Northeastern University
College *of* Professional Studies

Regulatory Strategy: Aveir™ VR Leadless Pacemaker System

Winter 2024 - Term Assignment

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RGA 6202: Medical Device Development: Regulatory Overview

(CRN: 20049, SEC 01 Winter 2024 CPS)

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I. Scope

Product Name	**Aveir™ VR Leadless System**
Product Description	A leadless pacemaker system designed for patients with bradycardia, providing rate-modulated pacing without the need for traditional leads. The system consists of the following: **1. Aveir™ Leadless Pacemaker**  **2. Delivery System Catheter**  **3. Aveir™ Link Module.**  ***Implantation procedure***: A small incision will be made at the top of patient's leg on the groin to gently pass the implant tool and the leadless pacemaker. The catheter will then guide the leadless pacemaker up through the femoral vein to enter the heart. Once inside the heart, the leadless pacemaker is carefully attached near the bottom of the right ventricle. Fluoroscopy (a type of X-ray) used as a guide. The leadless pacemaker is then wirelessly connected using the link module computer programmer to confirm if it is in a good place to deliver the therapy by using device settings as per needs.

II. Name of Device

Generic Name	**VR Leadless Pacing System; Implantable pacemaker pulse generator**
Trade Name	**Aveir™ VR Leadless System**

	Class	Rationale
Device Classification	**Class III Medical Device**	The Aveir™ VR Leadless System falls under the classification of a Class III medical device due to several reasons: ▪ It serves a critical role in either sustaining or supporting life. ▪ The device poses significant risks, potentially leading to severe complications if not utilized correctly. ▪ Prior to approval, extensive clinical trials/studies are necessary to establish the device's safety and effectiveness, weighing its benefits against potential risks. ▪ Its complexity restricts its use to trained healthcare professionals experienced in its intended applications. ▪ The insertion procedure involves greater invasiveness compared to other medical devices, requiring entry into the heart through cardiotomy. Considering these factors, the Aveir™ VR Leadless Pacemaker System is subject to the strictest regulatory oversight by the FDA. Hence, it is categorized as a Class III medical device and must undergo premarket approval (PMA) processes to confirm its safety and efficacy before it can be marketed and distributed commercially in the United States.

	Number	Description/Term
CFR Device Classification	**21 CFR 870.3610**	Aveir™ VR Leadless Pacemaker System is implanted in the human body and functions similarly to traditional pacemakers, it fits within the scope of the following in detail: **21 CFR PART 870** -- Cardiovascular Devices **Subpart D** - Cardiovascular Prosthetic Devices **Sec. 870.3610** Implantable pacemaker pulse generator.

III. Product Description

Manufacturing Site

Abbott Medical
15900 Valley View Court Sylmar,
CA 91342
+1 818 362 6822

Country of Origin

United States of America

Sterilization Information

The Aveir Leadless Pacemaker is an implant device and provided sterile for single use only. The Aveir Delivery Catheter is also, provided sterile and for single use only. Both devices are sterilized using ethylene oxide. The sterilization cycle was validated to meet the minimum Sterility Assurance Level (SAL) of 10-6. The Aveir Link Module is an external non-sterile medical device.

IV. Indications for Use and Intended Use

1. The Aveir™ VR Leadless Pacemaker is indicated for patients with bradycardia, a condition characterized by a slower than normal heart rate. It is suitable for patients with normal sinus rhythm who experience infrequent episodes of A-V block or sinus arrest. The device is also indicated for patients with chronic atrial fibrillation (AFib) who require single-chamber ventricular pacing and for those with severe physical disabilities who may not tolerate traditional pacemaker implantation.
2. Rate-Modulated Pacing: Rate-modulated pacing is a feature of the Aveir™ VR system that allows the pacemaker to adjust the pacing rate based on the patient's physical activity. This is particularly beneficial for patients with chronotropic incompetence, a condition where the heart does not appropriately increase its rate during exercise. The rate-modulated pacing ensures that patients receive appropriate pacing support during physical activities, enhancing their quality of life and overall cardiovascular health.
3. MR Conditional Safety: The Aveir™ VR Leadless Pacemaker is MR Conditional, meaning it is safe for patients to undergo magnetic resonance imaging (MRI) under specific conditions. This is a critical advantage for patients who may require diagnostic imaging during the lifetime of the device.

V. Contraindications

The use of Aveir Leadless Pacemaker (LP) is contraindicated in these cases:

- Presence of an Existing Pacemaker or ICD: Patients who already have an implanted pacemaker or implantable cardioverter-defibrillator (ICD) may not be suitable candidates for the Aveir™ VR Leadless Pacemaker due to potential interactions between devices.
- Severe Venous Occlusion: Patients with severe occlusion of the femoral veins or inferior vena cava may not be able to undergo the implantation procedure, which typically involves vascular access through these veins.
- Active Infection: Patients with an active systemic infection or sepsis should not receive an implantable device until the infection is adequately treated and resolved to prevent the risk of device-related infection.
- Hypersensitivity to Device Materials: Patients with known hypersensitivity or allergic reactions to materials used in the construction of the Aveir™ VR Leadless Pacemaker, such as the device casing or battery, should not receive the device.
- MRI Incompatibility: While the Aveir™ VR Leadless Pacemaker is MR Conditional, patients with specific medical conditions or implanted devices that are not compatible with MRI should avoid this pacemaker or consult their healthcare provider for further evaluation.

VI. Strategic Business Strategies

Sr. No.	Known Submission Risk	Planned Mitigation
1.	**Implantation Procedure**: The minimally invasive procedure for implanting the Aveir™ VR Leadless Pacemaker carries inherent risks such as vascular complications, bleeding, or infection.	**Clinical Testing**: Rigorous premarket clinical testing to evaluate the safety and efficacy of the device, identified potential risks, and established appropriate use guidelines. The Leadless II Study - Phase 2 met the pre-specified performance goals for both the confirmatory safety (freedom from serious adverse device effects) and effectiveness (acceptable pacing and sensing) endpoints. These results showed that the Aveir Leadless Pacemaker System is safe and effective for single chamber pacing indications.
2.	**Device Migration**: There is a risk of the leadless pacemaker migrating from its original implantation site within the heart, which could affect its performance and may require retrieval or repositioning.	**Post-Approval Studies**: Conducting post-market surveillance and studies to monitor the long-term performance of the device with monitoring and detection of any emerging risks or complications in a real-world setting. The patients with Aveir Leadless Pacemaker will continue to be followed through 10 years to assess long-term safety and efficacy following approval of the PMA approval.
3.	**Electromagnetic Interference (EMI):** The device may be susceptible to interference from strong electromagnetic fields, which could potentially disrupt its normal functioning.	**Clear Labeling**: The potential complications associated with the use of the Aveir Leadless Pacemaker System are provided in comprehensive labeling and instructions for use that detail the proper implantation technique, potential risks, MRI safety information, and guidelines for managing EMI.

Overall, The LCP demonstrates very stable performance and reassuring safety results during intermediate-term follow-up. The clinical and performance testing results support the use of the LCP as a promising alternative to conventional pacemaker systems. The leadless design and minimally invasive implantation procedure contribute to a better patient experience, with reduced recovery time and fewer post-procedural restrictions compared to traditional pacemakers.

VII. Specific Requirements

Applied Standards:

- ISO 14708-1: This standard specifies general requirements for active implantable medical devices, including aspects related to design, testing, and manufacture to ensure safety and performance.
- ISO 14708-2: Specifically focuses on implantable cardiac pacemakers, outlining requirements for device characteristics, testing methods, and performance criteria.
- Other Relevant Standards: Depending on the device's features, additional standards may apply, such as ISO 10993 for biocompatibility testing and ISO 14117 for electromagnetic compatibility (EMC) requirements. MRI safety of the MR Conditional Aveir Leadless Pacemaker has been tested per the requirements in ISO/TS 10974. The test results demonstrate that the Aveir Leadless Pacemaker is conditionally safe for use in MRI environments when used according to the instructions in the MRI Manual using the 1.5T and 3T MR scanner.

Guidances: FDA Guidance document: Aveir Leadless Pacing System – Aveir™ Leadless Pacemaker, Model LSP112V (Right Ventricular); Aveir™ Delivery Catheter, Model LSCD111; and Aveir™ Link Module, Module LSL02 – P150035 https://www.fda.gov/medical-devices/recently-approved-devices/aveir-leadless-pacing-system-aveir-leadless-pacemaker-model-lsp112v-right-ventricular-aveir-delivery

Testing Requirements:

Aveir™ VR Leadless System Testing Details and Results are as follows:

Test / Evaluation	Results/Outcomes
Clinical Testing	- **Study: Leadless II IDE study** assessing clinical safety and efficacy in patients requiring pacing therapy.
	- **Efficacy**: Met pre-specified primary endpoints, showing benefits for patients with abnormal heart rhythms.
	- **Implant Success**: 98% implant success rate with minimal dislodgments and low repositioning rates.
	- **Safety Endpoint**: Achieved primary safety endpoint of freedom from serious adverse device effects in 96% of participants.
In-vitro Engineering Testing	**Product Performance**: Testing aligned with specifications, IFU, and standards to demonstrate device performance.

Test / Evaluation	Results/Outcomes
Battery Longevity:	**Increased projected battery longevity** with an average estimated life of 17.6 years in Leadless II IDE study.
Biocompatibility Testing	**Safety Assessment**: Crucial testing to evaluate potential adverse effects on living tissue and ensure device safety for patient use.
ISO 10993 Compliance	**Biological Evaluation**: Ensuring compliance with ISO 10993 for biological evaluation based on intended use and contact duration.
Animal Testing	**Biocompatibility Assessment**: Conducting animal studies, like implantation studies, to evaluate biocompatibility in living systems.

The Aveir™ VR Leadless System has demonstrated strong safety and efficacy profiles based on various studies and evaluations. Clinical testing revealed high implant success rates, meeting safety endpoints, and showing efficacy in patients with abnormal heart rhythms. In-vitro engineering testing confirmed product performance aligned with specifications and standards, including increased battery longevity. Biocompatibility testing ensured safety for patient use, while compliance with ISO 10993 standards was maintained.

VIII. Clinical Requirement for Submission

Is Clinical Testing Req. (for submission): Yes

Justification:

- **High-Risk Device**: Clinical trials provide direct evidence of the Aveir™ VR Leadless system device's safety in the intended patient population. This includes monitoring for adverse events, device-related complications, and overall patient well-being.
- **Evaluating Effectiveness**: Clinical studies are essential for assessing the device's efficacy in managing bradycardia and improving patient outcomes. This involves measuring pacing performance, heart rate control, and patient quality of life.
- **Risk-Benefit Analysis**: In some cases, clinical trials may compare the leadless pacemaker's performance to traditional pacemakers, offering insights into potential advantages or unique benefits.
- **Regulatory Requirement**: For Class III medical devices like the Aveir™ VR Leadless Pacemaker, clinical data is a mandatory component of the PMA submission, providing the evidence base for regulatory decision-making.

IX. Regulatory Pathways

U.S. REGULATORY PATHWAY	
Type of Submission	**Modular PMA**
Submission Cost	**483,560 $**
FDA Classification	**Class III**
FDA Product Code(s)	**PNJ**
Product-Specific Guidance Document	**AVEIR VR Leadless Pacemaker and Delivery Catheter Instructions for Use, Patient Manual**
Marketed Version(s)	**Aveir™ VR Leadless System**
Estimated Submission Date	**August 27, 2021**
Estimated Clearance/Approval Date	**March 31, 2022**
Predicate Device Information	**N/A**

X. References

1. *FDA. (2023, November 21). Premarket Approval (PMA) for Aveir VR Leadless System. Retrieved from* https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P150035
2. *Abbott Cardiovascular. (n.d.). Why AVEIR Single Chamber Leadless Pacemakers.* Retrieved from https://www.cardiovascular.abbott/us/en/hcp/products/cardiac-rhythm-management/pacemakers/aveir-dr-dual-chamber-leadless-pacemaker-system/why-aveir.html
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5. *Product Classification database*. (2024, March 18). U.S. FOOD & DRUG ADMINISTRATION. Retrieved from https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/PCDSimpleSearch.cfm