



Memorandum

SUMMARY OF
P050023/S048, P950037/S100, P000009/S047, P070008/S028
Lumax 700/740 ICD, Lumax 600/640 CRT-D, PSW 1102.U Programmer Software
Biotronik, Inc.

EXECUTIVE SUMMARY

This PMA supplement was submitted to gain approval for a new version of the Lumax 700/740 and 600/640 devices. The sponsor is looking to approve a new SafeSync module which allows programming the device without the use of a telemetry wand for the entire session. The SafeSync module will be bundled as an accessory to the programmer. The wand is still used to initiate communication and “pair” the device to the programmer. In the amendment to the file the sponsor included a justification for not providing wireless performance data. This information is necessary since the device will perform programming of the device in the clinic. In a follow up email the requirements for wireless performance, In Band and Out Band testing, and RF Coexistence testing were included. The testing provided in the new document was deemed adequate by the consult reviewer.

The sponsor is also looking to provide an RV and LV Capture Control feature to the device. This feature uses the previously approved Automatic Threshold Management (ATM) feature to establish the Pacing Capture Threshold (PCT) and set the pacing therapy to the PCT + 1.0v (or 1.2v). The data submitted by the sponsor includes data from what the ATM feature analyzed and compared it to what was set by the clinician during the 3 month follow up. The study showed promising results and the clinician feels the data provided is adequate.

The sponsor is looking to implement a new LV pacing vector which includes an LV-tip to CRT-D can vector. Typically, for additional pacing vectors FDA requires a small clinical study to show effectiveness of the new vector. Safety is a minimal concern since the vector is setup in the clinic, and the clinician can evaluate if there is capture. The sponsor included information from the CELECSTIAL and Corox Over-the-Wire Lead Evaluation (OIVD) study. This information included followup data from patients out to 30 months with the unipolar LV threshold values. The limited data looks promising and there are no additional effectiveness concerns with the new pacing vector.

The electrical and firmware testing that the sponsor provided for the implant was initially incomplete. They have provided functional testing, but did not include any information regarding regression testing, hardware qualification, or the appropriate software documentation for the implant. In the amendment the sponsor provided additional information about their validation and verification methods for the hardware, software and firmware. In addition they have included all of the software documentation requirements from the Software Guidance Document.

The sponsor is also looking to include the Thoracic Impedance feature that was previously approved in the Lumax 5x0 device. A consult review was conducted to ensure the features were identical and that updated testing with the new implant was equivalent to the previous model. During his review he noted that the sponsor did include an updated longevity calculation for the 7x0/6x0 devices. The 7x0/6x0 device contain a different electronic module which would have different current consumption then the previous device. In the Amendment, the sponsor included updated information regarding the longevity calculations with the Thoracic Impedance feature turned on. This feature was initially approved on the 5x0 device, but the longevity was not calculated with the new HSK 4140 electronic module that is located in the 7x0/6x0 devices. The sponsor provided updated calculations and updated the labeling information.

In addition to responses to the deficiencies, the sponsor provided additional information and updates to the device and labeling. This included the following:

- Correction to the documentation for the NIPS (Non-Invasive Programmable Stimulation) parameter – The sponsor included updates for the S1-S2, S2-S3, and S3-S4 intervals for the Ventricular NIPS.
- Additional firmware update – The firm is providing an update to the firmware to correct the following two issues:
 - o DFT testing by the physician were reported as events and show up in the Home Monitoring Cardio Report
 - o Display of the IEGM is corrected to show if charging of the capacitor is terminated by the master switch and no shock is delivered
- Alternate supplier for the wand cover – The sponsor has a new supplier of the sterilized cover for the programming wand
- A new cardboard box – The new cardboard box is included due to the change to the packaging method provided in the submission. This is to allow the sterile cover to stay in place more easily.
- Update to the Lumax Family Technical Manual – This is to fix minor typo issues and only includes information for current devices. It removes information for non-Home Monitoring devices as they are no longer manufactured, along with other updates.
- Moving Clinical Studies into a separate pamphlet – All of the clinical information that was previously included in the Technical Manual will be a separate pamphlet that is included with the technical manual.

The information provided in the amendment and followup discussions with the sponsor have addressed the concerns of the review team. The sponsor provided the appropriate information for each of the concerns. The sponsor did include additional information with the amendment that had to be reviewed. While this is not typical for an amendment to a 180 day supplement, the additional information and testing provided in the amendment seem to be adequate and address the changes. Some of the changes in the amendment were minor document clarifications. The sponsor seems to have addressed all of the concerns and there are no additional concerns with this supplement.

BACKGROUND

The Lumax 700/740 (referred as to as 7x0 in this memo) and 600/640 (referred to as 6x0 in this memo) devices are based on the Lumax 500/540 (referred to as 5x0 in this memo). The main difference between the 7x0 series and the 6x0 series is the longer duration for recording AT/AF episodes in the 7x0 series of devices. Otherwise the sponsor states that they are identical.

The sponsor previously submitted a supplement to add the Thoracic Impedance (TI) feature in the Lumax 5x0 device. They are claiming that the feature in this supplement is the same as the one previously submitted for the 5x0. A consult for this file was assigned to review this feature and insure that they are equivalent. The consultant previously worked on the approval for the TI feature in the 5x0 device.

The statistical data provided in the submission is the same as that provided for the TI approval for the Lumax 5x0 device. Initially it seemed there was additional information provided. After discussion with the clinical consultant, it was deemed that re-analysis was not necessary. The sponsor also provided data from the CELESTIAL and GALAXY post approval/aftermarket clinical study which was deemed unnecessary for this submission as it was determined that the effectiveness of the TI feature is the same between the 5x0 and 7x0 devices. The TI feature does not affect safety since it does not change therapy or patient interactions.

INDICATIONS FOR USE

The Indications for Use are identical to the previously approved Lumax 5x0 ICD with only changes to the trade name of the device. It is included here for documentation purposes.

Indications for Use: The Lumax Family of Implantable Cardioverter Defibrillators (ICDs) is intended to provide ventricular antitachycardia pacing and ventricular defibrillation, for automated treatment of life threatening ventricular arrhythmias.

The Lumax 740 / 640 VR-T DX ICDs are part of a system that includes both the Kainox A+ and the Lumax 740 / 640 VR-T DX ICD devices.

The Indications for use are also identical for the CRT-D and is included here for documentation purposes.

Indications for Use: The Lumax CRT Ds are indicated for use in patients with all of the following conditions:

- *Indicated for ICD therapy*
- *Receiving optimized and stable Congestive Heart Failure (CHF) drug therapy*
- *Symptomatic CHF (NYHA Class III/IV and LVEF < 35%)*
- *Intraventricular conduction delay (QRS duration > 130 ms)*

Since the only changes to the indications for use is the change of the name there are no additional concerns.

CONTRAINDICATIONS

The Contraindications are identical to the currently marketed Lumax 5x0 device with only changes to the trade name of the lead for both the ICD and CRT-D versions of the device.

The Lumax ICDs and CRT Ds are contraindicated for use in patients with the following conditions:

- *Patients whose ventricular tachyarrhythmias may have transient or reversible causes such as:*
- *Acute myocardial infarction*
- *Digitalis intoxication*
- *Drowning*
- *Electrocution*
- *Electrolyte imbalance*
- *Hypoxia*
- *Sepsis*
- *Patients with incessant VF/VT*
- *Patients whose only disorder is bradyarrhythmias or atrial arrhythmias*

Since the changes to the contraindications do not have any changes, there are no additional concerns.

DESCRIPTION OF CHANGES

The following table shows which models the sponsor is looking to introduce in this supplement:

Produce Name	Device Type	Maximum Shock Energy
Lumax 700/740 Family of ICD / CRT-D devices		
Lumax 700 VR-T	Single Chamber ICD	30J
Lumax 700 DR-T	Dual Chamber ICD	30J
Lumax 700 HF-T	CRT-D	30J
Lumax 740 VR-T	Single Chamber ICD	40J
Lumax 740 DR-T	Dual Chamber ICD	40J
Lumax 740 HF-T	CRT-D	40J
Lumax 740 VR-T DX	Single Chamber ICD with Dual Chamber Sensing	40J
Lumax 600/640 Family of ICD / CRT-D devices		
Lumax 600 VR-T	Single Chamber ICD	30J
Lumax 600 DR-T	Dual Chamber ICD	30J
Lumax 600 HF-T	CRT-D	30J
Lumax 640 VR-T	Single Chamber ICD	40J
Lumax 640 DR-T	Dual Chamber ICD	40J
Lumax 640 HF-T	CRT-D	40J

Lumax 640 VR-T DX

Single Chamber
ICD with Dual
Chamber Sensing

40J

The following lists the new features in the 7x0/6x0 series of devices:

- RV and LV Capture Control
- SafeSync RF Telemetry (Wandless Telemetry)
- Asynchronous Pacing Modes
- Far-Field IEGM for Threshold Test
- Scheduling Periodic IEGM for Follow-up
- Advanced AT/AF Diagnostics (for 7x0 series devices only)
- Atrial NIPS
- Additional Left Ventricular (LV) Pacing Configuration
- Thoracic Impedance (TI)

The additional changes to the device include the following:

- A new analog IC and new digital IC
- New L.E.D. clipping diodes between the communication coil and the digital IC for future MR compliance
- New firmware
- Modified programmer software

The RV/LV capture control feature uses the previously approved Auto Threshold Management feature to evaluate the Pacing Capture Threshold of the device and set a safe margin (either 1.0v or 1.2v) above the threshold. The data provided by the sponsor shows that when set to 1.2v the device achieves 100% capture in the RV and LV.

The SafeSync RF Telemetry is an added accessory to the ICS3000 and Renamic programmer. The SafeSync module contains the hardware and wand connection to establish a connection with the implant and provide telemetry data. This module will allow the device to be interrogated without requiring a wand to be held to the device. The SafeSync module connects with the programmer through a USB connection. The module contains the hardware to communicate with the implant over the Medical Implant Communication System (MICS) frequency band and over GSM/UMTS/WLAN. The communication using the GSM/UMTS/WLAN system is not yet implemented and the firmware for the SafeSync module does not enable it. Therefore, this feature is “locked out” for US devices and requires a firmware update to add this functionality. The following tasks may be completed using the SafeSync module:

- Conduct sensing, pacing threshold and impedance tests
- Interrogate data of the implanted device such as program parameters, recorded statistical data and episodes, as well as real-time IEGMs
- Display, print-out, save and export data of the implanted device for analysis and reporting purposes
- Transferring parameters to the implants

The additional asynchronous pacing modes are for use during medical procedures such as cautery. They introduce the VOO, which provides asynchronous pacing in the ventricle, and DOO, which provides pacing in the atrium and ventricle with a fixed AV delay for conduction, pacing modes.

The 7x0/6x0 device introduces the automatic use of Far-field IEGM for threshold testing. This is in addition to the already approved near-field IEGM, conventional surface ECG, and leadless ECG.

The new device will also enable the ability to schedule remote monitoring transmission dates using the programmer. The programmer will setup 5 calendar dates with a minimum lab of 20 days between any two selected dates. After the 5 calendar dates have passed, the standard period of 30 day periodic IEGM will be enabled

For the 7x0 series devices only, there is an increase in the ability to record longer pre-history of atrial episodes. Currently, the device is can record up to 30 seconds of data. After this update, the device will be able to record up to 1 minute of information.

Atrial Non-Invasive Programmable Stimulation (NIPS) will be available in the both the 6x0 and 7x0 devices. This allows for manual stimulation of the atrium via the programmer.

This submission proposes a new Left Ventricle pacing vector. This vector will be from the LV-tip to CRT-D can and is only available for bipolar and unipolar HF-T devices.

The sponsor is looking to approve the Thoracic Impedance measurement system that was originally approved in the 5x0 Lumax devices. This system is exactly the same as the previous version, however it is running on updated Analog and Digital ICs.

BIOCOMPATIBILITY/MATERIALS

The sponsor states that all of the materials for the Lumax 7x0 and 6x0 devices are identical to the previous Lumax 5x0 pulse generator. They state that no other colorants, materials, or coatings have been added to the case and that the manufacturing process (b) (4) is also the same.

There is no suggestion in the submission that the patient contacting materials for the proposed device is different then the Lumax 5x0 series of devices. All of the device changes are to either the software or internal hardware of the device. Since the device follows the same manufacturing process with the same materials, there are no further concerns with Biocompatibility or materials.

SOFTWARE

Implant Software/Firmware

Version: ROM FW version 2.3 – RAM FW version 1.0.1
Level of Concern: Major (This is appropriate for this type of device and is consistent with other similar devices)

	Yes	No
<p>Software/Firmware Description:</p> <p>With this PMA Supplement, BIOTRONIK is also introducing a ROM firmware update for the Lumax 700/740 and 600/640 family of ICD and CRT-D devices. The firmware of the Lumax 7x0/6x0 devices is stored in the ROM and RAM of the updated digital IC "CIC_1". The sponsor states that the ROM firmware is identical in functionality of the ROM firmware in the Lumax 5x0 series of devices. The ROM covers the following features:</p> <ul style="list-style-type: none"> • Back up pacing • VF detection • Delivery of defibrillation shocks with maximum energy • Communication of the implant with the programmer and with the CardioMessenger II/II-S Home Monitoring patient device • The master switch • Manual emergency shocks. <p>The RAM implements the clinical functionality of the device and covers the following features:</p> <ul style="list-style-type: none"> • Bradycardia therapy • VT/VF detection • Atrial detection • Ventricular therapy sequences • Tachycardia therapy • EP test functionality • Holter and statistics • Home Monitoring • EOS detection and programmer communication <p>And the following additional features specific to the 7x0/6x0 devices:</p> <ul style="list-style-type: none"> • RV & LV capture control, • SafeSync Telemetry • Far-Field IEGM for threshold test asynchronous pacing modes • Advanced AT/AF Diagnostics • Atrial NIPS • Additional LV pacing configuration • Scheduling remote follow-ups <p><i>REVIEWER COMMENTS: The sponsor has stated that their testing methods for the device follow a three tier approach. This testing environment covers both</i></p> <div style="background-color: #cccccc; height: 150px; width: 100%; margin-top: 10px;"></div>	X	

(b) (4)

<p>Device Hazard Analysis:</p> <p>The sponsor did provide a device hazard analysis for the device firmware in their Risk Analysis document (RAN-111-175). The risk analysis plan is one provided for the entire system.</p> <p><i>REVIEWER COMMENTS: The documentation for the device firmware for the ROM and RAM seems to be adequate. It includes risk associated with the entire device and therefore addresses software concerns as well. There are no further concerns with this section.</i></p>	X	
<p>Software Requirements Specifications:</p> <p>The sponsor provided the Software Requirements Specification for the device firmware for both the ROM and RAM.</p> <p><i>REVIEWER COMMENTS: The documentation for the Software Requirements Specification for the ROM and RAM seems to be adequate. The sponsor did not provide documentation in the original submission and only included document numbers in the amendment. Further contact with the sponsor yielded the translated version of the document. After review of the document it seems the requirement specification is adequate and I have no further concerns with this section.</i></p>	X	
<p>Architecture Design Chart:</p> <p>The sponsor provided the Architecture Design Chart for the device firmware for both the ROM and RAM.</p> <p><i>REVIEWER COMMENTS: The documentation for the Architecture Design Chart for the ROM and RAM seems to be adequate. The sponsor architecture seems to support a method for keeping US and OUS features separate and locked out. There are no further concerns with this section.</i></p>	X	
<p>Design Specifications:</p> <p>The sponsor provided the Design Specification for the device firmware for both the ROM and RAM.</p> <p><i>REVIEWER COMMENTS: The documentation for the design specifications for the ROM and RAM seems to be adequate. There are no further questions or concerns with this section.</i></p>	X	

<p>Traceability Analysis/Matrix:</p> <p>The sponsor provided a Risk Management Plan which links possible hazards to mitigation measures and the appropriate verification activity. The document (RMP-115-034) contains mitigations for the programmer, hardware, and implant firmware.</p> <p><i>REVIEWER COMMENTS: The documentation for the Traceability Analysis for the ROM and RAM seems to be adequate. They have provided risks from their risk analysis, what mitigation measures were taken, and the appropriate verification activity document number. The mitigations and testing seem to be appropriate and I do not have any further concerns with this section.</i></p>	X	
<p>Development Environment:</p> <p>The sponsor provided documentation for the development environment for the device firmware for both the ROM and RAM. The sponsor states that the implant software represents a modification of he previously approved devices and utilizes the same development environment.</p> <p><i>REVIEWER COMMENTS: The description of the development environment seems to the complete. They have provided an overview of the life cycle for the development of the firmware. The sponsor states that this is the same as previously approved devices. There are no further concerns with the development environment.</i></p>	X	
<p>Verification & Validation Testing:</p> <p>The sponsor provided verification and validation testing for the device as part of the overall Verification and Validation Testing for the device. This testing included package, mechanical, shipping, and other tests.</p> <p><i>REVIEWER COMMENTS: The documentation for the testing for the firmware is mixed in with the hardware validation of the device. It is difficult to parse out the specific testing of the firmware or if they have done any regression testing of legacy features. In the amendment, the sponsor provided an overview of their testing, verification, and validation environment. This included the three tier approach described in the firmware description section of this table. This approach seems to cover all functions of both the hardware and firmware. They have conducted the entire range of testing for the device. The verification and validation testing of the device included brady and tachy testing, backup mode testing, accelerometer testing, threshold testing, ERI behavior, and therapy testing. The testing looks to be complete and shows that functions of the device meet the specifications. There are no further concerns with this section.</i></p>	X	
<p>Revision Level History:</p> <p>The sponsor provided the Revisions Level History for the device firmware for the ROM and RAM. They included a list of documents that have each revision listed.</p> <p><i>REVIEWER COMMENTS: The documentation for the device firmware for the ROM and RAM is adequate there are no further concerns with this section.</i></p>	X	

<p>Unresolved anomalies:</p> <p>The sponsor describes two anomalies in the device firmware. Both anomalies are rated as low significance and one anomaly is observed as a rare event.</p> <p><i>REVIEWER COMMENTS: The documentation for the device firmware for the ROM and RAM seems to be adequate.</i></p> <p><i>One anomaly is due to the transmission date for periodic IEGM messages being off by one day. The sponsor states that there is no data loss and that there is a low probability of occurrence. Since the data is off by one date, the user may adjust the date if this anomaly occurs. Also, since there is no data loss I do not see this being an issue.</i></p> <p><i>The second anomaly states that the Event Counter Statistics may be off with single counts of Vx events. They state that the printout is incorrect and that this is only diagnostic information without any risk of incorrect diagnosis. The sponsor states that this has a low probability of occurrence.</i></p> <p><i>Since there is a very low probability of these anomalies and that they do not impact safety and effectiveness, there is no additional concern. This section seems to be complete and there are no further concerns.</i></p>	X	
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Programmer Software

The sponsor has updated the programmer software to include the ability to recognize the new Lumax devices in this submission and to use the new SafeSync module. They are updating the software from the previous PSW 1101.U.

Version: ICS3000 and Renamic Programmer – PSW 1102.U		
Level of Concern: Major (This is appropriate for this type of device and is consistent with other similar devices)		
	Yes	No
Software/Firmware Description:		
The sponsor is looking to add the following features:		
<ul style="list-style-type: none"> • Addition of Lumax 7x0/6x0 device families • Support wandless telemetry and the SafeSync Module (External Communication Module) • Asynchronous Pacing Modes • Display of Far-Field IEGM • USB Barcode Scanner for scanning lead information • Scheduling periodic IEGM for Follow-up • Advanced AT/AF Detection • Atrial NIPS • Additional LV pacing configuration • Display of Thoracic Impedance • Support language selection English (JP) • Bug fixes for global applications 	X	
<i>REVIEWER COMMENTS: The addition of features to the programmer is congruent with the additions to this submission. The software information for the programmer is properly arranged. And I do not have any questions regarding the software description.</i>		
Device Hazard Analysis:		
<p>Biotronik has provided programmer software device hazard analysis in Appendix 1 and a risk analysis in Appendix 2 of the submission. They also included a summary of the most severe hazards and risks in section 11. The risk analysis has been updated for Lumax 7x0/6x0 which covers the changes included in this submission.</p> <p>REVIEWER COMMENTS: The risk analysis is appropriate for this type of system. All identified system hazard scenarios have been mitigated or are at an acceptable level of risk.</p>	X	

<p>Software Requirements Specifications:</p> <p>The sponsor has provided the Software Requirement Specifications (SRS) for the programmer which includes the requirements for the 1102.U, Tach50 programmer, Global Components Extensions, and GPMI Bootloader (SafeSync Module). This includes the lock-out features for OUS features.</p> <p><i>REVIEWER COMMENTS: The requirements appear to adequately define the software functionality associated with the implant. The requirements describe the user requirements that the system must meet and the description of the system features and components that satisfy these requirements. The software requirement specification defines functionality, response to inputs, and external interfaces. The information contained and provided is adequate.</i></p>	X	
<p>Architecture Design Chart:</p> <p>The architecture design chart is included in Appendices 85-89. This includes the design for the ICS3000 global components, the new Tach50 (this submission), updates, and wireless wand firmware.</p> <p>REVIEWERS COMMENTS: The architectural information provided for the implant seems adequate. The changes made in this submission build on the previous architecture and do not depart from it in any major way. The sponsor provided information is adequate.</p>	X	
<p>Design Specifications:</p> <p>The software design specifications are included in Appendix 77.</p> <p>REVIEWER COMMENTS: The sponsor seems to have provided a complete Design specification document for the programmer software. The sponsor provided information is adequate.</p>	X	
<p>Traceability Analysis/Matrix:</p> <p>The traceability analysis provided in section 11.7 table 33 covers the changes to the programmer software, states whether it is clinically relevant, if it poses a risk, and the test report to validate the feature.</p> <p><i>REVIEWER COMMENTS: This information demonstrates that the changes were tested during verification and the sponsor provided information is adequate.</i></p>	X	
<p>Development Environment:</p> <p>The overall software development environment has not changed as compared to version 1101.U for the changes / enhancements in this software version.</p> <p>REVIEWER COMMENT: The sponsor provided information is adequate.</p>	X	

<p>Verification & Validation Testing:</p> <p>The sponsor has provided the verification and validation test results for final version of programmer software. The test plan included functional testing of the programmer with the implant and SafeSync Module. Also, included testing for all of the changes. The summary was provided in section 11.9.1 Table 34.</p> <p><i>REVIEWER COMMENT: The Software Verification Reports were reviewed and the results look appropriate. The testing was done in-line with their usual testing for each module and seems complete. They have included their standard testing along with non-regression testing. This seems acceptable.</i></p>	X	
<p>Revision Level History:</p> <p>The sponsor has provided a revision level history for the proposed software. They state that the “U” designation is intended for US versions of the program and “A” designation for OUS. The US version includes the appropriate lockouts for OUS features and the revision level history includes all of the changes made to the software.</p> <p><i>REVIEWER COMMENTS: The sponsor provided information is adequate.</i></p>	X	

Unresolved anomalies:

A table in the submission states that there are still 12 unresolved anomalies that apply to the US version of the software. The sponsor has identified 2 High risk anomalies and 1 medium risk. The medium risk anomaly is associated with a drop in RF communication when a long episode is printed with high feed paper. The high risk anomalies are associated with a reduction in pacing rate during a reformation period. The second high risk anomaly states that an ineffective pacing program may continue in the threshold test if the device is borderline from the programming distance.

REVIEWER COMMENT: The drop of RF communication is said to have very low probability of occurrence and seems that the only issue would be the device has to renegotiate communication with the programmer.

The two high risk anomalies seem to be a big issue. The sponsor states that for dual chamber devices in DDDR mode the pacing may drop to the post shock pacing level during a reformation activity. If the patient has an elevated heart during the reformation, there could be a possible problem. The sponsor states that the post shock pacing rate could be set to 70ppm but does not provide any indication to the labeling to physicians discussing this issue. The following deficiency will be addressed to the sponsor regarding this anomaly.

In your submission you provide a list of anomalies related to the latest version of the programmer software. You include two anomalies that are rated as “High” significance, but only provide limited detail regarding postponing them. From the descriptions provided it seems that these issues are a significant risk to patients. Please provide the additional information below.

- a) For issue ID #19607 you state that a device may drop the pacing rate to a post shock pacing level during a reformation activity. This reformation activity is assumed to be a capacitor or battery reform. It is not indicated in your description how often this will occur and what the worst case scenario is for the patient. Also, please provide the longest possible duration for this under pacing event and which chambers would be affected. Please provide additional information as to how often this may occur and what effects it could have on the patient. Also, please provide how the post shock pacing level is determined.
- b) For issue ID # 17903 you state that a device during threshold testing may continue to pace at an ineffective pacing threshold if the device is being programmed at a distance that is close to the loss of communication. You state that lifting the wand will immediately revert the device back to previous permanent pacing program and capture condition. As this programming state is during a clinician visit, please identify if this could occurring during the use of the SafeSync Module. If it cannot occur with the SafeSync Module please indicate why. Also, please provide how often this anomaly can occur and additional information or mitigation taken to reduce the chance of this anomaly
- c) In your submission you have only listed new anomalies in the 1102.U software. Please provide a list of any previous anomalies that have not been fixed which may interact with the proposed version of the software. Please include information such as severity, possible occurrence rate, possible mitigations, and a detailed justification for acceptance.

X

REVIEWER COMMENTS: The sponsor responded stating that these anomalies are legacy anomalies and does not apply to the Lumax 7x0/6x0 devices. There are no further concerns with this deficiency.

EMC/EMI TESTING

The sponsor is adding a module to the ICS3000 programmer called SafeSync. This module is used to communicate with the implanted device through a Radio Frequency (RF) link in the 402-405 MHz Medical Implant Communication System (MICS) frequency band. The implanted device will also communicate with the Renamic programmer, which has the RF module already integrated. In the submission Mr. Seidman states that it is unclear if the Renamic programmer went through EMC and EMI testing. The Renamic programmer may have been approved prior to utilization of the built in RF module. Since it is not clear if the Renamic programmer had an EMC/EMI evaluation, this information will need to be evaluated to establish safety and effectiveness of the device. Also, Mr. Seidman did not find information regarding the use of the SafeSync module as a system with the ICS3000 programmer. Since the device is used as a system, it should be evaluated as such. The final concern regarding the programmer is to the performance of the device with other transmitters. There is no information in the submission regarding wireless coexistence testing of the ICS3000, Renamic programmer, and SafeSync Module.

The sponsor provided the information requested from the EMC/EMI consult. They gave an adequate summary of the testing performed with the Renamic programmer and SafeSync module. Since the SafeSync module connects with both the Renamic and ICS 3000 in the same manner, both programmers did not have to be tested. Also, the Renamic and ICS 3000 went through EMC/EMI testing prior to their approval. Since all devices pass the EMC testing there are no additional concerns with this deficiency.

The sponsor provided all of the requested information regarding wireless coexistence. They conducted the appropriate testing, which included testing in-band interference with 3 other devices operating in the same frequency band (in-band testing). They included comprehensive wireless testing showing that the communication link is self-recoverable. The testing provided is adequate and there are no further questions or concerns regarding this deficiency.

ELECTRICAL VERIFICATION AND VALIDATION TESTING

The sponsor provided a general section for hardware verification and validation testing. The device uses a new Digital IC (IC CIC_1) and Analog IC (IC DCAC_3). There is also an addition of two protection LEDs added as clipping diodes between the communication coil and CIC_1. The sponsor states that this is done for future MR Conditional devices.

The sponsor provided additional information in the amendment to the file. The information provided vendor information, inspection process, and part qualification information. There are no further concerns with this deficiency.

They currently are not seeking MR Conditional claims in this submission. The new electronic module in the Lumax 7x0/6x0 device is referred to as the HSK 4140. The previous design in the 5x0 device is referred to as the HSK 4130. The sponsor states that these are the only changes to the hardware of the device and that all other components (housing, connectors, HV capacitors, batteries, etc.) are identical to the 5x0 series of devices.

The sponsor has provided Table 24 and 25 which contains all Verification and Validation tests that were performed on the device. The Validation testing included testing such as packaging and environmental preconditioning, visual inspections, storage, brady functions, threshold management, and tachy detection with and without therapy.

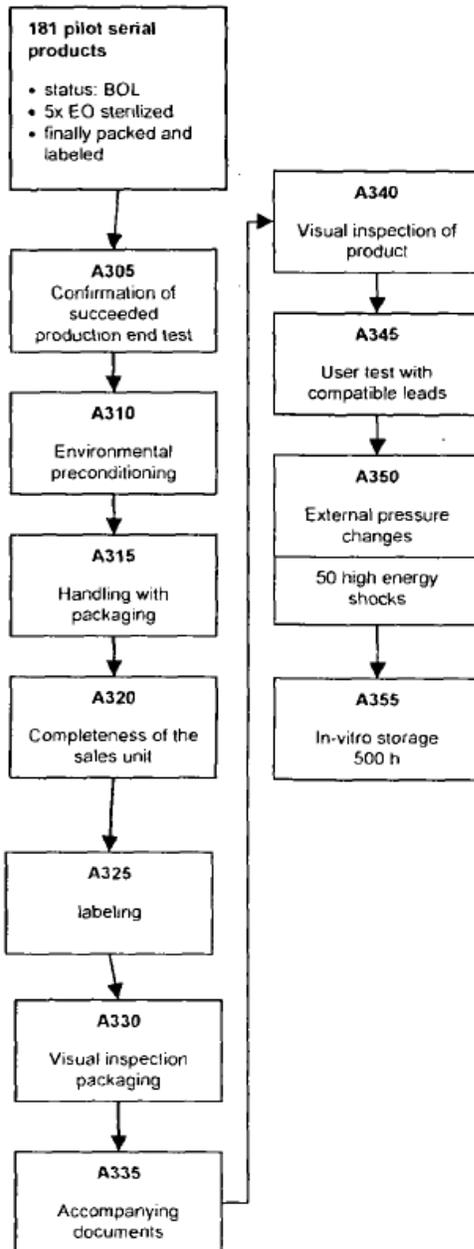
The Verification testing included testing such as success of sterilization, release of particles during use, biocompatibility (which was taken from the 5x0 devices), use of cautery in saline, protection from mechanical forces, accelerated aging, capacitor reform, EMI, ESD, and Internal/External defibrillation protection among others.

After review of the validation testing it seems the appropriate verification, validation, and part qualifications have been completed for this device. The testing of the device is congruent with other new release devices from the sponsor and seems to be appropriate.

During the first round of verification and validation testing performed by the sponsor it was found that 2 devices failed the elevated pressure test. The problem was root caused to damage that occurred during the Environmental Preconditioning phase. It was determined that packaging did not provide enough cushioning for the devices. A revised package was established and the devices were subject to the Environmental Precondition phase 3 times. The preconditioning included the following:

- Protection from temperature, pressure and moisture changes
- Transport test
- Drop Test

After this was completed there was a visual inspection of the packaging, handling of packaging, completeness of sales unit, and final visual inspection of the product. The sponsor does not state if there were any electrical tests done after this routine. The original failure occurred towards the end of the validation flow chart which is provided below:



Since the testing that found the failure (A350 in the chart above) was done later in the validation process the stress of testing may have brought marginal devices to failure. The retested devices may have exhibited the same failure. The retested devices only required visual inspection. It seems that the full validation cycle should have been completed on the repackaged devices to ensure that if the same device failure occurred it would be caught by testing.

The Environmental Pre-Conditioning test is the third test in their packaging test protocol. They reevaluated the packing material and placed the sterile blister pack between the labeling packet and the sterile cover. This provides additional cushioning of the device. The sponsor conducted the pre-conditioning tests an additional 3 times with the new

configuration and completed the rest of the protocol of testing. The testing was successful and all devices passed. The revalidation was performed with the same sample size as the original testing. The revalidation of the testing seems appropriate and the new method of packaging seems to be appropriate. There are no further concerns with this deficiency.

The verification and validation testing provided in the submission seems to combine all testing for the device. It is difficult to parse out which testing was done exclusively for the hardware, firmware, and software. It seems that all testing was done from a functional standpoint meaning that if each function worked as expected, all of the underlying systems must function as well. While this system seems to be appropriate it does raise concerns about various software anomalies that are detected and which functions have been testing. There does not seem to be a set of “regression” tests that are performed for each version of hardware/software followed by testing of new features. This clarification should be made to ensure that there are no reoccurring problems.

The sponsor provided an adequate table which included the pass/fail criteria. They also included a description of their tiered validation and verification strategy. This tiered approach seems to be adequate in covering the functionality of the device. The testing of the hardware and firmware takes place simultaneously while providing coverage of their Software Requirement Specifications. Since this covers the entire functionality of the device I do not see any additional concerns with the testing provided. Their response is adequate and I do not have any further concerns.

Thoracic Impedance Evaluation

The sponsor previously submitted an application for the TI feature in a supplement for the 5x0 series of devices. The consult was assigned to ensure that this feature is implemented the same in the 7x0/6x0 devices. After review, the consultant reviewer found that the features were equivalent. However, he did note that the battery longevity calculations were done based on the 5x0 series device which incorporates a slightly different electrical module compared to the 7x0/6x0 device. The change in the electrical module may affect battery longevity and should be addressed by the consult. In addition the he noted that in a separate calculation for battery longevity using the 7x0/6x0 device that the TI feature may not have been enabled.

The sponsor tested the Lumax HF-T device to find the additional current consumption of the Lumax 7x0/6x0 device. This is appropriate since the hardware is shared between all Lumax 7x0/6x0 devices. The testing is appropriate for this submission since they used the actual subject device. Prior information was collected from the Lumax 5x0 device did not accurately represent the Lumax 7x0/6x0 device. Since the updated information is from the subject device and they have included the updated current consumption and device longevity in their user manual there is no additional concern for this deficiency.

The sponsor stated that the information submitted in the original submission was not conducted with the TI feature enabled. The testing was done prior to the approval of the TI feature. Once the sponsor gained approval of the TI feature in the Lumax 5x0 device

series they conducted the appropriate testing with the Lumax 7x0/6x0 device. The information was included in the amendment and looks to be appropriate for the device and feature. There are no further concerns with this deficiency.

PACKAGING, SHELF LIFE, AND STERILIZATION

According to the submission the packaging method is identical to the previously market released Lumax Family of ICDs/CRT-Ds (Approved P050023/S1, December 7, 2006). The sponsor states that the sterile packaging materials fulfill the requirements for a non-toxic reaction with enclosed products. The sponsor also states that the Shelf Life of the device is 16 months which is consistent with current Lumax devices. The sponsor has performed long-term sterility testing on the packaging utilized for maintaining sterility of the ICD/CRT-Ds. The devices are sterilized with (b) (4). The sponsor states that the environmental controls, sterilization process, and sterility assurance procedures are identical to those used for previous Biotronik ICDs/CRT-Ds.

Although the sponsor indicates that there are no changes to the packaging in section 13 of the submission, they state that during validation and verification of the implant hardware they added additional padding. In section 10.1 of the submission they state the following:



The information provided is adequate. The sponsor only changed the ordering of the packaged material and this does not affect the sterilization of the device or packaging. There are no additional concerns with this deficiency.

LABELING

The labeling section was reviewed by the clinical consultant. He did not find any major issues with the labeling. His only concern is the inclusion of additional data required for the new LV pacing vectors which are described below.

MANUFACTURING DATA

No Manufacturing data was provided in this submission. The sponsor states that the device uses the same method of manufacturing as current devices. The changes described in this submission seem to agree with this statement.

ANIMAL STUDIES

There were no animal studies presented.

CLINICAL DATA

For this submission the sponsor is seeking approval for the following clinically relevant features:

- RV and LV Capture Control
- Asynchronous Pacing Modes
- Far-Field IEGM for Threshold Test
- Scheduling Periodic IEGM for Follow-up
- Advanced AT/AF Diagnostics
- Atrial NIPS
- Additional Left Ventricular (LV) Pacing Configuration
- Thoracic Impedance (TI)

The above features and the labeling submission was reviewed by a clinical consultant. The clinical consultant found the submission to be mostly approvable. The RV and LV capture control feature utilizes the previously approved Automatic Threshold Management (ATM) feature where the device intermittently collected Pacing Capture Threshold (PCT) data. The RV and LV Capture Control feature analyzes the PCT and adjusts the output to either PCT+1.2v or PCT+1.0v. The safety margin of 1.2v or 1.0v is set independently for the RV and LV and is selected by the physician. He notes in his review that RV capture must be ensured, as the patient may pass out or even die if the device is unable to capture. LV capture, while still very important, is not required for survival. The sponsor provided significant clinical data to show the safety and effectiveness of the ATM feature. Since the ATM feature assessed PCT, the sponsor was able to compare that output to the PCT set by the clinician. The study included 111 patients from 20 OUS sites and compared the two PCT levels. The average difference of PCT at 3 months was 0.02 +/- 0.18v. The data shows that the feature would provide capture 100% of the time with the output adjusted to the ATM PCT + 1.2v and 99.7% with the output adjusted to ATM PCT + 1.0v. The clinical consultant notes the very good agreement of the ATM PCT and the clinician assessed PCT for the RV. For the LV study there were 44 pairs of data and the study showed capture 100% of the time with the output adjusted to ATM PCT + 1.2v and 99.7% with the output adjusted to ATM PCT + 1.0v. The average difference of the PCT at 3 months was 0.06 +/- 0.35v. The sponsor also included data from the CELESTIAL and GALAXY post approval study. This data included 1199 RV pairs and 184 LV pairs. The clinical consultant states that it was very rare for disagreement to be large in the RV and uncommon in the LV. He states that as long as the engineering review shows that this feature functions as intended, RV and LV Capture Control does not add significant clinical risk.

The sponsor is also seeking approval for an additional LV pacing configuration. The new pacing vector is from the LV tip to the CRT-D can. The sponsor has not provided any performance data to support the addition of this pacing vector.

Typically some performance data to show that the pacing vector is effective is required. A deficiency was drafted by the clinical consultant and I revised the deficiency so that it was in line with previous deficiencies sent to other sponsors.

The sponsor is looking to include a Thoracic Impedance (TI) measurement feature. The sponsor previously submitted this feature for their Lumax 5x0 series of devices (P050023/S047) and state that this feature is exactly the same. The clinical consultant notes that the data submitted does not show any adverse events with this feature enabled. He notes that the impulse delivered for this feature is delivered by the approved Painless Shock Impedance feature and that the stimulation is not clinically concerning. Since this feature only reports the TI of the patient and does no special manipulation of the data, no clinical data is needed. Another consultant reviewed this information to ensure that the implementation of this feature is consistent with the previously approved TI measurement feature. His review is summarized above in this report.

The rest of the new features in this device are relatively mild updates. The clinical consultant did not find any clinical risks associated with the updates and felt that as long as they were functional from an engineering perspective, that he had no further concerns.

Additional information is needed for the new pacing vector. This information has been requested from other sponsors when they would like to introduce a new vector. The language for the deficiency was revised to be more in line with what was sent to other sponsors. Review of the TI feature found that the feature was implemented the same as it was for the 5x0 series of devices. However, the consultant noted that the power consumption information provided was from the 5x0 series device which uses a slightly different main board compared to the 7x0/6x0 device. The sponsor did not provide any justification as to the equivalency for the two devices.

The information provided in response to this request seems to be adequate. The PCT data for the device stayed consistent and were in an appropriate range. The data provided shows that the PCT for the new vector was grouped together for all leads provided in the data. The information provided seems to show that the effectiveness of the lead should not be a concern. As was previously establish in the first round review, safety is not a concern due to the normal testing procedure during implant and follow up. There are no additional safety or effectiveness concerns with this pacing vector and no additional concerns for this deficiency.

CONCLUSION

The sponsor has provided testing to show functionality of the device and has adequately responded to all of the deficiencies. The amendment included efficacy data for the new pacing vector and updated device longevity calculations based on the new hardware platform. The sponsor provided adequate performance data for the wireless coexistence testing and EMC/EMI testing. There are no additional concerns with this submission.