



April 14, 2022

Biosensors International USA, Inc.  
% Glenn Stiegman  
Senior Vice President, Clinical and Regulatory Affairs  
MCRA, LLC  
1050 K Street NW, Suite 1000  
Washington, District of Columbia 20001

Re: P190020  
Trade/Device Name: BioFreedom Drug Coated Coronary Stent System  
Product Code: NIQ  
Filed: October 1, 2019  
Amended: November 6, 2019, April 3, 2020, June 17, 2020, and January 4, 2021

Dear Glenn Stiegman:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the BioFreedom Drug Coated Coronary Stent System. This device is indicated for improving coronary luminal diameter in patients at high risk for bleeding with symptomatic ischemic heart disease due to de novo lesions of length  $\leq 32$  mm in native coronary arteries with a reference diameter ranging between 2.25 mm and 4.0 mm. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm> identifies combination product submissions.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 9-months.

Continued approval of the PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. This report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the PMA device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

You have agreed to provide the following non-clinical information in a report, which may be followed by a PMA supplement where applicable.

1. You will perform drug release testing of expired and variant samples using in vitro drug release (IVR) test conditions identified in your prior analysis (Step 1). To fulfill this condition of approval, you agree to use your smallest stent sizes (both diameter and length) for the determination of medium volumes in the planned Step 2 testing, inclusion of additional sampling time points of 12, 18, and 48 hours, and to report percent IVR profile data considering both drug load/amount normalized (where applicable) and percent of target label claim.
2. Long-term drug stability studies will be completed on five finished product batches representing the commercial process each year, with product codes rotating in a 4 year cycle. All batches for these studies will be stored at Long Term Conditions of  $25^{\circ}\text{C} \pm 2^{\circ}\text{C}/60\% \text{ RH} \pm 5\%$ , per ICH Q1A(R2). Testing for all studies will occur at 0, 3, 6, 9, 12, 18, 24, and 36 months.

Be advised that failure to comply with any post-approval requirement, including reporting of the study results, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

1. Final Reporting of the LEADERS FREE II (LFII) Clinical Study. The LFII Clinical Study (G130034) was a prospective, single arm, multi-center, multi-national, open label trial to evaluate the safety and effectiveness of the BioFreedom DCS in patients with coronary artery disease who were at high risk of bleeding. Patients received percutaneous coronary intervention (PCI) with the BioFreedom DCS followed by one month of dual antiplatelet therapy (DAPT) and followed through 36 months post-index procedure. To fulfill this condition of approval, you agree to provide the final clinical outcomes to FDA through 36 months post-procedure on patients enrolled in the LFII Clinical Study.

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Due to the ongoing COVID-19 pandemic, the Agency has been unable to conduct pre-approval inspections of the site involved in the manufacture of the BioFreedom Drug Coated Coronary Stent System. In lieu of the pre-approval inspection, the Agency has requested and considered additional information that would help it understand the adequacy of your Quality Systems and how they contribute to your device's safety. The

Agency has determined that there is sufficient Good Manufacturing Practices (GMP) information to support approval of your PMA at this time. However, approval is contingent upon the condition that Biosensors International USA should be readily available for an FDA GMP inspection with no other hindering factors when the affected sites are in a "Green" or "Yellow" zone and ORA resources are available to conduct an inspection. Furthermore, if upon inspection by FDA, the sites are deemed as not in compliance with the requisite FDA Current Good Manufacturing Practices (CGMPs) as outlined in 21 CFR 820, FDA has the authority to withdraw the approval of the PMA in accordance with 21 CFR 814.82(c).

Be advised that failure to comply with any post-approval requirement, including clinical studies results for all primary and secondary endpoints at 36-months, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.46(a)(3)-(4).

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage [https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma\\_pas.cfm](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm).

In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (<https://www.fda.gov/media/71327/download>).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website, <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system>.

Before making any change affecting the safety or effectiveness of the PMA device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" <https://www.fda.gov/media/81431/download>.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or post-marketing safety reporting (21 CFR 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems> and on combination product post-marketing safety reporting is available at (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at <https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls>.

CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet Home Page located at <https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals>. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft

form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Control Center - WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Samuel Raben, PhD at 240-402-6629 or [Samuel.Raben@fda.hhs.gov](mailto:Samuel.Raben@fda.hhs.gov).

Sincerely,

Brian Pullin  
Director  
DHT2C: Division of Coronary  
and Peripheral Intervention Devices  
OHT2: Office of Cardiovascular Devices  
Office of Product Evaluation and Quality  
Center for Devices and Radiological Health