SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Drug Eluting Permanent Right Ventricular (RV) or Right Atrial (RA) Pacemaker Electrodes

Device Trade Name: VEGA Steroid-Eluting Endocardial Leads
Lead Models: VEGA™ R45, VEGA™ R52, and VEGA™ R58

Device Procode: NVN

Applicant's Name and Address: MicroPort CRM USA, Inc.
5640 Airline Road, Arlington, TN 38002

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P130010

Date of FDA Notice of Approval: May 17, 2023

II. INDICATIONS FOR USE

VEGA leads are active straight leads indicated for anti-brady therapy according to applicable guidelines, and can be used in the ventricle or atrium. VEGA leads R45, R52 and R58 are suitable for MRI (allowing patients to safely undergo an MRI examination) with a MicroPort MR Conditional pulse generator device.

III. CONTRAINDICATIONS

Implantation of endocardial leads is generally contraindicated in patients with mechanical tricuspid valves.

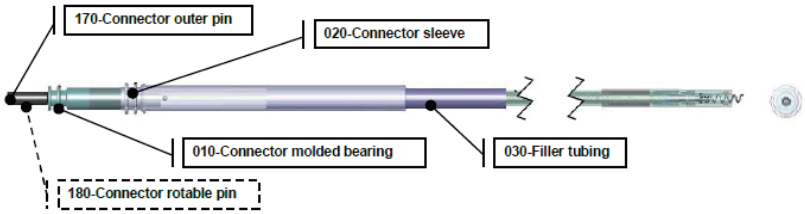
Do not implant in patients for whom a single dose of 310 µg of dexamethasone sodium phosphate may be contraindicated.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the VEGA lead labeling.

V. DEVICE DESCRIPTION

The VEGA Lead is a combination product consisting of two components: a device (pacing/sensing lead) and a drug (dexamethasone sodium phosphate). VEGA is a 7 French, transvenous, steroid-eluting, bipolar, IS-1 compliant active fixation endocardial lead intended for permanent sensing and pacing in either the right atrium or ventricle, for use with a single or dual chamber pacing system. VEGA leads are provided in straight configurations, but can be used with J-shaped stylets. The lead's body is a coaxial design with MP35N conductors and silicone outer insulation with a lubricious silicone coating Silglide® . The steroid collar is impregnated with a nominal dose of 310 µg of Dexamethasone Sodium Phosphate (DSP). A radiopaque marker is incorporated in the tip to enable x-ray facilitation of fixation. The lead's 2 mm body requires use of a 7F (2.33 mm) introducer sheath.



The system includes a straight stylet, J stylet, fixation tool, suture sleeve, funnel stylet guide and vein lifter as implant accessories.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of bradyarrhythmias, including in some situations, medications or surgery. Each alternative has its own specific indications as well as advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets their expectations and lifestyle. Cardiac pacing remains the most effective long-term treatment for symptomatic, irreversible bradycardia. Other non-MicroPort CRM pacing leads are commercially available to meet the needs of patients requiring an implantable pacing system.

VII. MARKETING HISTORY

VEGA Leads were first approved in April of 2017. They are CE marked and have been sold in Europe, Japan, EUA (emerging EU countries and Africa) and Latin America, Canada, and Australia. The lead has not been withdrawn from marketing in any country for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device. For the specific adverse events that occurred in the clinical study, please see Section X below.

Table 1: Most common events with possible adverse effects	
Events	**Possible Adverse Effect**
Lead displacement, conductor fracture	Intermittent or continuous loss of pacing and/or sensing
Rupture of insulation or helix electrode fracture	Pectoral stimulation, sudden fall in impedance, loss of efficacy of pacing, battery depletion
Cardiac perforation	Intermittent or continuous loss of pacing and/or Sensing Muscle or phrenic stimulation Tamponade
Threshold elevation	Loss of capture
Poor lead/pacemaker or defibrillator connection	Intermittent or continuous loss of pacing and/or sensing Pectoral stimulation
Arrhythmia at implantation	Extrasystoles, tachycardia, ventricular/atrial fibrillation
Introduction of air (with subclavian approach)	Air embolism
Clotting defect	Hematoma
Myocardial trauma	Chest pain
Contamination	Pocket infection, septicemia

IX. SUMMARY OF NONCLINICAL STUDIES

Non-clinical testing of the leads was conducted to ensure that the components and the finished device perform in accordance with their design specifications. Some of the supporting data is from PY2 and Beflex leads, which were predecessors to VEGA. PY2 was formerly marketed in the US; Beflex has been approved and marketed in Europe and other countries since 2009 but never introduced in the US. The most significant difference between PY2 and Beflex was the addition of a steroid component. The main difference between Beflex and VEGA is the addition of a lubricious coating (Silglide®) and ergonomic redesign of the accessories; therefore much of the Beflex test data is also applicable to VEGA.

Test	Purpose	Acceptance Criteria	Results
Abrasion Lead to Can and Lead to lead testing	Demonstrate the lead body is able to experience abrasion cycles between the can and the lead body	EN 45502-2-1: 2003 EN45502-1 : 1998	Pass

	or between 2 leads body without loss of insulation to the external environment.		
Tip pressure Testing	Check the compression force needed to buckle the lead in order to reproduce the heart beating.	EN45502-1 : 1998	Pass
Electrical testing	Check the electrical performance of the active fixation designs prior to implantation and after accelerated aging.	EN 45502-1: 1997 EN 45502-2-1: 2003 ASTM F (2007)	Pass
Lead Explant Axial Strength Testing	Verified the explant axial strength performance of the active fixation lead designs after accelerated aging.	EN 45502-1: 1997 EN 45502-2-1: 2003	Pass
Connector testing and Connector flexions fatigue validation test	Check the lead connector mechanical and electrical performance meets the product specification. Demonstrated the IS-1 conductors in the connector region of the lead can experience the cyclic test conditions.	ISO 5841-3 EN 45502-1: 1997 EN 45502-2-1: 2003	Pass
Corrosion Performance Testing	Check the current induced corrosion performance of the active fixation lead designs and materials. Verify the electrical, and corrosion performance of electrical lines at the distal end of the lead after being subjected to 10 years of pacing equivalent in an accelerated period in saline water.	EN 45502-2-1 : 2003 EN 45502-1: 1997	Pass
Lead Body Flexion Fatigue Mechanical Testing	Demonstrate that the uniform lead body region of the lead can experience flexion cycles in a bell-mouth without conductor fatigue fracture.	EN 45502-2-1 : 2003 EN 45502-1: 1997	Pass
400 million cycles flexion in the lead distal section	Demonstrate that the transition zone can experience 400,000,000 flexes that represent movement during heart contractions through 10 years of implant at a mean heart rate of 75 bpm.	EN 45502-1: 1997 EN 45502-2-1 : 2003	Pass
Biological tests	Bacterial endotoxin determination and determination of the population of microorganism on/in products.	USP 31 – NF 26 ISO 11737 - 1	Pass
Packaging	Check the packaging meets requirements of packaging, and sterile tray content. Verify the resistance of the packaging to the transportation impact and temperature variation.	EN45502-1: 2015	Pass
Particulates	Demonstrated that the lead conform to particulates standards in-vivo during implantation or in-	EN 45502-2-1 : 2003	Pass

	vivo use. The size and the quantity of particulates is analysed during this test.		
Mechanical tests	Verified the mechanical performance of Vega leads prior to implantation.	EN 45502-2-1 : 2003	Pass
Sterilization	Conducted to ensure that the VEGA lead meets the EO residual, particulate release, bioburden and bacterial endotoxin requirements with acceptable results. Validated cycle to a minimum sterility assurance level (SAL) of 10^{-6}.	ISO11135: 2014/A1: 2019	Pass
MRI	Conducted to ensure performance with MR conditional pacemakers when used as a system in the MR environment (includes, static, RF gradient fields and heating)	ISO 10974:2018	Pass

Shelf-life testing applicable to VEGA Leads

Test	Summary	Requirements	Results
Electrical testing	Check the electrical performance of the active fixation designs prior to implantation and after accelerated aging.	EN 45502-1: 1997 EN 45502-2-1: 2003 ASTM F 1980 (2007)	Pass
Lead Explant Axial Strength Testing	Verified the explant axial strength performance of the active fixation lead designs after accelerated aging.	EN 45502-1: 1997 EN 45502-2-1: 2003	Pass
Particulates	Demonstrated that the lead conform to particulates standards in-vivo during implantation or in-vivo use. The size and the quantity of particulates is analysed during this test.	EN 45502-2-1 : 2003	Pass
Biological tests	Bacterial endotoxin determination and determination of the population of microorganism on products.	ANSI AAMI ST 72 ISO 11737 - 1	Pass

Drug Component

The stability study of the drug component (ref. J900) mounted on VEGA lead was conducted following the ICH guidelines for stability studies.

The samples were prepared and packaged as finished leads, and sterilized according a validated EtO cycle before being put in storage conditions.

The steroid collar was successfully verified against specifications for a shelf life of 36 months in long term conditions (25°C, 60% (relative humidity (RH), according to ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use)

guideline definition) and for 6 months in accelerated conditions (40°C, 75% RH, according to ICH guideline definition).

Biocompatibility

Summary of Biocompatibility Testing			
Biological effect	**Source**	**Test description**	**Result**
Cytotoxicity	ISO 10993-5	ISO MTS cytotoxicity test ISO MTT cytotoxicity test	PASS
Sensitization	ISO 10993-10	ISO Guinea Pig Maximization Sensitization Test (Two Extracts)	PASS
Irritation or intracutaneous reactivity	ISO 10993-10	ISO Intracutaneous Irritation Study - Extract	PASS
Acute Systemic Toxicity	ISO 10993-11	Systemic Toxicity Study in Mice	PASS
		E&L study and Toxicological Risk Assessment	PASS
Material-Mediated Pyrogenicity	ISO 10993-11 and USP	USP Rabbit Pyrogen Study, Material Mediated	PASS
Subchronic/Subacute toxicity	ISO 10993-11	ISO Systemic Toxicity Study in Rats Following Subcutaneous Implantation, 13 Weeks	PASS
		Bacterial reverse mutation test (Ames testing)	PASS
		Chromosomal aberration study in mammalian cells	PASS
		E&L study and Toxicological Risk Assessment	PASS
Implantation	ISO 10993-6	ISO Muscle Implantation Study in Rabbits, 4 Week	PASS
		ISO Muscle Implantation Study in Rabbits, 13 Week	PASS
		ISO Muscle Implantation Study in Rabbits, 26 Week	PASS
		ISO Subcutaneous Implantation in Rats, 26 Weeks	PASS
Hemocompatibility	ISO 10993-4	ASTM Hemolysis Study - Extract and Direct Contact Method	PASS

Summary of Biocompatibility Testing			
Biological effect	**Source**	**Test description**	**Result**
	& ASTM	SC5b-9 Complement Activation Assay	PASS
		ASTM Partial Thromboplastin Time (PTT)	PASS
		Heparinized Blood Platelet and Leukocyte Count Assay (ISO)	PASS
		Standard Thrombogenicity in Ovine (ISO)	PASS
		Chronic Evaluation in Ovine Model GLP study	PASS
Chronic toxicity	ISO 10993-11	ISO Systemic Toxicity Study in Rats Following Subcutaneous Implantation, 26 Weeks	PASS
		Genotoxicity Studies	PASS
		E&L study and Toxicological Risk Assessment	PASS

X. SUMMARY OF PRIMARY CLINICAL STUDIES

Clinical data supporting the VEGA leads was obtained on a predecessor lead, Beflex RF. The only difference between the VEGA leads and the Beflex RF leads is the addition of a lubricious outer coating intended to improve handling during implant. The Beflex RF have been sold in Europe and other OUS markets since 2012. Clinical data for the Beflex RF leads was obtained in the PLEASURE-S premarket clinical trial, which was conducted in Europe.

The initial phase of PLEASURE-S was a non-randomized, prospective trial, which studied 203 Beflex RF leads, models RF46D and RF45D. The study was designed to demonstrate with 95% confidence that the proportion of subjects free from lead complication (serious device-related adverse effect) is greater than 90%. Setting the Type 1 error to 0.05%, the statistical power to 80%, the one-sided test-expected rate success to 97% and using "proc power" of SAS 9.1, the sample size required was 89.

203 Beflex leads were implanted in 123 patients at 18 centers located in France, Spain and Germany, in either or both the atrial (98) and ventricular (105) chambers. The study evaluated the safety and performance of the leads by:

- Demonstrating the absence of excessive risks related to the lead or its use, when used in accordance with the lead's manual/instructions for use (IFU).
- Demonstrating that the device meets expectations regarding electrical performance.

A. Study Design

Patients were treated between June 9, 2009 and January 1, 2011. The database for this PMA reflected data collected through January 1, 2011 and included 203 patients. There were 22 investigational sites. The study was a prospective, multi-center, single arm clinical study.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the PLEASURE-S study was limited to patients who met the following inclusion criteria: patients who were candidates for single or dual chamber pacemaker indications.

   Patients were not permitted to enroll in the PLEASURE-S study if they met any of the following exclusion criteria:
   - Ventricular tachyarrhythmias
   - Chronic atrial fibrillation
   - Tricuspid valvular disease or tricuspid mechanical heart valve

2. Follow-up Schedule

   All patients were scheduled to return for follow-up examinations at pre discharge, 1 month and 3 months postoperatively.

   Preoperatively, medical history and inclusion criteria compliance were assessed. Postoperatively, the objective parameters measured during the study included pacing threshold, R-wave or P-wave amplitude, and impedance. Adverse events and complications were recorded at all visits.

3. Clinical Endpoints

   Primary objective and results:
   The primary (safety) objective was to assess the complication rate per lead model with a confidence interval, and also measure the rate of other adverse events. The objective was to demonstrate that the complication free rate at 3 months is greater than 90%. There were two (2) lead complications recorded in two (2) patients with atrial implants, resulting in a 98% rate of patients free of lead complications at 3 months. The lower 95% confidence bound was 93.7% (p=0.002). In the ventricle, four (4) lead complications occurred in separate patients, resulting in a rate of 96.2% of patients free of lead complications at 3 months. The lower confidence bound was 91.5% (p=0.0167).

   A second study phase was added to gather additional data on ventricular implants. Fifty one (51) additional patients were implanted with ventricular leads and followed for 3 months. Within this group, two (2) lead complications occurred in two patients, resulting in cumulative safety results of 96.3% rate of patients free of lead complications at 3 months. The lower 95% confidence bound was 92.1% (p=0.002).

Secondary Endpoint #1 - Electrical performance:
The secondary (performance) objective was to document the pacing threshold, sensing amplitudes and impedance at implant, one month and three month follow up visits, as well as document the stimulation threshold at 3 months. Electrical performance was stable and as expected in both heart chambers, and the overall rate of observations/non-device related adverse events was also comparable to performance of predecessor leads.

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety and Effectiveness Conclusions

The risks of the device are based on nonclinical laboratory testing and data collected in a clinical study conducted to support post market OUS requirements, as described above. Bench testing verified that the lead conformed with and performed to its design specifications. Since the VEGA leads are an evolution of the Beflex lead with no significant design changes that impact the clinical evaluation, clinical data was leveraged from Beflex. The initial clinical trial confirmed safety by meeting the acceptance criteria for lead complications and adverse events at 3 months post-implant in the target patient population.

Effectiveness of the VEGA lead was demonstrated by bench tests as well as three-month clinical trial endpoints for pacing and sensing performance and lead handling.

Based on successful completion of bench testing and a clinical trial that met all primary and secondary endpoints in the target patient population, the probable benefits of the lead outweigh the potential risks of lead failure or injury to the patient, when used in accordance with the directions for use.

B. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study as described above. When the device performs as intended, the lead paces appropriately and provides the necessary benefit to maintain a normal heart rate.

The probable risks of the device are also based on data collected in a clinical study as described above. The risks include lead dislodgement or lead failure. This may require an additional invasive approach to place the new lead. Threshold increases and infection are also risks. If the patient is pacemaker-dependent and the lead suddenly fails, it could result in syncope, hemodynamic collapse or death. Risks such as perforation either acutely or after the procedure can also result in prolonged hospital stay or pericardial effusion with tamponade. The proposed leads have demonstrated through bench testing and a long history of reliability in the market that the benefits outweigh all those risks and provide a better life to the people with heart problems.

1. Patient Perspective
   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the indication for use of the device the probable benefits outweigh the probable risks.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Based on successful completion of bench testing and a clinical trial that met all primary and secondary endpoints in the target patient population, the probable benefits of the lead (delivery of pacing and sensing as needed to maintain a normal heart rate) outweigh the potential risks of lead failure or injury to the patient, when used in accordance with the directions for use.

XIII. CDRH DECISION

CDRH issued an approval order on May 17, 2023.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.