DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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September 19, 2016

Bio2 Medical, Inc.
Ms. Julie Ross
Director, Quality Assurance and Regulatory Affairs
4670 Table Mountain Drive
Golden, CO 80403

Re: K160747
Trade/Device Name: Angel Catheter
Regulation Number: 21 CFR 870.3375
Regulation Name: Cardiovascular Intravascular Filter
Regulatory Class: Class II
Product Code: PNS
Dated: June 24, 2016
Received: June 27, 2016

Dear Ms. Ross:

This letter corrects our substantially equivalent letter of July 28, 2016.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in

the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carmen G. Johnson -S

for Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K160747/S001

Device Name
Angel® Catheter

Indications for Use *(Describe)*
The Angel® Catheter is intended to provide the combined functions of an inferior vena cava (IVC) filter and a multi-lumen central venous catheter.
The Angel® Catheter is intended for short term use for the prevention of clinically significant pulmonary embolism (PE) in critically ill patients at high risk for PE or recurrent PE, and recognized contraindications to standard pharmacological thromboprophylaxis therapy.
The Angel® Catheter is also intended to provide access to the central venous system.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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I. SUBMITTER

Applicant Name:	Bio2 Medical, Inc.
Address:	4670 Table Mountain Drive Golden, CO 80403
Phone:	(720) 833-5660
Fax:	(303) 422-4182
Contact Person:	Christopher E. Banas

II. DEVICE

Trade Name:	Angel® Catheter
Catalog Number:	AC3930A
Common or Usual Name:	Inferior Vena Cava Filter and Central Venous Catheter
Classification:	Short-Term Intravascular Filter Catheter (21 CFR 870.3375)
Device Class:	II
Product Code:	PNS

III. PREDICATE DEVICES

The Angel® Catheter combines the functions of a retrievable inferior vena cava (IVC) filter and a multi-lumen central venous catheter (CVC). These functions have not been previously combined in a single device. Therefore, there are separate predicate devices identified with each function.

The Angel® Catheter legally marketed predicates, to which Bio2 Medical, Inc. is claiming equivalence, are listed below.

Predicate Devices for the Angel® Catheter		
	Predicate Device Name	**FDA 510(k) Number**
Inferior Vena Cava (IVC) Filters	Cook® Celect® Vena Cava Filter	K073374
	Bard Eclipse™ Vena Cava Filter	K093659
Central Venous (CVC) Catheters	Edwards Multi-Med Central Venous Catheter	K091709
	ARROWG+ARD Blue Quad-Lumen Central Venous Catheter	K962577

IV. DEVICE DESCRIPTION

The Angel® Catheter is a retrievable vena cava filter permanently attached to a central venous access catheter. The conical, self-expanding, Nitinol filter has wide proximal openings that allow the capture of clots in the distal end of the filter. The filter is 50 mm long at its maximum expanded/unconstrained diameter of 30 mm. The distal end of the filter is free floating on the central venous catheter so that the filter can expand to the diameter of the vena cava.

The catheter is designed to constrain the IVC filter component in an unexpanded state for delivery to the IVC and to function as the sheath for retrieval of the IVC filter. It has '1 cm' depth markers indicating the depth the catheter has been inserted into the patient. For ease of placement, the catheter has a hydrophilic coating applied to the outer diameter up to the 24 cm depth marker.

The filter is permanently attached to the multi-lumen catheter to ensure secure positioning, while simultaneously providing access to the central venous system for administration of medications, fluids, or blood products; blood sampling; and monitoring of central venous pressure. The multi-lumen catheter and sheath connections are standard color-coded luer fittings, compatible with current ICU pressure monitoring equipment and other accessories. The Distal Tip Port and Proximal Sheath Port may be used for power injection of contrast media, and these luers contain specific pad printing indicating the maximum power injection rates.

Performance and Principle of Operation

The Angel® Catheter combines the functions of an inferior vena cava (IVC) filter and a multi-lumen central venous access catheter (CVC). It is designed for bedside percutaneous placement in the inferior vena cava, via the femoral vein, for the prevention of pulmonary embolism. Placement of the device is similar to a standard central venous catheter, followed by an abdominal radiograph to assess proper position of the catheter and filter. While in place, the catheter is maintained using the same techniques as a central venous catheter. When the indications for IVC filtration and/or central venous access are no longer present, the permanent attachment of the filter to the catheter ensures that the filter will be retrieved with the catheter at the time of removal. The Angel® Catheter is intended for short term use (less than 30 days).

V. INDICATIONS FOR USE

The Angel® Catheter is intended to provide the combined functions of an inferior vena cava (IVC) filter and a multi-lumen central venous catheter.

The Angel® Catheter is intended for short term use for the prevention of clinically significant pulmonary embolism (PE) in critically ill patients at high risk for PE or recurrent PE, and recognized contraindications to standard pharmacological thromboprophylaxis therapy.

The Angel® Catheter is also intended to provide access to the central venous system.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICES

The Angel® Catheter is substantially equivalent to both the vena cava filter and central venous catheter predicate devices identified with regard to the indications for use, technological characteristics, and performance characteristics. The major technological similarities and differences are summarized below:

Technological Comparison of Angel® Catheter to Predicate Devices

	Angel® Catheter	**Inferior Vena Cava (IVC) Filters**		**Central Venous Catheters (CVC)**	
		Cook® Celect® Vena Cava Filter	**Bard Eclipse™ Vena Cava Filter**	**Edwards Multi-Med Central Venous Catheter**	**ARROWG+ARD Blue Quad-Lumen Central Venous Catheter**
FDA 510(k) Number	-	K073374	K093659	K091709	K962577
Indications for use	*Per Section V*	Similar	Similar	Similar	Similar
Placement Duration	<30 Days	Optional Retrieval	Optional Retrieval	Identical	Identical
Principle of Operation	Bedside Placement	Under Fluoroscopic Guidance	Under Fluoroscopic Guidance	Similar	Similar
Venous Access Site	Femoral	Femoral/ Jugular	Femoral/Jugular /Subclavian	Jugular/ Subclavian	Femoral/ Jugular/ Subclavian
Indicated Caval Diameter	15 mm - 30 mm	Similar	Similar	NA	NA
Filter Material	Nitinol (Laser Cut from NiTi Tube)	Conichrome	Nitinol (NiTi Wire)	NA	NA
Filter Dimensions	30 mm diameter x 50 mm length	Similar	Similar	NA	NA

Continued on next page

	Angel® Catheter	Inferior Vena Cava (IVC) Filters		Central Venous Catheters (CVC)	
		Cook® Celect® Vena Cava Filter	Bard Eclipse™ Vena Cava Filter	Edwards Multi-Med Central Venous Catheter	ARROWG+ARD Blue Quad-Lumen Central Venous Catheter
Filter Securement	Permanently Attached to Catheter	Hooks	Hooks	NA	NA
Catheter Securement	Standard Suture Wing/ Overclamp	NA	NA	Identical	Identical
Catheter Lumen	3	NA	NA	4	4
Catheter/ Delivery System Profile	9.0F	8.5F	Femoral: 7.0F Jugular/ Subclavian: 10.0F	8.5F	8.5F
Useable Length	30 cm	Not Specified	Not Specified	20 cm	30 cm
Sterilization Method	EtO	Identical	Identical	Identical	Identical
Device Usage	Single Use only	Identical	Identical	Identical	Identical

VII. PERFORMANCE DATA

The following performance testing was completed to demonstrate that the Angel® Catheter met applicable design and performance requirements, and is therefore equivalent to predicate devices.

Biocompatibility Testing

All blood contacting materials for the Angel® Catheter were identified. The following list summarizes the biocompatibility testing performed for the device:

Biocompatibility Testing
Two week Systemic Toxicity Study in the Rat, Repeated Parenteral Administration of Two Extracts
Bacterial Reverse Mutation Assay – Extracts
Mouse Peripheral Blood Micronucleus Study
Genotoxicity: Mouse Lymphoma Assay – Extract
ISO Guinea Pig Maximization Sensitization Test - Extract
Cytotoxicity Study Using the ISO Elution Method
ASTM Hemolysis Study
USP Rabbit Pyrogen Study-Material Mediated
ASTM Partial Thromboplastin Time-1
ASTM Partial Thromboplastin Time-2
SC5b-9 Complement Activation Assay-1
SC5b-9 Complement Activation Assay-2
ISO Systemic Toxicity Study in Mice
ISO Intracutaneous Study in Rabbits
C3a Complement Activation Assay-1
C3a Complement Activation Assay-2

In conclusion, the biocompatibility evaluation of the Angel® Catheter met the applicable ISO 10993 and ASTM test standards.

Performance Bench Testing

The following list summarizes the performance bench testing completed for the Angel® Catheter:

Performance Testing
Dimensional, Visual, and Compatibility
Lumen Flow Rate
Tensile Testing
Pressure Monitoring
Aspiration
Multilumen Leakage
Catheter Burst/Hemostasis
Particulate
Power Injection Capability
Force to Deploy/Retrieve
Simulated Use - Pre-Clinical GLP Animal Study
Catheter Stiffness
Catheter Flexural Fatigue Tolerance
Catheter Coating Lubricity and Durability
Catheter Coating Coverage and Adhesion
Clot Trapping/Filter Efficiency
Filter Migration Resistance
Filter Durability (Fatigue)
Corrosion
Filter FEA
Magnetic Resonance Imaging (MRI) Compatibility
Radial Force
Active A_f (BFR)
Nickel Leaching

In conclusion, the performance bench testing for the Angel® Catheter conformed to the product specifications and met the applicable acceptance criteria.

Animal Studies

Multiple Non-GLP and GLP studies were conducted for the Angel® Catheter on porcine and ovine animal models. The results from these studies supported the safety and performance of the Angel® Catheter for use in human clinical studies.

Clinical Studies

Multiple clinical studies were performed with the Angel® Catheter including a First in Man (FIM) Pilot Study, a European Post-Market Registry Study, an Early Feasibility Study under FDA's Early Feasibility Program (EFP), and a Pivotal Study.

The primary objective of the Pivotal Study was to evaluate the safety and effectiveness of the Angel® Catheter in critically ill subjects at high risk for PE, and with recognized contraindications to standard pharmacological therapy. This study followed the Early Feasibility Study that was conducted to obtain initial insights into the safety of the Angel® Catheter in critically ill subjects with high risk of venous thromboembolism (VTE) disease and not receiving pharmacological thromboprophylaxis.

With a Pivotal Study goal of 150 evaluable subjects, the primary endpoint was freedom from clinically significant PE or fatal PE at the time of discharge or up to 72 hours post device removal, whichever was first. Secondary safety endpoints were: 1) Incidence of acute proximal deep vein thrombosis; 2) Incidence of catheter related thrombosis; 3) Incidence of catheter related blood stream infections; 4) Incidence of major bleeding event; and 5) Incidence of PEs averted.

The device was successfully placed in 163 eligible subjects [intention-to-treat (ITT) population], 151 of these subjects had the device in place for at least 48 hours [per-protocol (PP) population]. The most common indication for placement of the device was recognized contraindication to the use of anticoagulation in 160/163 (98.2%) of subjects. Refer to the list below.

Indications for Angel® Catheter Placement		
Subject Characteristics	**ITT Population (N=163)**	**PP Population (N=151)**
Subject has recognized contraindications to standard pharmacological thromboprophylaxis including	98.2% (160/163)	98.0% (148/151)
Active bleeding or at high risk for bleeding	95.6% (153/160)	95.3% (141/148)
Hypersensitivity to pharmacological thromboprophylaxis	0.0% (0/160)	0.0% (0/148)
History of severe heparin induced thrombocytopenia	0.0% (0/160)	0.0% (0/148)
Severe thrombocytopenia	0.6% (1/160)	0.7% (1/148)
Other	6.9% (11/160)	7.4% (11/148)
Subject has a confirmed acute proximal lower extremity DVT or a confirmed acute PE as diagnosed by site with recognized contraindication to anticoagulation	4.9% (8/163)	5.3% (8/151)
Subject requires a temporary interruption (>24 hours from last dose) of pharmacological thromboprophylaxis for a surgical or medical procedure	6.2% (10/162)	6.7% (10/150)
Prophylactic use of the Angel® Catheter*	98.2% (160/163)	98.0% (148/151)
* Defined as subjects without a confirmed ongoing PE.		

Freedom from clinically significant PE and fatal PE were reported for all subjects (i.e., no clinically significant or fatal PEs were reported in any of the study subjects as determined by the CEC). Thus, the primary effectiveness endpoint of the study was met. Of the secondary safety endpoints, there were 30/163; 18.40% ITT (30/151; 19.87% PP) acute proximal DVT including the 20/163; 12.27% ITT (20/151; 13.25% PP) catheter-related DVTs, 0/163; 0.00% ITT (0/151; 0.00% PP) catheter-related blood stream infection, and 5/163; 3.07% ITT (4/151; 2.65% PP) rate of major bleeding events. In addition, the averted PE rate was 14/163; 8.59% ITT (14/151; 9.27% PP). The study device had no reported events related to filter fracture, migration or embolization. There were no serious adverse events (SAE) reported as a result of the device insertion. There were no infectious complications associated with the use of the Angel® Catheter and no device-related SAEs occurred during the insertion or removal of the device.

There were no Unanticipated Adverse Device Effects reported. No serious Angel® Catheter-related clinically significant PEs, deaths, CRBSIs, or major bleeding occurred in any subjects during the study period. All SAEs are discussed below.

System Organ Class/Preferred Term	Number of Events, ITT Population	Number of Subjects, ITT Population (N= 163)
Any Serious Adverse Event	66	49 (30.1%)
Cardiac Disorders	5	5 (3.1%)
Cardiac Arrest	4	4 (2.5%)
Supraventricular Tachycardia	1	1 (0.6%)
General Disorders And Administration Site Conditions	5	5 (3.1%)
Brain Death	2	2 (1.2%)
Multi-Organ Failure	3	3 (1.8%)
Hepatobiliary Disorders	1	1 (0.6%)
Chronic Hepatic Failure	1	1 (0.6%)
Infections And Infestations	11	8 (4.9%)
Abdominal Sepsis	1	1 (0.6%)
Lobar Pneumonia	1	1 (0.6%)
Pneumonia	6	6 (3.7%)
Sepsis	2	2 (1.2%)
Septic Shock	1	1 (0.6%)
Injury, Poisoning And Procedural Complications	7	7 (4.3%)
Craniocerebral Injury	4	4 (2.5%)
Post Procedural Haemorrhage	1	1 (0.6%)
Subdural Haematoma	1	1 (0.6%)
Subdural Haemorrhage	1	1 (0.6%)
Nervous System Disorders	9	9 (5.5%)
Brain Hypoxia	1	1 (0.6%)
Brain Oedema	1	1 (0.6%)
Cerebrovascular Accident	1	1 (0.6%)
Haemorrhage Intracranial	1	1 (0.6%)
Intracranial Pressure Increased	5	5 (3.1%)
Renal And Urinary Disorders	2	2 (1.2%)
Renal Failure	1	1 (0.6%)
Renal Failure Acute	1	1 (0.6%)
Respiratory, Thoracic And Mediastinal Disorders	9	9 (5.5%)
Acute Respiratory Distress Syndrome	1	1 (0.6%)
Pleural Effusion	1	1 (0.6%)
Pulmonary Embolism	1	1 (0.6%)
Respiratory Failure	6	6 (3.7%)
Vascular Disorders	17	17 (10.4%)
Deep Vein Thrombosis	10	10 (6.1%)
Haemodynamic Instability	1	1 (0.6%)
Hypotension	1	1 (0.6%)
Pelvic Venous Thrombosis	2	2 (1.2%)
Vena Cava Thrombosis	3	3 (1.8%)

Numbers are % (counts/sample size).

In conclusion, the Pivotal Study demonstrated that the bedside insertion of the Angel® Catheter is safe and that this device is an effective alternative for the prevention of clinically significant PEs in a high risk population of critically ill patients with contraindications to anticoagulation.

The use of the device for an average of 6.79 days provided protection from PE in this population that was similar to that reported with the use of anticoagulation in the PROTECT study in critically ill subjects with no contraindications to anticoagulation, providing protection for the period with the highest risk of thromboembolic events. There were no clinically significant PEs reported in the study, which is lower than the anticipated rate of these events in this critically ill population with high rates of DVTs and contraindications to anticoagulation.

The Angel® Catheter was not associated with any catheter related blood stream infections. The number of acute lower extremities DVTs as well as the number of catheter related thrombosis (CRT) are within the expected frequency of these events in critically ill patients with central venous catheters. The device malfunctions were mostly related to the non-functionality of one of the access ports and none of them resulted in a serious adverse event.

Thus, this Pivotal Study successfully met all pre-specified primary and secondary endpoints of the clinical trial, and demonstrated an acceptable safety profile for the Angel® Catheter.

VIII. CONCLUSIONS

Based on clinical data, performance testing, and similarities in indications for use, materials, technological characteristics, principle of operation and design features, Bio2 Medical, Inc. considers the Angel® Catheter performance to be substantially equivalent to the legally marketed predicate devices listed above in terms of safety and performance. Device differences do not raise any new issues of safety or effectiveness.