DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

April 20, 2017

Penumbra, Inc.
Ms. Michaela Mahl
Senior Manager of Regulatory Affairs
One Penumbra Place
Alameda, California 94502

Re: K162901
Trade/Device Name: Penumbra 3D Revascularization Device
Regulation Number: 21 CFR 870.1250
Regulation Name: Percutaneous Catheter
Regulatory Class: Class II
Product Code: NRY
Dated: March 20, 2017
Received: March 21, 2017

Dear Ms. Mahl:

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,

Carlos L. Pena -S

Carlos L. Peña, PhD, MS
Director
Division of Neurological
and Physical Medicine 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)*
K162901

Device Name
Penumbra 3D Revascularization Device

Indications for Use *(Describe)*

Penumbra Reperfusion Catheters and Separators

As part of the Penumbra System, the Reperfusion Catheters and Separators are indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. Patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment.

Penumbra 3D Revascularization Device

As part of the Penumbra System, the Penumbra 3D Revascularization Device is indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral-Ml and M2 segments) within 8 hours of symptom onset. Patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment.

Penumbra Aspiration Tubing

As part of the Penumbra System, the Penumbra Sterile Aspiration Tubing is indicated to connect the Penumbra Reperfusion Catheters to the Penumbra Aspiration Pump.

Penumbra Aspiration Pump

The Penumbra Aspiration Pump is indicated as a vacuum source for Penumbra Aspiration Systems.

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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510(k) Summary

(as required by 21 CFR 807.92)

Pursuant to Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, Penumbra Inc. is providing the summary of Substantial Equivalence for the Penumbra System 3D Revascularization Device.

1 Sponsor/Applicant Name and Address

Penumbra, Inc.
One Penumbra Place
Alameda, CA 94502 USA

2 Sponsor Contact Information

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3 Date of Preparation of 510(k) Summary

April 19, 2017

4 Device Trade or Proprietary Name

Penumbra 3D Revascularization Device

5 Device Classification

Regulatory Class:	II Classification Panel: Neurology
Classification Name:	Percutaneous Catheter
Regulation Number:	21 CFR §870.1250
Product Code:	NRY (Catheter, Thrombus Removal)

6 Predicate and Reference Devices

510(k) Number/ Clearance Date	Name of Predicate Device	Name of Manufacturer
Predicate Device		
K160449 [25May2016]	Penumbra System and Penumbra Pump MAX	Penumbra, Inc.
Reference Devices		
K153071 [23Dec2015]	Solitaire™ Platinum Revascularization Device	Micro Therapeutics, Inc. d/b/a ev3 Neurovascular
K161640 [12Jul2016]	Penumbra System ACE 68 Reperfusion Catheter	Penumbra, Inc.

7 Predicate Comparison

	Predicate Device	Primary Reference Device	Subject Device
Predicate 510(k)	Penumbra System : K160449	Solitaire™ Platinum Revascularization Device: K153071	Penumbra 3D Revascularization Device: K162901
Classification	Class II, NRY	Same	Same
Indication for Use	Penumbra Reperfusion Catheters and Separators As part of the Penumbra System, the Reperfusion Catheters and Separators are indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. Penumbra Aspiration Tubing As part of the Penumbra System, the Penumbra Sterile Aspiration Tubing is indicated to connect the Penumbra Reperfusion Catheters to the Penumbra Pump MAX. Penumbra Pump MAX The Penumbra Pump MAX is indicated as a vacuum source for Penumbra Aspiration Systems.	The Solitaire™ Platinum Revascularization Device is intended to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset. Patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment.	Penumbra Reperfusion Catheters and Separators As part of the Penumbra System, the Reperfusion Catheters and Separators are indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. Patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment. Penumbra 3D Revascularization Device As part of the Penumbra System, the Penumbra 3D Revascularization Device is indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments) within 8 hours of symptom onset. Patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for

	Predicate Device	Primary Reference Device	Subject Device
Predicate 510(k)	Penumbra System : K160449	Solitaire™ Platinum Revascularization Device: K153071	Penumbra 3D Revascularization Device: K162901
			treatment. <u>Penumbra Aspiration Tubing</u> As part of the Penumbra System, the Penumbra Sterile Aspiration Tubing is indicated to connect the Penumbra Reperfusion Catheters to the Penumbra Aspiration Pump. <u>Penumbra Aspiration Pump</u> The Penumbra Aspiration Pump is indicated as a vacuum source for Penumbra Aspiration Systems.
System Components	Aspiration Pump	N/A	SAME as Predicate
	Aspiration Tubing	N/A	SAME as Predicate
	Reperfusion Catheter	Micro Catheter	SAME as Predicate
Materials	Separators	Solitaire™ Platinum	3D Revascularization Device
Push-wire			
Core wire	304 Stainless Steel **or**	N/A	SAME as Predicate
	Nitinol	SAME	N/A
Outer coil	304 Stainless Steel	N/A	SAME as Predicate
Solder joint	Silver Solder (95% Sn / 5% Ag) Gold Solder (80% Au / 20% Sn)	N/A	SAME as Predicate
Coating	PTFE Green (PC 8-403G)	N/A	SAME as Predicate
Shrink tubing	N/A	PTFE	N/A

	Predicate Device	Primary Reference Device	Subject Device
Predicate 510(k)	Penumbra System : K160449	Solitaire™ Platinum Revascularization Device: K153071	Penumbra 3D Revascularization Device: K162901
Distal Tip			
Outer coil	304 Stainless Steel	N/A	SAME as Predicate
Inner coil / Marker coils	Platinum Alloy (92% Pt / 8% W)	90% Platinum / 10% Iridium	SAME as Predicate
Attachment tip	N/A	Unknown	304 Stainless Steel
Solder joint	Gold Solder (80% Au / 20% Sn) Silver Solder (95% Sn / 5% Ag)	N/A	Gold Solder (80% Au / 20% Sn) Silver Solder (96.5% Sn / 3.5% Ag)
Stent	N/A	Nitinol	Same as Primary Reference
Radiopaque Markers	N/A	4 - 5	Same as Primary Reference
Separator tip	Pebax 40D: green (026) ,yellow (032), blue (041), purple (054)	N/A	N/A
ID band	Polyolefin (PET)	N/A	N/A
Introducer sheath	Pebax / Nylon	PTFE / Grilamid	FEP
Dimensions			
- Distal OD [Cone]	0.022" – 0.045" [0.56mm – 1.14mm]	N/A	N/A
- Device OD	N/A	4mm & 6mm	4.5 mm
- Device Usable Length	N/A	20mm & 40mm	20 mm
- Push Wire Length	175 cm – 200 cm	180 cm	200 cm
Sterilization	**EO**	**SAME**	**SAME**
Shelf-Life	**36-Months**	**24-Months**	**36-Months**

8 Device Description

The Penumbra 3D Revascularization Device is an additional component to the currently available Penumbra System. The Penumbra System's fundamental mechanism of action is aspiration. Aspiration draws clot into the Penumbra Reperfusion Catheter to remove the clot. The 3D Revascularization Device is designed to assist the Reperfusion Catheter with thrombus removal if needed. The device is provided sterile, non-pyrogenic, and intended for single use only.

9 Indications for Use

Penumbra Reperfusion Catheters and Separators

As part of the Penumbra System, the Reperfusion Catheters and Separators are indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. Patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy are candidates for treatment.

Penumbra 3D Revascularization Device

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Penumbra Aspiration Tubing

As part of the Penumbra System, the Penumbra Sterile Aspiration Tubing is indicated to connect the Penumbra Reperfusion Catheters to the Penumbra Aspiration Pump.

Penumbra Aspiration Pump

The Penumbra Aspiration Pump is indicated as a vacuum source for Penumbra Aspiration Systems.

10 Summary of Non-Clinical Data

As required under Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, a summary of any information regarding substantial equivalence of the device follows.

Included in this section are descriptions of the testing, which substantiates the safe and effective performance of the Penumbra 3D Revascularization Device as well as its substantial equivalence to the predicate devices:

- Biocompatibility
- Design Verification (Bench-Top Testing)
- Design Validation (GLP Animal Testing)

The subject Penumbra 3D Revascularization Device met all established requirements.

10.1 Biocompatibility Testing

Evidence of the biocompatibility of the Penumbra 3D Revascularization Device is derived from the testing used to support the current FDA cleared Penumbra System Separators and a series of studies listed and summarized in the table below.

Biocompatibility tests conducted on the materials of the Penumbra 3D Revascularization Device were selected in accordance with EN ISO 10993 -1 guidelines (Biological Evaluation of Medical Devices) for limited duration (<24 hours), external communicating devices, contacting circulating blood. All studies were conducted pursuant to 21 CFR, Part 58, Good Laboratory Practices. In summary, non-clinical testing found the Penumbra 3D Revascularization Device to be biocompatible according to the requirements of EN ISO 10993 requirements.

Test	Method	Results
In Vitro Cytotoxicity	ISO Elution Test (MEM Extract)	No evidence of cell lysis or toxicity
Sensitization	ISO Maximization Test for Delayed Hypersenitivity	Non-Sensitizing
Acute Intracutaneous Reactivity (Irritation)	ISO Intracutaneous (Intradermal) Injection Test	No evidence of irritation
Acute Systemic Toxicity	ISO Acute Systemic Injection Test	No evidence of systemic toxicity
Rabbit Pyrogen Study	USP Material-Mediated Rabbit Pyrogen Test	No evidence of material-mediated pyrogenicity
Hemo-compatibility		

Test	Method	Results
- In Vitro Hemolysis	ASTM Methode (Extraction & Direct Contact)	Non-Hemolytic
- In Vitro Coagulation (PT, PTT)	Prothrombin Time (PT) Assay	Coagulation times are not significant different than corresponding control
	Partial Thromboplastin Time (PTT) Assay	Non-Thrombogenic
Complement Activation	C3a and SC5b-9 through Enzyme Assay	No greater biological response than corresponding control
Dog Thrombogenicity	Thrombogenicity Study in Dogs - ISO	Non-Thrombogenic
Genotoxicity		
- Mouse Lymphoma	Mouse Lymphoma Mutagenesis Assay - ISO	Non-Mutagenic
- Ames Mutagenicity	Ames Test	Non-Mutagenic
- *In Vivo* Mouse Micronucleus	Micronucleus Assay - ISO	Non-Mutagenic

In summary non-clinical testing substantiates that the Penumbra 3D Revascularization Device is non-cytotoxic, non-sensitizing, non-irritating, non-toxic, non-pyrogenic, non-hemolytic, and non-thrombogenic.

10.2 Bench-top Testing

The physical and mechanical properties of the Penumbra 3D Revascularization Device was assessed using standard test methods and pre-determined acceptance criteria. The following tests were performed and all tests passed successfully:

Attribute	Specification	Result
Pouch Seal Strength	Minimum value per specification	Pass
Dimensional / Visual Inspection	These evaluations confirm that the units used in this Design Verification testing meet all product specifications.	Pass
Simulated Use [Intracranial Access, Vessel Access Entry Performance, Delivery/Retrieval Forces & Clot Removal]	Simulated use testing of the Penumbra 3D Revascularization Device was performed with accessory devices in an anatomical model which simulated the tortuosity of the neurovasculature. Devices were delivered through the tortuous anatomical model to evaluate the effectiveness of the devices to remove clots and that the Reperfusion Catheter does not collapse under vacuum.	Pass
Particulate Testing	≥ 10 μm will be ≤ 6000 particles	Pass
	≥ 25 μm will be ≤ 600 particles	Pass
	≥ 75 μm will be measured for informational purposes only (FIPO)	FIPO
	≥ 125 μm will be measured for informational purposes only (FIPO)	FIPO

Attribute	Specification	Result
Radial Pressure	Value within the specification range	Pass
Device A_f	Maximum value per specification	Pass
Tensile Strength - Markerband	Minimum value per specification	Pass
Tensile Strength - Wire Attachment	Minimum value per specification	Pass
Corrosion	Specimens will be free from signs of corrosion.	Pass
Kink Resistance	No kinking when formed in a defined radius.	Pass
Torsion Response	Minimum value per specification	Pass

The results of the tests appropriately address the physical and mechanical performance expectations of the device. This is further supported by the surgical handling and performance results reported in the *in vivo* study. Based on these overall results, the physical and mechanical properties of the subject Penumbra 3D Revascularization Device is acceptable for the intended use and substantially equivalent to the predicate device.

10.3 Animal Study

Two animal studies were conducted to evaluate the safe use of the Penumbra 3D Revascularization Device, one study in a rabbit model [Chronic Safety Study] and one study in a swine model [Acute Performance Study]. The studies concluded that:

- No vessel injury was noted on the final angiograms following the vessel response procedure.
- No abnormal gross or histology findings were noted in test vessel segments.
- The use of the Penumbra System 3D Revascularization Device resulted in no significant vascular response in these experimental conditions.

11 Clinical Study

The Penumbra 3D Trial was a non-inferiority study that compared the safety and effectiveness of the Penumbra 3D Revascularization Device, used with the Penumbra System aspiration devices, to that of Penumbra System alone for the revascularization of acute ischemic stroke patients with a large vessel occlusion.

Penumbra 3D Trial CLINICAL DATA SUMMARY

The Penumbra 3D Trial was a non-inferiority study that compared the safety and effectiveness of the Penumbra 3D Revascularization Device, used with the Penumbra System aspiration devices, to that of Penumbra System alone for the revascularization of acute ischemic stroke patients with a large vessel occlusion. This was a prospective, randomized, concurrent controlled, non-inferiority design, multi-center study. Patients presenting with symptoms of acute ischemic stroke and evidence of a large vessel occlusion (>2.5mm in diameter) in the cerebral circulation were assigned to either the 3D Revascularization Device with Penumbra

System arm (3D/Penumbra System) or the Penumbra System alone arm. Each treated patient was assessed for 3 months after randomization.

Statistical Analysis

The objective of the statistical analysis was to assess if the effectiveness of 3D/ Penumbra System was non-inferior to Penumbra System alone as defined by a modified Thrombolysis In Cerebral Infarction scale (mTICI) score of 2-3. The pre-specified primary efficacy analysis was conducted in the per protocol population. The primary effectiveness analysis was the difference between the 3D/ Penumbra System group and the Penumbra System alone group (control). A binomial comparison was used to test the null hypothesis that the difference in proportions was less than or equal to -0.15 (H_0: $P_{3D} - P_{Control} \leq -0.15$; i.e., that revascularization in the 3D/ Penumbra System group is worse than for the Penumbra System alone group) vs. the one-sided alternative (H_1: $P_{3D} - P_{Control} > -0.15$). This was equivalent to evaluating that the lower bound of the 90% confidence interval for the difference was above -15%. The sample size calculations assume that 80% of the standard Penumbra System patients experience success (mTICI of 2 to 3) and 80% of the 3D/Penumbra System patients experience success.

Study Procedures

Acute ischemic stroke patients presenting within 8 hours of onset with NIHSS score ≥8 underwent 1:1 randomization to 3D/ Penumbra System or Penumbra System alone. The primary effectiveness endpoint was mTICI score of 2-3 with a 15% margin for non-inferiority. Device and procedure-related serious adverse events (SAEs) at 24 hours were the primary safety endpoint. Key secondary endpoints were functional independence at 90 days defined by a modified Rankin Scale (mRS) score of 0-2, symptomatic intracranial hemorrhage (sICH) and all cause mortality. All patients were followed for 90 days.

Key Inclusion Criteria

- From 18 to 85 years of age
- Present with symptoms consistent with an acute ischemic stroke for revascularization within 8 hours from symptom onset
- Refractory to or not eligible for IV rtPA therapy, e.g., presenting between 0 and 3 hours from symptom onset AND contraindicated for IV rtPA, or presenting between 3 and 8 hours of symptom onset, or evidence from vascular imaging of persistent occlusion after IV rtPA
- Evidence of a large vessel (≥2.5mm in diameter) occlusion in the cerebral circulation
- NIH Stroke Scale (NIHSS) score ≥8
- Signed informed consent

Key Exclusion Criteria

- History of stroke in the past 3 months
- Females who are pregnant

- Pre-existing neurological or psychiatric disease that could confound the study results such as a pre-stroke mRS score ≥1
- Known severe allergy to contrast media
- Uncontrolled hypertension (defined as systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg)
- CT evidence of the following conditions at randomization:
  - Significant mass effect with midline shift
  - Large infarct region >1/3 of the middle cerebral artery territory
  - Evidence of intracranial hemorrhage
- Angiographic evidence of an arterial stenosis proximal to the occlusion that could prevent thrombus removal
- Angiographic evidence of preexisting arterial injury
- Rapidly improving neurological status prior to enrollment
- Bilateral stroke
- Intracranial tumors
- Known history of cerebral aneurysm or arteriovenous malformation
- Known hemorrhagic diathesis, coagulation deficiency, or on anticoagulant therapy with an International Normalized Ratio (INR) of >1.7
- Baseline platelets <50,000
- Use of IV heparin in the past 48 hours with PTT >1.5 times the normalized ratio
- Baseline glucose <50mg/dL or >300mg/dL
- Life expectancy less than 90 days prior to stroke onset
- Participation in another clinical investigation that could confound the evaluation of the study device

Summary of reasons for exclusion of enrolled subjects, especially those based on angiographic criteria

Of the 198 patients enrolled, a total of 15 patients were excluded for angiographic reasons. These patients along with 5 patients who did not meet key inclusion/exclusion criteria and 5 patients who did not receive the assigned treatment were excluded from the Per Protocol analysis.

Patient Disposition
Summary of Patient Disposition

	Randomized (ITT)*			Primary Effectiveness Cohort+		
	All Patients (N=198)**	**3D / Penumbra System (N=98)**	**Penumbra System (N=100)**	**All Patients (N=150)**	**3D / Penumbra System (N=74)**	**Penumbra System (N=76)**
Completed Study	70.2% (139/198)	68.4% (67/98)	72.0% (72/100)	68.7% (103/150)	63.5% (47/74)	73.7% (56/76)
Died prior to 90 day follow-up	22.7% (45/198)	19.4% (19/98)	26.0% (26/100)	24.0% (36/150)	23.0% (17/74)	25.0% (19/76)
Early termination						
Subject Lost to Follow-Up	5.1% (10/198)	8.2% (8/98)	2.0% (2/100)	6.0% (9/150)	10.8% (8/74)	1.3% (1/76)

	Randomized (ITT)*			Primary Effectiveness Cohort+		
Subject Withdrawal	2.0% (4/198)	4.1% (4/98)	0% (0/100)	1.3% (2/150)	2.7% (2/74)	0% (0/76)

*All patients who were consented and randomized were included in the intent to treat (ITT) population. The ITT population included all subjects with data for a given endpoint; results were assessed according to randomized assignment regardless of the treatment actually received.

**There were 8 patients not treated with any component of the Penumbra System due to the resolution of thrombus, inability to access target vessel due to tortuous anatomy and angiographic exclusion.

+The primary effectiveness cohort excluded patients that did not meet angiographic criteria (n=15), inclusion or exclusion criteria was not met (n=5), treatment was not as assigned (n=5), patients received tPA > 3 hours (n=14) or patients that had a baseline TICI ≥ 2a (n=9), which resulted in a primary effectiveness cohort of 150 patients.

The large vessel occlusions randomized include the following target vessels.

Patient Target Vessels in Penumbra 3D Trial

	Randomized (ITT)			Primary Effectiveness Cohort		
Target Vessel	**All Patients (N=198)**	**3D / Penumbra System (N = 98)**	**Penumbra System (N = 100)**	**All Patients (N=150)**	**3D / Penumbra System (N =74)**	**Penumbra System (N =76)**
ICA	19.7% (39 / 198)	15.3% (15 / 98)	24.0% (24 / 100)	19.3% (29/150)	14.9% (11/74)	23.7% (18/76)
MCA M1	63.6% (126 / 198)	66.3% (65 / 98)	61.0% (61 / 100)	68.7% (103/150)	71.6% (53/74)	65.8% (50/76)
MCA M2	13.6% (27 / 198)	15.3% (15 / 98)	12.0% (12 / 100)	10.7% (16/150)	13.5% (10/74)	7.9% (6/76)
PCA	1.0% (2 / 198)	1.0% (1 / 98)	1.0% (1 / 100)	0.7% (1/150)	0% (0/74)	1.3% (1/76)
Basilar	1.0% (2 / 198)	1.0% (1 / 98)	1.0% (1 / 100)	0.7% (1/150)	0% (0/74)	1.3% (1/76)

Primary Effectiveness Endpoint

The Primary Effectiveness Endpoint was revascularization of the occluded target vessel. Revascularization was defined by a mTICI score of 2 to 3 following use of the 3D/Penumbra System and prior to the use of any additional therapies or adjunctive devices. Use of IA lytic was considered a treatment failure. Patients administered IV rtPA > 3 hours from stroke symptom onset or having an mTICI score of 2a or greater prior to intervention are excluded. Angiographic results were adjudicated by an independent Core Laboratory.

Primary Effectiveness Endpoint	All Patients	3D / Penumbra System	Penumbra System	Difference (90 % CI)†
mTICI score of 2 to 3, Per Protocol, % (n/N)	86.0% (129/150)	86.5 % (64/74)	85.5% (65/76)	1.0 % (-8.4%, 10.3%)

†Wald confidence intervals

Primary Safety Endpoint

The Primary Safety Endpoint was incidence of device and procedure-related serious adverse events that occurred within 24 hours post-procedure. The primary safety endpoint was adjudicated by a Clinical Events Committee. Each site was permitted two roll-in patients and these patients were the first patients the physicians used the 3D Revascularization Device. The primary safety endpoint data for the roll-in patients is included.

	Roll-In	Randomized (As Treated)		
Primary Safety Endpoint (As Treated)	**Roll-In**	**All Patients**	**3D / Penumbra System**	**Penumbra System**
Procedure Related Serious Adverse Event, % (n/N)	7.9% (6/76)	12.7% (23/181)	10.2% (9/88)	15.1% (14/93)
Device Related Serious Adverse Event, % (n/N) SAE during the procedure	6.6% (5/76)	5.0% (9/181)	4.5% (4/88)	5.4% (5/93)

Secondary Endpoint

The Secondary Endpoint was functional outcome at 90 days post-procedure. Patients administered IV rtPA > 3 hours from stroke symptom onset (n=14) or having an mTICI score of 2a or greater prior to intervention (n=9) are excluded. Eight (8) patients who were not treated with any component of the Penumbra System are also excluded. Patients who received any additional therapies or adjunctive devices following the use of the Penumbra System (+3D) are imputed as an outcome failure.

Functional Outcome at 90 Days Post-Procedure (modified ITT)

Outcome (ITT)	All Patients (N=167)	3D / Penumbra System (n=82)	Penumbra System (n=85)	p-value
mRS 0-2	37.5% (57/152)	38.0% (27/71)	37.0% (30/81)	1.0

Note: P-value from two-sided Fisher's Exact test for categorical assessment between groups.

Each specific SAE through 90 days occurring in more than 2% of patients (As Treated)

Serious Adverse Event MedDRA Preferred Term	All Patients (N=181)	3D / Penumbra System (N=88)	Penumbra System (N=93)
Stroke in evolution	15.5% (28/181)	12.5% (11/88)	18.3% (17/93)
Haemorrhagic transformation stroke	2.8% (5/181)	2.3% (2/88)	3.2% (3/93)
Haemorrhage intracranial	2.2% (4/181)	2.3% (2/88)	2.2% (2/93)
Respiratory failure	5.0% (9/181)	2.3% (2/88)	7.5% (7/93)

Serious Adverse Event MedDRA Preferred Term	All Patients (N=181)	3D / Penumbra System (N=88)	Penumbra System (N=93)
Acute respiratory failure	2.8% (5/181)	4.5% (4/88)	1.1% (1/93)
Pulmonary embolism	2.2% (4/181)	2.3% (2/88)	2.2% (2/93)
Dysphagia	8.3% (15/181)	9.1% (8/88)	7.5% (7/93)
Atrial fibrillation	3.3% (6/181)	3.4% (3/88)	3.2% (3/93)
Deep vein thrombosis	2.2% (4/181)	1.1% (1/88)	3.2% (3/93)
Renal failure acute	2.2% (4/181)	4.5% (4/88)	0.0% (0/93)
Anaemia	2.2% (4/181)	2.3% (2/88)	2.2% (2/93)

Categorization of SAEs through 90 days by Body System (As Treated)

Serious Adverse Event by Body System	All Patients (N=181)	3D / Penumbra System (N=88)	Penumbra System (N=93)
Number of Patients with at Least one Serious Adverse Event	48.1% (87/181)	43.2% (38/88)	52.7% (49/93)
Nervous system disorders	26.0% (47/181)	21.6% (19/88)	30.1% (28/93)
Respiratory, thoracic and mediastinal disorders	11.0% (20/181)	10.2% (9/88)	11.8% (11/93)
Gastrointestinal disorders	9.9% (18/181)	9.1% (8/88)	10.8% (10/93)
Cardiac disorders	9.4% (17/181)	11.4% (10/88)	7.5% (7/93)
Vascular disorders	5.5% (10/181)	1.1% (1/88)	9.7% (9 /93)
Infections and infestations	4.4% (8/181)	2.3% (2/88)	6.5% (6/93)
Renal and urinary disorders	2.8% (5/181)	4.5% (4/88)	1.1% (1/93)
Blood and lymphatic system disorders	2.2% (4/181)	2.3% (2/88)	2.2% (2/93)
Injury, poisoning and procedural complications	2.2% (4/181)	2.3% (2/88)	2.2% (2/93)
Metabolism and nutrition disorders	1.7% (3/181)	2.3% (2/88)	1.1% (1/93)
Endocrine disorders	0.6% (1/181)	0.0% (0/88)	1.1% (1/93)
General disorders and administration site conditions	0.6% (1/181)	1.1% (1/88)	0.0% (0/93)
Immune system disorders	0.6% (1/181)	0.0% (0/88)	1.1% (1/93)
Investigations	0.6% (1/181)	0.0% (0/88)	1.1% (1/93)

12 Summary of Substantial Equivalence

The subject Penumbra 3D Revascularization Device is substantially equivalent to the predicate device with regard to intended use, operating principle, design concept, materials, shelf-life, packaging and sterilization processes.