# *Validation of a New Procedure for a Pacemaker Component*

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***Abstract*** *— Company X manufactures pacemakers in Puerto Rico. Over the past years, Company X has been having a significant amount of complaints due to the septum component contained in its pacemakers. Doctors have claimed that during the surgical process of implanting the pacemaker device in the patient, the septum component detaches itself from the device, rendering the device unusable. This validation project presents both the Product Performance Qualification (PPQ) and Installation Operational Qualification (IOQ) of the new septum that will replace the current one that is presenting complaints and its corresponding Controlled Environmental Humidity Chamber.*

***Key Terms*** *— Pacemaker, Septum, Controlled Enviromental Humidity Chamber and Medical Adhesive (Med A).*

## PROBLEM BACKGROUND

Recently in Company X, there have been several field complaints from surgeons who claim that the septum tears from the device when they are in the process of tightening the lead and the pacemaker together with the torque wrench used in the surgery. In an effort to improve customer satisfaction, a test was conducted where the septums used for the defibrillators manufactured by Company X (Septum A), where inserted into the pacemakers and tested under normal conditions against the current Septum B. It has been proven that this septum (Septum A) with bigger diameter has delivered a comparable amount of fewer complaints than the smaller one currently being used in pacemaker manufacturing (Septum B). The study included testing all pacemaker models and testing them under different conditions that a normal pacemaker would undergo, such as saline soak, impedance test and lead interaction test. Given the favorable results from the study, the research was approved and the new process will need to be validated for all the pacemaker device models in Company X. This project will present the validation of Septum A for the pacemaker manufacturing process.

## IMPORTANCE OF THE STUDY

This project is very important, given that it will validate a new procedure that will use new equipment in order to reduce field complaints that will, consequently, make the product more robust. It is clear that it will not make the product perfect, since there will always be complaints, but it will decrease the field complaints and will improve product quality, which will improve customer demand; instead of decreasing it due to poor product quality.

## SUPPORTING THEORY

Figure 1 below shows the key components of a pacemaker such as casting header, case and septum.

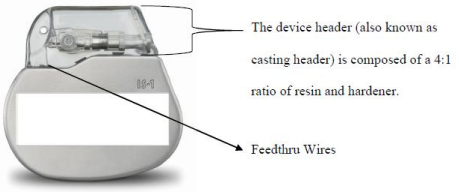



**Figure 1**
**Pacemaker Anatomy**

Table 1 (shown in the next page) shows the quantity of pacemakers that have been returned to Company X due to defective/ damaged septum that has torn or detached from the device at the moment when the surgeon is manipulating it in order to securely tighten the lead in the pacemaker device from January 2011 until June 2012.

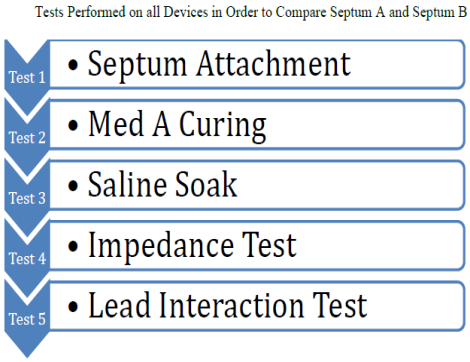
**Table 1**
**Field Complaints due to Defective Septum**

| Month | Quantity Field Complaints Due to Defective Septum |
|---|---|
| Jan-11 | 59 |
| Feb-11 | 56 |
| Mar-11 | 67 |
| Apr-11 | 88 |
| May-11 | 76 |
| Jun-11 | 45 |
| Jul-11 | 67 |
| Aug-11 | 77 |
| Sep-11 | 88 |
| Oct-11 | 97 |
| Nov-11 | 78 |
| Dec-11 | 94 |
| Jan-12 | 83 |
| Feb-12 | 78 |
| Mar-12 | 69 |
| Apr-12 | 75 |
| May-12 | 78 |
| Jun-12 | 89 |

The engineering tests performed for both Septum A and Septum B consisted of a series of tests that simulate the conditions undergone by a pacemaker. The tests are shown in the next column in Table 2 for both Septum A and B:

- Septum Attachment- the septum is placed in the septum cavity contained in the device header and two shots of Med A are placed in the circumference in the space between the device header and the septum border, therefore sealing the space between the two components in order to avoid body fluids from entering the device once it is installed inside the patient's body.
- Med A Curing- The Mead A cures for a minimum of two hours in the controlled environmental chamber.
- Saline Soak- The devices are submerging the devices in saline water for 45 minutes in order to test the integrity of the cured Med A adhesive and see if it resists normal body fluid conditions without septum detachment. Saline is used because it is the closest component that there is that could simulate bodily fluid properties.
- Impedance Test- measured in a pacemaker device in order to measure the magnitude of its conductivity and test whether it will monitor the patient's heartbeat correctly and conduct the proper voltage needed per device model and, obviously, per patient needs.
- Lead Interaction Test- performed in order to verify if the lead cable can easily enter the connector/ chamber opening without difficulty. The only way a lead would have difficulty entering the chamber is if there is a Med A adhesive leakage inside the chamber/ connector barrel.

**Table 2**
**Functional Tests for Septum A and B**




Both septums were submitted to the same process in order to draw robust conclusions concerning their performance and functionality for the intended use. The sample size consisted of all the models manufactured by the Medical Device Company in Puerto Rico and other countries where pacemakers are made.

As far as the individual sequence followed by Septum A and Septum B is concerned, Figure 2 shows the individual conditions due to individual and functional capabilities.

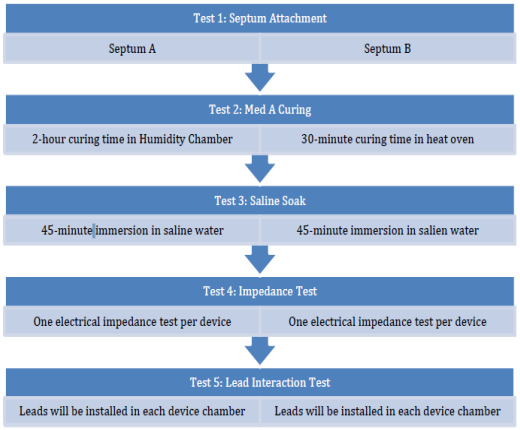



**Figure 2**
**Test Flowchart Comparison: Septum A vs. Septum B**

## PROCESS VALIDATION & EQUIPMENT QUALIFICATION METHODOLOGY

Since the data from the Engineering Test Report (ETR) concluded that that it is favorable to use Septum A not only for defibrillator manufacturing, but also for pacemaker manufacturing in company X, given the notable results of devices that passed the septum attachment test (93% with Septum A versus 70% with Septum B); the next step to follow would be to validate the new procedure for pacemaker manufacturing in Company X and to qualify the Controlled Environmental Humidity Chamber for use with the new pacemaker septum A. The Controlled Environmental Chamber is used to accelerate the Med A adhesive curing time, by providing a controlled environment at a temperature range of 37ºC ±5ºC and relative humidity range of 60% ±10% as per pacemaker procedure XXX.

## INSTALLATION OPERATIONAL QUALIFICATION (IOQ)

The Installation Qualification (IOQ) will be conducted before the Product Performance Qualification (PPQ) given that in order to validate the process, the equipment used in the process (i.e. controlled environmental chamber) must be qualified first.

### Installation Qualification (IQ)

The Installation Qualification (IQ) will be conducted to verify that the equipment is installed properly as per manufacturer's specifications, procedure XXX for pacemakers; and that all utilities/ connection requirements are available to operate the system. Supporting utilities will be verified and documented evidence will be included in the IOQ Results Report. Figure 3 below shows the Controlled Environmental Chamber used for this qualification.

**Figure 3**
**Controlled Environmental Chamber**

Table 2 below shows the Installation Qualification (IQ) Criteria used for the Chamber.

**Table 2**
**Installation Qualification Criteria**

| Utilities | Requirement |
|---|---|
| Electrical Power | Line to Neutral Voltage: 120±10% VAC(50/60 Hertz, 15Amps) |
| Electrical Ground for Safety | Presence of grounding |
| Verify Humidifier Connection | Tubing and connection free of visible cracks / defects and leaks |
| Verify Humidifier Water Level | Assure that the humidifier is filled with process water to at least 50% |
| Desiccant Air Dryer | Verify that the desiccant Air dryer material is blue |

### Operational Qualification (OQ)

The Controlled Environmental Chamber (Temperature/ Relative Humidity Chamber) will be verified for proper operation under operating parameters of 37˚C ± 5˚C and 60 ± 10% Relative Humidity. The Controlled Environmental Chamber controller will be set at this temperature and relative humidity in order to obtain their respective profiles. The operational qualification (OQ), will

provide assurance that the Controlled Environmental Chamber (Temperature/ Relative Humidity Chamber) functions as required per procedure XXX for pacemakers. Table 3 below shows the operational criteria used to qualify the Controlled Environmental Humidity Chamber.

**Table 3**
**Operational Qualification Criteria**

| Test Instructions | Expected Results |
|---|---|
| Turn Power Switch ON (Controller) | The controller should power ON. Red power indicator illuminates. |
| Humidifier and Humidity Controller both function normally. | Green power indicator illuminates on ultrasonic humidification system and steam shall appear on the upper vapor port. Humidity demand indicator (Green LED) illuminates. |
| Dehumidifier pump system functions normally. | Inlet is lower port, exhaust chamber is upper port. |
| Temperature controller and heater function | Temperature controller and heater indicator lights (yellow and amber LEDs) function. |
| Turn switch for internal circulation fan ON | Fan activates internal circulation fan. |
| Turn Light Switch ON | Light switch activates internal illuminator. |
| Turn Power Switch OFF | The machine must not operate. |

As part of the OQ, temperature and humidity consistency of the Chamber must be proved. In order to test this consistency profile tests will be conducted. The chamber must operate at 37˚C ± 5˚C and 60 ± 10% Relative Humidity. The controller will be set at this temperature and relative humidity for the profile.

Five (5) thermocouples were placed inside the Controlled Environmental Chamber. Four (4) in the corners and one (1) in the middle of Controlled Environmental Chamber as shown in Figure 4 below.

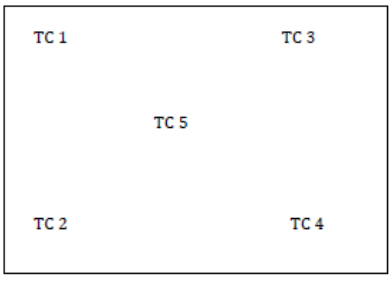



**Figure 4**
**Thermocouples Layout**

Phase I will consist of three empty chamber runs of a two-hour period. The thermocouples will gather humidity and temperature data on a per minute basis.

Phase II will consist of three loaded chamber runs where the chamber will be loaded with 59 pacemakers (Septum Drying process has a severity of "3" as per FME000. As per SOP YYY (SOP, Validation/ Qualification), for attribute data and a severity of "3" it is required a minimum sample size of 59.). Data will also be recorded on a per minute basis.

## Product Performance Qualification (PPQ)

The PPQ will consist of manufacturing the pacemaker with the new core sleeve A and the new septum A, also following the new septum attachment procedure established in SOP XXX. Figure 14 below shows the anatomy of Core Sleeve A and B; both core sleeves are made of the same stainless steel material.

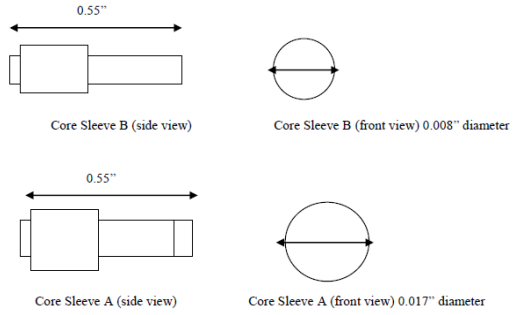



**Figure 5**
**Core Sleeve Anatomy**

The only processes that will change with the new septum A attachment procedure are:

- Mold preparation & assembly- here is where the new core sleeve A with the bigger diameter will be installed into the silicone mold where the device will be:
- Septum Attachment- the new septum A will be installed, Med A dispensing machine parameters will change to 90+/- 10 psi and sequence will be different.
- Septum Curing- new two-hour curing time in a humidity chamber.
- Quality Control (QC) Inspection-will inspect lead interaction.

The Test Rationale will be as follows: the product performance qualification (PPQ) will consist of a visual inspection that will be conducted on a microscope under 7-10x magnification. Devices must be visually inspected as per SOP ZZZ. The septum seal must be free of nicks and pits. Also, the septum slit opening must not be separated. Gauge Test and Setscrew verification will be performed as per SOP ZZZ. After new septum installation a lead interaction test must be conducted by inserting the test leads into the header samples. Afterwards, an X torque wrench must be inserted through the septum as per SOP XXX.

Acceptance Criteria for this PPQ will ensure that all 59 devices are submitted to100% visual inspection of the septums before and after the lead interaction test. All 59 samples must pass visual inspection criteria established in procedure XXX.

The visual inspection, gauge test and setscrew verification will consist of the following:
Can and header must be free of medical adhesive, cracks and bore leaks. Septum bond must be free of voids.

## RESULTS

The following sections will present the tabulated and graphical results for the Installation Qualification (IQ), Operational Qualification (OQ) and Product Performance Qualification (PPQ) of the septum attachment process and the controlled environmental chamber for the pacemaker Medical Device Company.

### Installation Qualification (IQ)

The IQ tested proper installation conditions and resources were available for the Controlled Environmental Chamber to function properly, per manufacturer and company specifications. Electrical power, ground safety, humidifier water level and equipment connections were evaluated. Table 4 in the next column shows the installation qualification results for the Controlled Environmental Chamber:

**Table 4**
**Installation Qualification Results**

| Utilities | Requirement | As Found | Pass/ Fail |
|---|---|---|---|
| Electrical Power | Line to Neutral Voltage: 120±10% VAC(50/60 Hertz, 15Amps) | 118 V | Pass |
| Electrical Ground for Safety | Presence of grounding | Grounding present | Pass |
| Verify Humidifier Connection | Tubing and connection free of visible cracks / defects and leaks | Tubing free of leaks and cracks | Pass |
| Verify Humidifier Water Level | Assure that the humidifier is filled with process water to at least 50%. | Humidifier water level filled at 60% | Pass |
| Desiccant Air Dryer | Verify that the desiccant Air dryer material is blue | Desiccant material is blue | Pass |

All criteria for the Installation Qualification were met.

### Operational Qualification (OQ)

Table 5 in the next column shows the operational qualification results for the Controlled Environmental Humidity Chamber. As can be observed, all criteria were met.

**Table 5**
**Operational Qualification Results**

| Test Instructions | Requirements | As Found | Pass/ Fail |
|---|---|---|---|
| Turn Power Switch ON (Controller) | The controller powered ON. Red power indicator illuminates. | ON with Red light illuminated | Pass |
| Green and Humidity LED Lights Functionality | Green power indicator illuminates on ultrasonic humidification system and steam shall appear on the upper vapor port. Humidity demand indicator (Green LED) illuminates. | Green power indicator illuminated on ultrasonic humidification system and steam appeared on the upper vapor port. Humidity demand indicator (Green LED) | Pass |
| Humidifier and Humidity Controller both function normally. | Humidifier and Humidity Controller both must function normally. | Humidifier and Humidity Controller both functioned normally. | Pass |
| Dehumidifier pump system functions normally. | Inlet is lower port, exhaust chamber is upper port. | Dehumidifier pump system functions normally. | Pass |
| Temperature controller and heater function | Temperature controller and heater indicator lights (yellow and amber LEDs) function. | Temperature controller and heater indicator lights (yellow and amber LEDs) function. | Pass |
| Turn switch for internal circulation fan ON | Fan activates internal circulation fan. | Fan activates internal circulation fan. | Pass |
| Turn Light Switch ON | Light switch activates internal illuminator. | Light switch activates internal illuminator. | Pass |
| Turn Power Switch OFF | The machine must not operate. | The machine did not operate. | Pass |

## Product Performance Qualification (PPQ)
## Temperature and Humidity Profiles

Table 6 below presents the range of values that the five thermocouples detected during every single minute of the three (3) empty and loaded chamber test runs that lasted 120 minutes each.

**Table 6**
**Temperature and Humidity Profile Results**

| | Run | Temperature Range (°F) | Relative Humidity Range (%RH) |
|---|---|---|---|
| Phase 1 | 1 | 33-37 | 58-61 |
| | 2 | 35-39 | 57-61 |
| | 3 | 34-38 | 59-63 |
| Phase 2 | 1 | 34-38 | 58-60 |
| | 2 | 33-38 | 58-62 |
| | 3 | 34-39 | 59-61 |

The graphs in the following page show the results for the temperature and humidity profiles in comparison to acceptable process parameters. As can be observed, all observations remained within process specifications. Figure 6 in the next page shows the Temperature Profiles for the three empty chamber runs. As can be observed there is a degree of variance among the profiles, but the temperature and humidity profiles remain within specifications regardless.

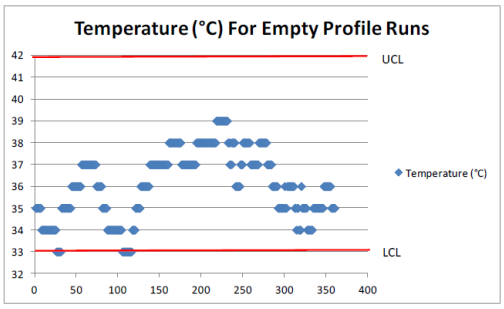



**Figure 6**
**Temperature Empty Chamber Runs**

Figure 7 in the next column shows the Humidity Profiles for the three empty chamber runs.

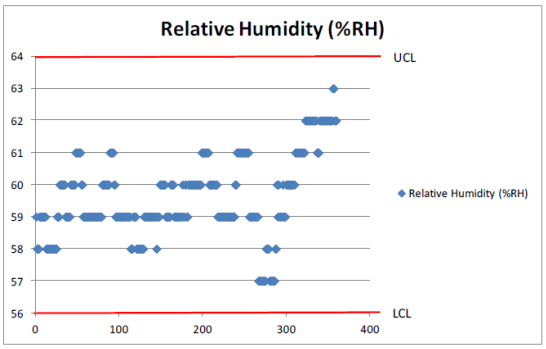



**Figure 7**
**Humidity Empty Chamber Runs**

The following graphs show the results for the temperature and humidity profiles in comparison to acceptable process parameters. As can be observed, all observations remained within process specifications. Figure 8 in the following column shows the Humidity Profiles for the three empty chamber runs.

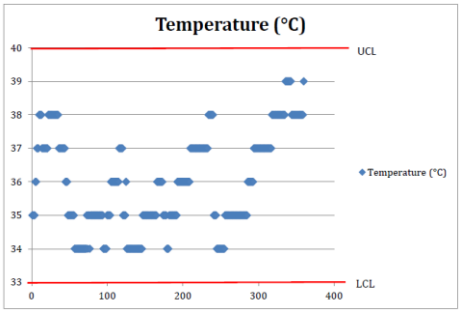



**Figure 8**
**Temperature Loaded Chamber Runs**

Figure 9 below shows the Humidity Profiles for the three empty chamber runs.

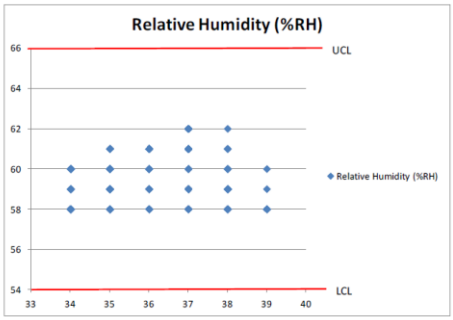



**Figure 9**
**Humidity Loaded Chamber Runs**

The red lines present the Upper Control Limit (UCL) and the Lower Control Limit (LCL) established by the process in Company X. Since the relative humidity parameters are and 60 ± 10%, that means that the limits will be defined by 54% RH as the LCL and 66% RH as the UCL. As can be observed, all temperature points gathered on a minute basis for the three runs remained within parameters and closer to the LCL than the UCL. The X-axis shows values for the amount of observations made (3 profile runs of 120 minutes/ 120 observations; 3x120=360 total observations). The Y-Axis shows the relative humidity values observed during the three empty chamber profile runs.

## CONCLUSIONS

After reviewing the results from the IOQ and the PPQ, conclusions were made concerning the Controlled Environmental Chamber and the new septum component. The conclusions are as follows:

### Installation Operational Qualification (IOQ)

After verifying the equipment functionality and the installment conditions required by the Controlled Environmental Chamber; it was observed that the equipment is not only fit for use for the Septum curing process, but it is also properly installed with the required conditions per manufacturer and process specifications. Even though this new process will reduce field complaints, it will have an economic impact caused by less efficiency, given that it will take one extra hour and a half to execute a process that originally took only thirty minutes. I propose that we investigate deeper into the situation and test whether it is viable to decrease the curing time to one hour and hopefully half an hour.

### Product Performance Qualification (PPQ)

The Product Performance Qualification (PPQ) consisted of testing a total of fifty-nine (59) pacemaker devices representing all models currently manufactured in the Puerto Rico site of Company X. All fifty-nine (59) devices passed the functional and visual tests, which qualifies the septum component fit for use for pacemaker manufacturing. Figure 10 and 11 show an example.

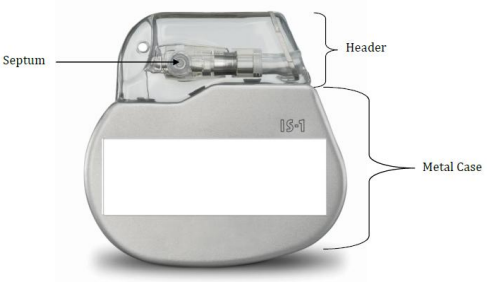



**Figure 10**
**Pacemaker Anatomy**

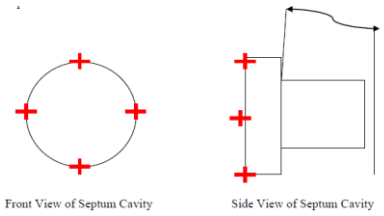



**Figure 11**
**Septum Anatomy**

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