermined acceptance criteria corresponding to [redacted] This is due to the fact the documentation incorrectly referenced Study [redacted] which was performed in 2004 (submitted to FDA as part of [redacted] in 2005) with two objectives – 1. [redacted] and, 2. [redacted] As such, it contained acceptance criteria corresponding to two objectives, and not corresponding to either [redacted] Observation 3A, b. states that that were 4 instances of [redacted] and 1 instance of "device acquired [redacted] The study [redacted] that was incorrectly referenced, employed a total of ove[redacted] leads (including control leads) to study [redacted] As such approximately [redacted] leads were implanted in each subject, including placement of some of the leads at the Inferior Vena Cava (IVC). The IVC is a known weak location of cardiac tissue offering higher propensity to perforate. Furthermore the leads utilized in the study had a construction that was significantly different from the Durata in that it lacked [redacted] The lead body was purposefully constructed solely of [redacted] to assess [redacted] relative to the controls.
Completed Actions:	We have revised the Durata risk analysis 60003937 Rev. T, Risk Analysis Data Table Sec. 2, with the appropriate references to [redacted] for [redacted] (See Attachment 3.7). In this version of the Durata risk analysis 60003937 Rev. T, Study [redacted] has been listed as mitigation to [redacted] in the Risk Analysis Data Table, Sec. 5.
Planned Actions:	1) As part of the remediation activities we will conduct a review of risk analyses, i.e., review risks and the appropriateness of the mitigations stated, corresponding to all products that are currently being marketed in the US. (Expected completion: April 30, 2013) 2) In addition we will establish a process to provide for systematic control and evaluation of all our risk analyses as linked to our design and process FMEAs. This is described further in our response to Observation 3B with more details and completion timelines presented as part of our response to Observation 7B.

B. Your Durata design risk analysis [redacted] is inadequate in that it combines different recalled and not recalled devices, for example:

a. Your [redacted] out for all [redacted] leads states a severity of [redacted] and a probability of [redacted] when your design team stated the Durata design decreased the risk of this [redacted] root cause.

b. Your [redacted] for all [redacted] leads states a severity of [redacted] and a probability of [redacted] when your design team stated the Durata design decreased the risk of this [redacted] root cause.

Response

Background:	The Clinical Use FMEA (CUFMEA) for all leads, as well as CUFMEAs for our other implanted devices such as pacemakers and ICDs, were approved and released in August 2012. The intent of the CUFMEA was to provide the manufacturing sites with a unified approach to assigning severities and probabilities to field issues. It was not intended to be used as a Design FMEA; however, it had been referenced in a recently revised Durata Risk Management Report. During the inspection, the investigator observed in the CUFMEA for leads that individual failure modes were noted but that severities and probabilities, and therefore risk, were not separated for different lead model families. For example, in the (b) (4) lead section of the CUFMEA, failure modes for Riata were not separated from those of Durata. Instead, the severity and probability assignment was made generically for (b) (4) Note that for the (b) (4) CUFMEAs, this issue did not exist as failure modes and their severities and probabilities were identified separately for individual product families.
Completed Actions:	The CUFMEA for leads has been revised to separately identify failure modes by product family based on field experience (See Attachment 3.8). For (b) (4) leads, individual severities and probabilities are listed separately for different product families (Riata, Riata ST, Riata ST Optim, Durata). For item a) (b) (4) the severity is listed as (b) Per our "Global Risk Management Procedure" SOP 4.7.2 a severity (b) is defined as (b) (4) and a severity (b) is defined as (b) (4) A severity (b) is assigned to (b) (4) while a severity (b) is assigned to (b) (4) These severity assignments apply equally to Riata and Riata ST which are our recalled product, as well as to Riata ST Optim and Durata, our non-recalled product, and are now reflected for each of the product family models. Similarly, probability assignments based on field experience have been made separately for the individual product family models. For (b) (4) the probability had been assigned a value of (b) defined as (b) (4) per SOP 4.7.2, for our recalled product Riata and Riata ST. For Riata and Riata ST (b) (4) we have also now taken the opportunity to update the latest CUFMEA (See Attachment 3.8, page 3 of Table 1: (b) (4) Leads) with occurrence rates from our (b) (4) results which indicate that the rate of (b) (4) (See Attachment 3.9). This corresponds to a probability value of (b) (4) for Riata and (b) (4) for Riata ST.

	For our non-recalled product Riata ST Optim and Durata, the probability category is (b) defined as (b) (4) per SOP 4.7.2, for (b) (4) Hence the risk of (b) (4) is lower on Riata ST Optim and Durata as compared to Riata and Riata ST, based on actual field experience out of over (b) (4) Riata leads sold worldwide since 2002, over (b) (4) Riata ST leads sold worldwide since 2005, over (b) (4) Riata ST Optim leads sold worldwide since 2006, and over (b) (4) Durata leads sold worldwide since 2007. For item b, (b) (4) a similar correction was made in the revised CUFMEA for leads. The severity assignment remains applicable for all of the (b) (4) lead product families (Riata, Riata ST, Riata ST Optim, and Durata). The probability assignment is (b) defined as (b) (4) for our recalled product Riata and Riata ST, and is (b) defined as (b) (4) for our non-recalled product Riata ST Optim and Durata, based on field experience. Hence the risk of (b) (4) is lower on Riata ST Optim and Durata as compared to Riata and Riata ST.
Planned Actions:	As a long term remediation, we will review and revise Failure Mode Effects and Analysis (FMEA) for all product families. This FMEA will be used as a "living document" from design and development to field usage, specifying severities and probabilities for each failure mode identified. A team comprised of Quality, Clinical, and Development personnel will review existing severity and probability assignments for appropriateness to avoid situations such as the one noted here. It is expected that these "living document" FMEAs will be completed for high voltage leads by January 31, 2013 with the rest of our product lines completed by March 31, 2013.

Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 4

Design Change:

(b) (4) *Design Change:*
You documented (b) of (b) devices failed your "(b) (4) test" predetermined acceptance criteria of (b) (4) during your design verification testing. You then changed your (b) (4) in the (b) (4) from (b) (4) to (b) (4) inches, produced and tested (b) newly manufactured (b) (4) leads and approved your design verification without determining the validity of any of your other design verification activities that were conducted using the (b) (4) leads manufactured under previously approved specifications (design inputs).

Response:

Background:	We believe the concern stemmed from the usage of the terminology "Corrective Action" being used within our procedure "Product Verification and Validation" SOP 4.4.3 Rev. R (See Attachment 4.1) (Sec. 6.2.5 flow chart and Sec. 6.2.5.2) instead of "Design Change" or "Process Change". The product was still within the development phase. Additionally, there was no perceived need to complete a determination on the validity of the design verification activities because the affected verification tests were repeated. We recognize that this choice of wording is suboptimal and can easily be confused for the 21 CFR Part 820 definition of a "Corrective Action" which was not our intention. As part of our process within "Global Product Development Protocol" SOP 2.1 Rev. R, section 8.8 and 8.9, (See Attachment 4.2) each development program is required to complete traceability to ensure all design inputs have been appropriately verified and validated. Either a drawing, specification, or manufacturing operation must be updated in order to incorporate a "design change" or "process change" and would have been subsequently traced as part of the process. Therefore the only remaining action would be to update the process document wording given that the necessary design inputs, verification and validation are already in place.
Completed Actions:	In order to improve the clarity of how we perform our process "Product Verification and Validation" SOP 4.4.3 Rev. T (See Attachment 4.3) was revised to assure the following: (completed: November 2, 2012) 1) The correct usage of terminology replacing "Corrective Action" with "Design or Process updates" (Sec. 6.2.5 flow chart and Sec. 6.2.5.2). 2) A descriptive flow chart that requires us to document our change impact assessment which reviews the impact of the change to the design inputs, outputs, verification, and validation (Sec. 6.2.5 flow chart and Sec. 6.2.5.2). Training to "Product Verification and Validation" SOP 4.4.3 Rev. T was completed on November 2, 2012. (see Attachment 4.4)
Planned Actions:	A plan will be developed to conduct a review of implemented "Corrective Actions" (Design Changes and Process Changes) and to perform an assessment of any impact of the change(s) on the validity of other verification activities (Expected completion: November 30, 2012).

Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 5

Design History File:
Your firm was unable to clearly identify the full content of your Durata design history file, for example: I was unable to determine when your firm approved your Durata design inputs, outputs, verification, validation, design transfer and when you conducted your final approval of your Durata design. I was also unable to determine which inputs were changed or unchanged from 1997 onward which is the origination of your Durata design.

Response:

Background:	The Durata lead was developed from the (b) (4) lead by completing design changes involving (b) (4) All other design aspects of the lead (b) (4) Given the nature of the changes, many of the design inputs, design verification, and design validation from the (b) (4) (b) (4) were deemed applicable and not repeated. These activities, which occurred in support of previously approved products, and a summary of the dates for each phase were not available in one record. Thus the items were referenced in various test reports, and may not have been referenced directly in the Durata Design History File. All the documents and testing were available during the inspection, and required tracing through the reports.
Planned Actions:	The corrective action for this observation will be handled as part of Observation 2C under item "1" of the remediation and the actions are repeated below. A systematic review will be conducted on currently manufactured products to assess if the associated Design History Files require remediation. Design History Files identified for remediation will be prioritized and the activities will include the following: 1. A summary document that outlines the gate completion dates for design inputs, design outputs, design verification, design validation, and design transfer will be added to each design history file. (Expected completion: June 30, 2013)

Observation 6

Training:
A. Internal Auditor Training:
Your training of your internal auditors is inadequate in that your audit team audited the Durata design project in January of 2012 when after 6 days of inspectional requests of your firm to provide the Durata design history file I was unable to determine when your firm approved your Durata design inputs, outputs, verification, validation, design transfer and when you conducted your final approval of your Durata design. I was also unable to determine which inputs were changed or unchanged from 1997 onward which is the origination of your Durata design.

Response:

Background:	We reviewed the internal audit report conducted in January 2012. Here we briefly recap the audit approach. The auditors reviewed the procedures and project related documents for design development planning, design input, design output, design review, design verification, design validation, design transfer, design changes and the design history file.
Planned Actions:	The procedures that comprise the above listed design development activities will be further improved to ensure that approval of the phases of development is clearly required and documented. Among the personnel to be trained to the design development procedures will be the internal auditors and the training will emphasize the requirement to examine documents for the required approvals, and any changes to design inputs. (Expected completion: November 30, 2012)

B. Design Training:
You have inadequate training of design controls, for example:
a. After 6 days of inspectional requests I was unable to determine which design inputs were changed or unchanged from 1997 to present day.

Response:

Planned Actions:	We will develop a training plan for personnel performing and documenting design control activities. (Expected completion: November 30, 2012)

b. 4 personnel approved your design validation study with an ambiguous input

Response:

Background:	Note: No correction necessary because the initial ambiguous input in "(b) (4) (b) (4) (b) (4) ", Sec. 5 Objectives, dated June 2004 (See Attachment 6.1), had been subsequently amended in November 2004 (See Attachment 6.2, Sec. 2.0 Updated Study Summary). The amendment of the study was done before the analysis of the results that assured the primary study objectives were met.

Planned Actions:	We will develop a training plan for personnel performing and documenting design control activities. (Expected completion: November 30, 2012)

Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 7

CAPA system:

A. Your CAPA system is inadequate in that in reviewing 11 of your recently closed CAPAs I found:

a. two were closed and did not state a verification of the effectiveness would be performed.

Response:

Background	In the "Corrective Action and Preventive Action Procedure" SOP 3.3.5, Rev. Y in effect at the time of the inspection, the requirement for a CAPA effectiveness check on any closed CAPA (internally referred to as a Product Improvement Request (PIR)) was stated in Sec. 7.4.4 and 7.4.6, as summarized below: Sec. 7.4.4 states: "An effectiveness check shall be performed on any PIR that has been closed, unless there is justification that no effectiveness check is required. Effectiveness check activities may include a review of field returns, manufacturing data, technical service call logs, etc. for those products or processes that had CAPA(s) implemented as stipulated by the PIR. Documentation of effectiveness check activities shall be included in the PIR file." Sec. 7.4.5 states: "For PIRs and corrective actions associated with a recall/advisory, the failure rate shall be assessed twice after the PIR/corrective action has been closed. To allow sufficient time to fully assess the failure rate, the first assessment shall be done 6 to 9 months after PIR/corrective action closure, with the second assessment done 6 to 9 months apart from the first assessment. If a death is reported at any time during this assessment period, or if the failure rate is inconsistent with the rate that had been stated in the recall/advisory communication, then the issue will be escalated to management with executive responsibility (SOP4.1.3)."
Completed Actions:	The two CAPAs associated with this observation PIR 12-004 and PIR 11-013 were retrospectively reviewed and revised to include a memorandum containing effectiveness check criteria and the resulting determination of CAPA effectiveness (See Attachments 7.1 and 7.2). Both PIR 12-004 and PIR 11-013 met the criteria and thus, effectiveness was verified. While the PIR review was retrospective, the effectiveness criteria were established prior to review of data from the prescribed data source. A revision was completed on November 2, 2012 to the "Corrective Action and Preventive Action Procedure" SOP 3.3.5, Rev. AA (See Attachment 7.3). Section 7.4.1 "Closure of PIRs" now includes requirements for a Verification of Effectiveness (VOE) Plan for an opened PIR. The VOE Plan shall include predetermined effectiveness criteria. Training to "Corrective Action and Preventive Action Procedure" SOP 3.3.5, Rev. AA for Product Improvement Board (CAPA Board) membership occurred on November 2, 2012 (See Attachment 7.4 for Training Records).

Planned Actions:	CAPAs opened between October 31, 2010 – October 31, 2012 not already remediated will be retrospectively reviewed to identify any missing VOE plans and/or checks and will be remediated as follows: 1) A protocol will be developed that defines the process for how to review CAPAs retrospectively and address gaps in VOE activities per the latest "Corrective Action and Preventive Action Procedure" SOP 3.3.5, Rev. AA. (Expected completion: November 30, 2012) 2) Perform review of individual CAPA files per the above protocol. (Expected completion: January 31, 2013)

b. two were closed and stated "no effectiveness check is required" with no justification, which is required by your procedures if no verification check is performed.

Response:

Completed Actions:	The two CAPAs, PIR 12-008 and PIR 12-007, were retrospectively reviewed to add an effectiveness check be performed to assess the data sources affected by the CAPA against predetermined effectiveness criteria. Predetermined effectiveness criteria were set for PIR 12-008 (See Attachment 7.5) and for PIR 12-007 (See Attachment 7.6).
Planned Actions:	For PIR 12-008, while it was verified all communications were completed to affected SJM field staff, the vendor has not yet reconciled all product returns for purchasers outside of SJM, and thus, the PIR remains in a monitoring period. Due to the implementation date of the inspection criteria clarification in September 2012 for PIR 12-007, the additional check will be completed after receipt of at least (b) (4) (b) (4) of the vendor supplied component. This level of component receipts is expected no later than December 31, 2012. Additional planned actions to address 7(b) will be performed as part of the planned actions in 7(a).

c. six of the CAPAs are closed and state an effectiveness check is going to be done in 6-9 months. None of the 11 CAPAs reviewed, including these 6, specify how you are going to verify your effectiveness.

Response:

Completed Actions:

Since the inspection we revised Sec. 7.4.4 of our "Corrective Action and Preventive Action Procedure" SOP 3.3.5 to Rev. AA (See Attachment 7.3) to include a requirement for a Verification of Effectiveness (VOE) Plan containing predetermined effectiveness criteria prior to CAPA closure including:

- When the effectiveness check occurs or when there is a quantity of product to assess
- Identification of the data source(s) to review
- Specific criteria necessary to demonstrate effectiveness.

The Verification of Effectiveness will be overseen by the CAPA Administrator or designee to assure the completeness of the execution of the VOE Plan. If the CAPA effectiveness verification performed did not meet the predetermined criteria, then the CAPA will remain open and subject to additional investigation and CAPA.

The 11 CAPA records, PIR 10-007, PIR 11-011, PIR 11-012, PIR 11-013, PIR 11-016, PIR 12-001, PIR 12-002, PIR 12-003, PIR 12-004, PIR 12-007, and PIR 12-008, reviewed during this inspection were subsequently reviewed and remediated to include retrospectively defined predetermined effectiveness criteria. Each PIR demonstrated effectiveness or continues in a monitoring phase per the stipulations of the predetermined effectiveness criteria. A summary is shown in the following Table:

PIR#	Effectiveness Demonstrated	Monitoring Phase	ECD to Complete Monitoring Phase	Attachment Number
11-011		X	Jun-2013	7.7
11-012		X	Apr-2013	7.8
11-013	X		N/A	7.2
11-016		X	Apr-2013	7.9
12-001		X	Apr-2013	7.10
12-002		X	Apr-2013	7.11
12-003		X	Apr-2013	7.13
12-004	X		N/A	7.1
12-007		X	May-2013	7.6
12-008	X		N/A	7.5
10-007	X		N/A	7.12

Planned Action

See the Table in Completed Actions for this response, above, for PIRs which are currently in the monitoring phase. Expected remediation dates for these PIRs are also shown in this previous Table.

CAPA files not already remediated which were opened between October 31, 2010 and October 31, 2012 will be remediated as per planned action above in 7(a).

d. PIR10-007 was closed on 03/25/2011 and an employee documented that the CAPA was not effective on 10/20/2011 and the problem of (b) (4) *in your lead continued, implemented two actions to correct the original problem and requested a new effectiveness check be performed at a later date. This CAPA was not re-opened nor was there a separate CAPA opened after the original CAPA action taken was determined to be ineffective. There is no document control dictating which documents are part of or not part of this CAPA.*

Response:

Completed Actions:	The CAPA Board staff reviewed CAPA file PIR 10-007 which found the CAPA for (b) (4) originated from returns analysis. This review also determined the employee who performed the October 20, 2011 effectiveness check erred in that he did not use the correct data source where the CAPA originated. Instead, the effectiveness check was based on a (b) (4) (b) (4) The data source was corrected to returns analysis during the October 2012 review which found a five-fold reduction in occurrence in the population sold after the PIR closure date on March 25, 2011 compared to the population sold prior to March 25, 2011. The sold lead population after the PIR closure exceeded (b) (4) and found (b) occurrences within this population. Thus the CAPA Board deemed the CAPA performed effective based on meeting the predetermined criteria based on the correct data source. (See Attachment 7.12) Additional CAPA files opened since October 31, 2010 were reviewed by the CAPA Board Chair and this review found no similar event where CAPA was incorrectly deemed ineffective or where additional action was performed without a new, separate CAPA issuance or reopening of the original CAPA file.
Planned Actions:	As a response to Observation 10a, an index, form number 60046468, Revision A will be added to CAPA files not already remediated which were opened between October 31, 2010 and October 31, 2012. The index will specify the contents required and added to each CAPA file. It is estimated a file index will be added to these CAPA files opened within this time period by December 31, 2012. See associated actions and attachments 10.1 through 10.12.

e. you failed to re-evaluate and update your risk analysis for CAPA PIR 10-007 when the mitigation identified in the risk analysis failed and you continued to have the problem of (b) (4) (b) (4) *and then implemented further actions to solve the problem*

Response:

Completed Actions:	1) A review of CAPA PIR10-007 was completed and a risk analysis update was performed (see Attachment 7.14) which indicated the mitigation associated with the (b) (4) was effectively resolved. 2) We reviewed other CAPAs initiated since October 31, 2010 – October 31, 2012 (see Attachment 7.15) and found no other similar events where re-evaluation and update of a risk assessment was deemed necessary. We consider Observation 7.A.e. to be closed.

Appendix -1
Response to FDA-483 dated November 7, 2012

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B. Your Corrective Action #PIR-10-005 for your Riata lead was inadequate in that you failed to evaluate the validity of some of your Durata lead design verification and validation activities.

Response:

Background:	Corrective action #PIR10-005 pertains to the incidence of (b) (4) associated with Riata leads. The current revision of SOP 4.7.2 Global Risk management, Rev. R -Section 5.5 Sustaining (Manufacturing and field usage) - requires a review and an update to the risk management documentation as appropriate for current and future products concerning new failure modes. Our approach to risk management prior to the inspection was to develop Failure Mode Effects and Analysis (FMEA), per SOP 4.7.2 Global Risk Management Rev. R, during the design stage, and then employ individual Risk Analyses on specific failure mechanisms that are discovered during field usage. While an individual Risk Analysis is typically generated during the course of carrying out a CAPA investigation, the original design FMEA is not automatically updated with these risk(s).
Completed Actions:	We revised the procedure SOP 4.7.2 Global Risk Management, from Rev. R to Rev. T (See Attachment 7.16) on November 2, 2012 to specify the following: • A FMEA shall be the primary tool used to perform the risk analysis (Sec. 5.3.1) • The criteria to initiate a review of the FMEA is stated in the Risk Control section (Sec. 5.3.3) and the Sustaining section (Sec 5.5) • The FMEA is a specified deliverable in the Risk Management File (Sec. 7.0) Training for the revised procedure was completed on November 2, 2012 (See Attachment 7.17)
Planned Actions:	To improve and streamline the Risk Management process • We will enhance our Failure Mode Effects and Analysis (FMEA) across all product families. • The FMEA will be considered a "living document" from design and development to field usage, specifying severities and probabilities for each failure mode identified. • A team comprised of Quality, Clinical, and Development personnel will review existing severity assignments for appropriateness, and also assign probabilities based on empirical field data. Criteria such as a) a new or previously unforeseen hazard, b) a product recall, c) initiation of a CAPA, or d) an ineffective CAPA implementation would initiate a review of the FMEA which in turn could lead to a re-evaluation of the validity of some of the previously performed verification and validation activities.

	We will enhance the "living document" FMEA for product families that are currently being sold in the United States. This activity will include the following: • Review existing risk analysis and transfer the individual failure modes into the new FMEA • Re-assess the severity assignment for each identified failure mode • Using field performance data, develop a probability of harm estimate for each failure mode • Specify the risk of each failure mode based on the above severity and probability values • Review the existing mitigations and re-assess for appropriateness, including re-evaluation of the validity of any previously performed verification and validation activities • Any new risks identified subsequently shall be added by appending to the FMEA tables in each revision. The estimated timeframe to develop the "living document" FMEA is summarized below: • High Voltage Leads: January 31, 2013 • Cardiac Resynchronization Therapy Leads: January 31, 2013 • Low Voltage Leads: February 28, 2013 • Implantable Cardioverter Defibrillators: March 31, 2013 • Pacemakers/Implantable Cardiac Monitors: March 31, 2013 • Leads Delivery Tools: March 31, 2013 Once these FMEAs are completed, SOP 3.3.5 CAPA procedure will be updated to specifically require the Risk Analysis to include assessment of these FMEAs as part of the CAPA investigation. Also, it will specify that if a CAPA implementation is deemed ineffective, or if a CAPA is associated with a recall, then the FMEA will be evaluated to determine the validity of some of the verification and validation activities previously performed to mitigate risk. Risk analysis arising from CAPA activities in the interim period will be included in these FMEAs. Following the next revision of the CAPA procedure training will be provided to appropriate personnel. (Expected Completion: December 31, 2012)

Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 8

CAPA Procedures:
Your CAPA procedures are inadequate in that they do not address:

1. Determining whether the action taken adversely affects the finished device,

Response:

Completed Actions:	"Corrective Action and Preventive Action" SOP 3.3.5 has been revised to Rev. AA to explicitly state in Sec. 7.4.1 that as part of the CAPA process, a determination will be made as to whether the action taken adversely affects the finish device (see Attachment 7.3). Training to SOP 3.3.5, Rev. AA was completed on November 2, 2012 (see Attachment 7.4). The training was performed for Product Improvement Board (PIB) membership (i.e., the CAPA board), which includes representatives from QA, Clinical, Regulatory, Development, and Manufacturing.
Planned Actions:	CAPA files opened between October 31, 2010 and October 31, 2012 will be updated to document that prior actions undertaken as part of a CAPA did not adversely affect finished devices. (Expected Completion: December 31, 2012.)

2. Identify data sources you are going to analyze; such as complaints and MDRs.

Response:

Background:	In the "Corrective Action and Preventive Action" SOP 3.3.5, Rev. Y (See Attachment 8.1) in effect at the time of the inspection, Sec. 2.0 specified the data sources of the CAPA system, including Field Issues, Manufacturing, Operational Site data, Supplier Quality, and Audits. Section 5.4 specified that on a monthly basis, a listing of non-conformances from these data sources shall be provided to the CAPA Board.
Planned Actions:	A Data Trending and Analysis Department Work Instruction will be developed to include identification of specific data to be analyzed for review by the CAPA Review Board and personnel will be trained. It is estimated that release of this work instruction and related training will be completed by December 31, 2012. The next revision to the "Corrective Action and Preventive Action" SOP 3.3.5, will identify the exact data source and the expected content to be provided after investigation from within each of the larger groups of data sources (e.g. field complaints, MDRs, clinical studies, manufacturing operations, supplier quality, auditing). Once the specific content from each of the data sources are identified, the procedure will be updated and the respective functional groups will be trained to begin providing this data per the Procedure and Work Instruction to the CAPA Review Board. . The revision to SOP 3.3.5 and related training is expected to be completed by December 31, 2012.

3. verifying or validating the effectiveness of a CAPA
And the procedures state you will determine the effectiveness of the CAPA after the CAPA is closed

Response:

Background:	In the "Corrective Action and Preventive Action" SOP 3.3.5, Rev. Y (See Attachment 8.1) in effect at the time of the inspection, Section 7.4.4 required that an effectiveness check be performed on product that had CAPA implemented, and that such activities could "include a review of field returns, manufacturing data, technical service call logs, etc. for those products or processes that had CAPA(s) implemented as stipulated by the PIR."
Completed Actions:	"Corrective Action and Preventive Action" SOP 3.3.5, Rev. Y, Section 6.1 was revised to Rev. AA to require verifying or validating the effectiveness of a CAPA (see Attachment 7.3). Requirements for a Verification of Effectiveness (VOE) Plan and specification of predetermined criteria for effectiveness have also been added to Section 7.4.4 and 7.4.5, respectively. The procedure now includes a work flow where the CAPA file is considered closed only after meeting the predetermined effectiveness criteria, as depicted in Section 7.5 of "Corrective Action and Preventive Action" SOP 3.3.5, Rev. AA. Training to "Corrective Action and Preventive Action" SOP 3.3.5, Rev. AA was completed on November 2, 2012 (see Attachment 7.4). The training was performed for Product Improvement Board (PIB) membership (i.e., the CAPA board) and representatives from Quality Assurance, Development, Operations, and Regulatory Affairs. We consider Observation 8.3 to be closed.

Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 9

Complaint Files:

Your complaint handling procedures are inadequate in that:

a. Your procedures do not dictate that you will make a decision as to whether an investigation is necessary.

Response:

Background:	The "Complaint Handling Processes", DWI 9.0.4.1, Rev. AA, is the procedure that was in effect at the time of the inspection (See Attachment 9.1). The DWI had a section on complaints investigations which required making a decision as to whether an investigation was necessary; however, it was not a clearly defined decision point in the process. Appendix A, section 7 (p20-21) of DWI 9.0.4.1 Rev. AA stated that Product Reporting personnel must assess if any further action, including "investigation", was required. The prior version of the coversheet, "Product Reporting Event Review Form", Form 0500197, Rev. J (See Attachment 9.2) in use at the time of the inspection, required the Product Reporting team to make a decision as to whether an investigation was necessary. A check box labeled "investigation" appeared on the Product Reporting Event Review Form of each complaint, thus demonstrating that this decision was required from a procedural point-of-view for each complaint.
Completed Actions:	The "Complaint Handling Processes", DWI 9.0.4.1 has been revised to Rev. AB to further clarify that a decision is needed as to whether an investigation is necessary (See attachment 9.3). Section 5.1.13 (p.10) of this updated version of our process includes the comprehensive language from the regulations, section 820.198(b), indicating, "All complaints are reviewed and evaluated to determine whether an investigation is necessary. When no investigation is made, PR team shall maintain a record that includes the reason no investigation was made and the name of the individual responsible for the decision not to investigate..." Additionally, Appendix A, section 3 (p.21) within DWI 9.0.4.1 elaborates on types of investigations that can be completed. The "Product Reporting Event Review Form", Form 0500197, has been revised to Rev. K (See attachment 9.4). Here, we have implemented an improved format to capture our decision for each complaint by having definitive selections for whether to investigate, including "yes" and "no", and a section called "other/more info (please explain)" which is intended to capture additional information and the reasons for the decision to or not to investigate. Training to DWI 9.0.4.1 Rev. AB and "Product Reporting Event Review Form" 0500197 Rev. K was completed on November 2, 2012 (see Attachment 9.5).

b. A review of your Durata Model 7121 SN AHD32782 complaint found:
1. you did not specify whether an investigation was necessary

Response:

Background:	Although this complaint record did not clearly specify whether an investigation was necessary, a comprehensive, multi-functional investigation was completed, including: 1) analysis on the returned product, 2) a CAPA investigation, and 3) an investigation within the manufacturing site on root cause and corrective actions.
Completed Actions:	The "Product Reporting Event Review Form", Form 0500197, was revised to Rev. K (see attachment 9.4). In the investigation section, which will be filled out for each complaint, we have implemented an improved format for how we capture our decision for whether to investigate by having definitive selections "yes", "no" and "other/more info". We have also included a step to define the investigation type to be performed (i.e., (b) (4) (b) (4) Additionally, the "Complaint Handling Processes", DWI 9.0.4.1, Appendix A, Rev. AB section 3 now includes steps for making decisions on whether to investigate and what types of investigations to perform. Training for the revised procedure and form was provided for the Product Reporting team on November 2, 2012 (See attachment 9.5).

2. Your decision of whether this complaint was a medical device reportable event was conflicting in that you stated "not implanted" as a justification for the non-reportable event when the lead was implanted and then removed during the implant procedure.

Response:

Background:	This observation specifically challenges our brevity and definition of the phrase "not implanted" for this complaint, since the lead was (b) (4) during the implant procedure. Please note, the definition we use for "implanted" is based on a definition we identified in "FDA, Guidance for the Submission of Research and Marketing Applications for Permanent Pacemaker Leads and for Pacemaker Lead Adaptor 510(k) Submissions", under "definitions of terms" (See Attachment 9.6). The guidance states, "A lead is considered implanted when the surgical incisions are closed". In the complaint on the Durata lead, Model 7121, serial number AHD32782, a lead implant was attempted. The lead exhibited (b) (4) (b) (4) upon tests at the desired implant site. The Durata labeling indicates, "If desired, evaluate one or more potential fixation sites using the helix tip prior to extending the Helix", suggesting a routine part of an implant procedure includes testing several times/sites, until desired values are obtained (Attachment 9.7, p. 15). Since the test values were undesirable, the lead was not sutured in place and the surgical incisions were not closed; instead a different lead was used. There were no negative clinical outcomes for the patient, and the only result was a slightly longer procedure. On the form that Product Reporting uses to summarize a complaint, under the "not reportable" section, the Product Reporting coordinator listed

	"not implanted" to mean "decision not to use the product during implant attempt before closing the surgical incision". When the lead was returned, (b) (4) which explains the observations reported in the complaint, since the helix (b) (4)
Completed Actions:	Since the inspection, we have updated our "Complaint Handling Processes", DWI 9.0.4.1 to Rev. AB (see Attachment 9.3) to improve completeness of detail regarding the justification for non-reporting decisions. Appendix C (p.33) of DWI 9.0.4.1 Rev. AB indicates that stating "not implanted" by itself is not adequate, and it requires a Product Reporting employee to indicate "decision not to use product (b) (4) for justification for future similar cases. It provides additional elaboration on what that statement means, including that (b) (4) Additionally, the Product Reporting team was trained on the updated process on November 2, 2012 (see Attachment 9.5).

Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 10

Document Control:
Your document control is inadequate in that while reviewing:

a. CAPA #PIR 10-005 I was unable to determine which document were included in the CAPA and which were not, for example the attachment pages are not identified as being associated with the CAPA and a separate "knowledge transfer to future HV lead designs" memorandum was not identified as being part of your CAPA.

Response:

Completed Actions:	To improve our records management process, a "PIR File Page Index" was added to the standard requirements for a CAPA file as defined in our recently updated procedure, "CAPA SOP" 3.3.5 Rev. AA, effective November 2, 2012 with training completed on November 2, 2012. (See Attachment 7.3) This PIR file page index is based on a standard form, document number 60046468, Rev. A, released on October 29, 2012. The file page index reflects the document name, any unique associated identifiers such as document numbers, subjects, the author, and the associated revision. The file page index was used to remediate PIR 10-005, where documents associated to the PIR were indexed. (See Attachment 10.1). Additional PIR files subject to review discussed in Observation 7 were also remediated to include this file page index and are attached for review per the following Table:
Planned Actions:	Additional CAPA files opened between October 31, 2010 and October 31, 2012 will be remediated to include the PIR File Page Index. The estimated completion date the file page index for these additional files is December 31, 2012. The indexing methodology will also be included in the future revision of the CAPA procedure described in the response to Observation 8(2), and will be the responsibility of the CAPA Owner or Designee to create and maintain this index throughout the life of the CAPA.

PIR#	Attachment Number
11-011	10.2
11-012	10.3
11-013	10.4
11-016	10.5
12-001	10.6
12-002	10.7
12-003	10.8
12-004	10.9
12-007	10.10
12-008	10.11
10-007	10.12

b. Durata Model 7121 SN AHD32782 complaint I was unable to determine which documents were included in the complaint as the documents are not identified as being linked to the complaint and there is no individual complaint identifier.

Response:

Background:	Our "Complaint Handling Processes", DWI 9.0.4.1, Rev. AA, (See Attachment 9.1 section 5.1.3) and "Product Reporting Event Review Form" 0500197 Rev. J (See attachment 9.2) that were in effect during the inspection, require complaints be identified by the unique combination of the product model number and serial number. Our process was to compile a physical complaint file as a collection of records related to that complaint. Additionally, at the time of closing complaint files, each complaint was scanned as a unit, into an electronic file. Therefore the complaint file was electronically bound, which would ensure all documents within the file are contained. This was already taking place at the time of the inspection. During the inspection the investigator was presented with information either extracted directly from the complaint file or from an original record referenced in the complaint file. The unique complaint number did not appear on each page in the file.
Completed Actions:	In the future, complaints will be identified by a unique complaint ID, comprised of the product's serial number, model number, and complaint open date. If multiple complaints are received against the same product (serial number) and occur in the same day, one complaint record will be opened for the complaints on that day in order to best evaluate associated complaints. The Complaint Handling Process, DWI 9.0.4.1, Rev. AB now indicates the enhanced unique complaint identifier and elaborates on the fact that the file will be electronically bound (See Attachment 9.3, section 4.4, p. 6). The Product Reporting team was trained on this enhanced process on November 2, 2012 (See Attachment 9.5). We consider Observation 10.b. to be closed.

Appendix -1
Response to FDA-483 dated November 7, 2012

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Observation 11

Control of Inspection, Measuring, and Test Equipment

Your calibration procedure and implementation is inadequate in that your procedures dictate calibration and you are performing verification, unless it falls out of your tolerances upon which you calibrate the equipment; for example:

Response:

Background:	The (b) (4) ensures the inspection, measuring, and test equipment (IM&TE) remains calibrated for use. Our calibration process at the time of the inspection included the implementation of calibration and verification activities. While the below definitions were not documented in our Metrology Manual, see below for how we interpreted and applied definitions of calibration and verification at the time of the inspection: • (b) (4) • (b) (4) *Note: We have interpreted and applied the above definitions of calibration and verification as defined in ANSI/NCSL Z540.3, "American National Standard for Calibration" and VIM (JCGM 200:2012) "International vocabulary of metrology – Basic and general concepts and associated terms". In the event of an out of tolerance condition, the IM&TE is subject to adjustment, repair or retirement and an "Out of Tolerance Notification" Form 9191348 Rev. F (See Attachment 11.1) is completed that requires a product and process impact assessment. These activities at the time of the inspection were defined in our procedure "Metrology Manual", SOP4.6.1 Rev. AC (See Attachment 11.2), Section 6.0 for steps to be completed for adjustment, repair or retirement.

Completed Actions:	• We have revised the procedure, "Metrology Manual" SOP4.6.1 from Rev. AC to Rev. AD on November 2, 2012. Section 2.0 of the revised procedure now contains the following in order to improve clarity of our current process. (See Attachment 11.3)
	  • Definitions for calibration and verification:
	  • (b) (4)
	  • (b) (4)

	• Training for "Metrology Manual SOP" 4.6.1 Rev. AD was provided to the Metrology Department on November 2, 2012. (See Attachment 11.4)
Planned Actions:	1) As an additional control measure, a plan will be established by November 30, 2012 to implement Preliminary Out of Tolerance Alerts for the inspection, measurement and test equipment. These will allow for the adjustment of IM&TE prior to the equipment exceeding established tolerances.

a. You failed to follow your procedures which require you to calibrate the (b) (4) *in* (b) *of your* (b) (4) *used to* (b) (4) *leads. In actuality you* (b) (4)

Response:

Background:	While we were performing the correct steps of calibration of instruments and verification of (b) (4) at the time of the inspection, the phraseology used in the procedure did not clearly state our process. As stated below: our calibration process for "Calibration (b) (4) " entails: 1) Comparing an installed (b) (4) to a controlled (b) (4) The result is evaluated to determine if it meets acceptance criteria or the installed (b) (4) requires adjustment. (Note: We consider this to be calibration.) 2) The (b) (4) is measured by the (b) (4) (b) (4) to assure the (b) (4) meets the tolerance specification or the (b) (4) requires adjustment. (Note: This is verification.)
Completed Actions:	1) "Calibration (b) (4) " has been updated on November 2, 2012 to include SWMP5002. This is reflected in "Calibration Procedure for (b) (4) (b) (4) 60029715 Rev. C (see Attachment 11.5) pertaining to the calibration and verification of the (b) (4) system included the following: • Improving clarity and assuring the correctly stated process for how (b) (4) is verified and instruments are calibrated. • Referencing the "Calibration Procedure" which defines verification and calibration. 2) Training to the Calibration Procedure for (b) (4) (b) (4) " 60029715 Rev. C was provided to the Metrology Department on November 2, 2012. (See Attachment 11.6)