SUMMARY OF SAFETY AND EFFECTIVNESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Cutting/Scoring Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheter
Device Trade Name:	Scoreflex NC Scoring PTCA Catheter
Device Product Code:	NWX
Applicant's Name and Address:	OrbusNeich Medical (Shenzhen) Co., Ltd. No. 1 Jinkui Road, Futian Free Trade Zone Shenzhen, 518038, China
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P200041
Date of FDA Notice of Approval:	December 21, 2021

II. INDICATIONS FOR USE

The Scoreflex NC Scoring PTCA Catheter is indicated for:
Balloon dilatation of a de novo stenotic portion of a coronary artery and in-stent restenosis in coronary arteries in patients evidencing coronary ischemia for the purpose of improving myocardial perfusion

III. CONTRAINDICATIONS

The use of the Scoreflex NC Scoring PTCA Catheter is contraindicated in the following patient types:

- Patients with an unprotected left main coronary artery
- Patients with coronary artery spasm in the absence of a significant stenosis

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Scoreflex NC Scoring PTCA labeling.

V. DEVICE DESCRIPTION

The Scoreflex NC Scoring PTCA Catheter (Scoreflex NC) is a sterile, single use rapid exchange (RX) catheter consisting of a non-compliant Nylon balloon, a Nickel-titanium alloy (Nitinol) scoring wire, a soft tip, a distal shaft, and a proximal shaft. The nominal and rated burst pressure of the Scoreflex NC balloon is 12 atm and 20 atm, respectively. The proximal shaft of the catheter

is composed of a female luer connector bonded to a Polytetrafluoroethylene (PTFE) coated stainless steel hypotube and the scoring wire is laser welded to the distal end of the hypotube. The distal shaft is composed of an outer nylon tube with the balloon/tip tube and scoring wire welded at the distal tip. The cutting section of the scoring wire is located outside of the balloon. Two radiopaque platinum/iridium marker bands are positioned on the scoring wire and aligned with the balloon shoulders to ensure accurate positioning of the balloon and facilitate fluoroscopic visualization. A hydrophilic coating composed of Polyvinylpyrrolidone and Polyethylene glycol covers the outer surface of the distal catheter tip and the distal shaft; the inside of the guidewire lumen (tip lumen) and the outer surface of the balloon are lubricated with a silicone coating. A figure of the device is provided below.

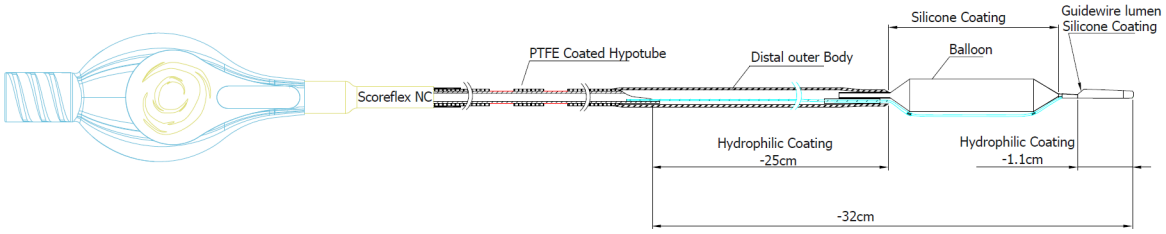

Figure 1. Scoreflex NC Scoring PTCA Catheter

The Scoreflex NC Scoring PTCA Catheter is compatible with ≤0.014" (0.36mm) guide wires and ≥5F (1.75mm to 3.5mm balloon diameters) or ≥6F (4.0mm balloon diameters) guiding catheters. The working length of the device is 139cm.

Table 1. Scoreflex NC Scoring PTCA Catheter Device Characteristics

Characteristic	OrbusNeich Scoreflex NC
Available balloon Lengths (mm)	10, 15, 20
Available balloon Diameters (mm)	1.75, 2.0, 2.25, 2.5, 2.75, 3.0, 3.5, 4.0
Catheter Working Length (cm)	139
Catheter Design	Rapid Exchange
Balloon Inflation Pressure (atm)	Nominal: 12 Rated Burst Pressure: 20
Guiding Catheter Compatibility	5F 6F
Catheter Shaft Outer Diameter (nominal)	Proximal: 2.1F Distal: 2.7F

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of coronary artery disease including medical therapy, atherectomy, stenting, bypass graft (CABG) surgery or the use of other commercially available PTCA catheters and scoring balloons catheters. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Scoreflex NC has been available for distribution in the European Union (EU) since the CE Mark was first issued on May 12, 2016. The device has been introduced to foreign markets

outside of the United States as listed in the table below.

Table 2. Scoreflex NC in Foreign Markets Outside of the United States

Australia	Iran	Republic of Serbia
Austria	Ireland	Romania
Belgium	Israel	Russian Federation
Brunei Darussalam	Italy	Singapore
Bulgaria	Japan	Slovakia
Chile	Jordan	Slovenia
Cyprus	Kuwait	South Africa
Czech Republic	Lithuania	Spain
Denmark	Malaysia	Sweden
Egypt	Myanmar	Switzerland
Finland	Nepal	Thailand
France	Netherlands	Turkey
Germany	Norway	Ukraine
Hong Kong	Philippines	United Kingdom
Indonesia	Poland	Vietnam

The Scoreflex NC has not been withdrawn from any country for reasons relating to device safety and 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 Scoreflex NC Scoring PTCA Catheter:

- Death
- Acute myocardial infarction
- Total occlusion of the coronary artery
- Coronary vessel dissection, perforation, rupture, or injury
- Acute vessel closure
- Restenosis of the dilated vessel
- Unstable angina
- Stroke, air embolism and embolization of fragmentation of thrombotic or atherosclerotic material
- Arrhythmias, including ventricular fibrillation
- Hypertension
- Hypotension
- Coronary artery spasm
- Hemorrhage or hematoma
- Arteriovenous fistula
- Drug reactions, allergic reaction to contract medium
- Infection
- Need for blood transfusion

For the specific adverse events that occurred in the clinical studies, please see Sections X and XI below.

IX. SUMMARY OF NONCLINICAL STUDIES

A series of non-clinical laboratory studies were performed to ensure that the Scoreflex NC met the specified performance characteristics as defined via design inputs and recommendations of the guidance document for Certain Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheters (issued on September 8, 2010) and per applicable international and domestic standards. Although the scope of the 2010 PTCA guidance does not include cutting/scoring catheters, many of the non-clinical testing recommendations are still applicable.

Test	Description/Purpose	Acceptance Criteria	Summary of Test Results
Bench testing			
Visual Inspection	To demonstrate that the appearance of the product would meeting corresponding specifications	Catheter, including proximal markers, pulling wire, tip and hydrophilic/silicone lubricant should be free from anomalies.	Passed
Dimensional verification	To demonstrate that the device dimensions meet corresponding specifications	Device dimensions must meet the established engineering drawing specifications	Passed
Balloon preparation, deployment, and retraction	To demonstrate that the product could be safely and reliably delivered to the intended location according to the IFU	Balloon catheter preparation, delivery, balloon inflation/ deflation, and catheter retraction steps must not damage the balloon catheter.	Passed
Balloon Rated Burst Pressure	To establish the rated burst pressure	Burst pressure> 20 atm No evidence of radial burst and balloon burst shall be before shaft burst	Passed
Shaft Burst	To demonstrate that the shafts of all catheters burst at or higher than 30 atm	Catheter shaft shall have no evidence of leak at 30 atmospheres	Passed
Balloon Fatigue	To determine the cyclic reliability of the catheter	Balloon shall withstand 20 cycles of repeated inflation/ deflation to RBP without failure	Passed
Balloon Compliance	To determine how the diameter of a balloon varies with applied inflated pressure and to establish the labeled compliance values	Compliance should be approximately 0.8% per atm	Passed
Balloon Inflation/Deflation time	To verify that the balloon inflates and deflates within a specified time	Balloon Inflation＜10 seconds Balloon Deflation ＜15 seconds	Passed

Catheter bond strength	To ensure that all bond joints on the catheters would meet strength specification	Pulling Wire/Tip Tube: 0.674 lbs Balloon Distal Leg/Tip Tube: 0.674 lbs Balloon Proximal Weld: 0.674 lbs Marker Band: 0.8 lbs Pulling Wire/Hypotube: 2.0 lbs Transition Weld: 2.0 lbs Hub Bonding: 2.25lbs	Passed
Tip Pull Strength	To demonstrate that the catheter tip bond would meet tensile strength specifications	>0.674 lbs	Passed
Flexibility and kink	To assess the ability of product to withstand flexural forces that are typical of clinical use	Each catheter must be free of kinks.	Passed
Torque Strength	To assess the ability of product to withstand torque when the distal tip is not free to rotate	Catheter must withstand a minimum of three (3) rotations of the proximal hub without any break or fracture	Passed
Coating Integrity	To demonstrate that delamination or degradation of the coating would not occur during simulated use	No significant increase in the frictional forces after simulated use and no gross changes in the visual appearance after simulated use	Passed
Particulate	To evaluate the quantity of particles generated during simulated use	Data will be compared to USP<788> requirements for small volume, single- dose infusions	Passed
Balloon Rated Burst (In-Stent)	To establish the rated burst pressure within an expanded stent	＞20 atm.	Passed
Balloon Fatigue (In-Stent)	To determine the cyclic reliability of the catheter within an expanded stent	10 cycles of repeated inflation/ deflation to RBP without failure	Passed
Radiopacity	To demonstrate visibility of the balloon marker bands	Marker bands must be clearly visible and indicative of the balloon landmarks	Passed
Biocompatibility			
Cytotoxicity (ISO 10993-5)	To evaluate the test article for cytotoxicity to mammalian cells in culture	Non-cytotoxic	Passed
Sensitization (ISO 10993-10)	To evaluate the allergenic potential or sensitizing capacity of the test article in guinea pigs	Non-sensitizing	Passed
Intracutaneous Reactivity (ISO 10993-10)	To assess the potential of the test article to cause local irritation in the dermal tissues of rabbits	Non-irritating	Passed
Acute Systemic Toxicity (ISO 10993-11)	To assess for potential toxic effects as a result of a single-dose systemic injection in mice	Non-toxic	Passed
Hemolysis (Direct and Extract; ASTM F756)	To evaluate the hemolytic potential of the test article and test article extracts	Non-hemolytic	Passed

Complement Activation (ISO 10993-4)	To evaluate the potential to activate the complement system	Not a complement activator	Passed
Thrombogenicity (ISO 10993-4)	To evaluate the thromboresistance of the test article in comparison to a negative control device	Non-thrombogenic	Passed
Material Mediated Pyrogenicity (ISO 10993-11; USP<151>)	Determination of potential pyrogenic response induced by an extract of the test article following injection into the marginal ear vein in rabbits	Non-pyrogenic	Passed
Genotoxicity: AMES (ISO 10993-3)	To evaluate the mutagenic potential of the test article using bacteria strains in the presence and absence of microsomal enzymes	Non-mutagenic	Passed
Genotoxicity: In Vitro Mouse Lymphoma Assay (ISO 10993-3; OECD 490)	To evaluate the ability of the test article to induce forward mutations at the thymidine kinase (TK) locus of mouse lymphoma cells in the presence of trifluorothymidine (TFT)	Non-mutagenic and non- clastogenic	Passed
Packaging			
Visual Inspection	To ensure that the package maintains a sterile barrier following thermal cycling and transportation simulation	Seal width ≥ 7 mm	Passed
Integrity		No damaged component	Passed
Burst		Pouch burst pressure ≥12.2 inch H2O	Passed
Sterilization			
Sterilization Validation	Overkill approach (half cycle method) per ISO 11135-1	Sterility Assurance Level (SAL) of 10^{-6}.	Passed
Shelf life			
2-year Simulated Aging	Repeat of bench testing to assess the effect of aging on the Scoreflex NC	Test results after 2-year simulated aging shall meet the same criteria as those of bench testing.	Passed

Animal Studies

The objective of the in vivo animal study was to confirm the safety and efficacy of the device by histopathological assessments using miniature pig coronary arteries. Balloons were inflated in the left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX), or right coronary artery (RCA) at or near the maximum inflation pressure while under fluoroscopy. Sapphire II NC and Scoreflex were selected as the control devices. Sapphire II was selected as a control device because it is a non-compliant balloon catheter and Scoreflex was selected as it is considered the first generation of this scoring device. These are appropriate because they represent comparable angioplasty platforms. The goals of the study were to assess comparative histopathological examination and performance characteristics.

Following balloon treatment, there were no problematic findings in the coronary artery blood flow state or treatment site perforations, dissections, or other disorders, with no significant differences noted among the Scoreflex NC and the control devices (Sapphire II NC and Scoreflex). Histopathological examination as measured by the Schwartz score for the Scoreflex NC and Sapphire II NC balloon catheters had equivalently low scores of 0 to 1, demonstrating a low vessel injury post-angioplasty.

With respect to performance characteristics, no significant difference was observed among the scores for the Scoreflex NC, Sapphire II NC, and Scoreflex balloon catheters.

The histopathological assessment performed by the third-party contract research organization found that overall arterial injury was absent or confined to focal IEL disruption(s) with no medial involvement. Mechanical overstretch noted by accumulated proteoglycan was absent to minimal. Minor indentations in the medial wall were noted primarily from the Scoreflex NC study balloon and Scoreflex control balloon. There was an absence of fibrin, inflammation, and medial hemorrhage for all treated segments. Review of the original EVG slides confirmed essentially normal vessel elements with no indication of lacerations/dissections. H&E staining showed a relative absence of inflammation for all vessels, indicating that healing in the porcine coronary artery model would be complete by 28 days without clinical consequence.

Based on the findings from the analysis, the Scoreflex NC balloon catheter demonstrated acceptable safety and device performance. Furthermore, based on the histopathological analysis, there were no concerns regarding the use of the Scoreflex NC in a human clinical study.

X. SUMMARY OF CLINICAL STUDIES

OrbusNeich performed a clinical study to assess the acute safety and device procedural success of the Scoreflex NC Scoring PTCA Catheter in its intended use for the dilatation of coronary artery stenosis (>70% diameter stenosis). The study was performed in the United States under an approved IDE in accordance with Good Clinical Practice guidelines, ISO 14155, 21 CFR 812, as well as local regulations, and applicable regulatory requirements. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Subjects were treated between 15 February 2019 and 27 December 2019. The database for this PMA reflected data collected through 27 December 2019 and included 200 subjects. There were 12 investigational sites in the USA.

The study was a prospective, open label, multi-center, single arm, observational study designed to evaluate the acute safety and device procedural success of the Scoreflex NC Scoring PTCA Catheter in subjects with stenotic coronary arteries during percutaneous coronary intervention.

The evaluation of safety and clinical effectiveness was performed through a primary endpoint of device procedural success and secondary endpoint of assessment of angiographic efficacy as shown through a clinically significant reduction in diameter stenosis as determined by an independent Core Lab using Quantitative Coronary Angiography (QCA). The primary endpoint was assessed using descriptive statistics on the Intention To Treat (ITT) patient population. The primary endpoint was reported using frequencies, percentages, and a two-sided exact 95%

confidence interval.

Secondary endpoints were evaluated in the ITT subject population set using descriptive statistics. The secondary endpoints have been summarized using the mean, median, standard deviation, minimum, maximum, and two-sided 95% confidence intervals. Frequencies, percentages and two- sided exact 95% confidence intervals have been reported for binary endpoints as appropriate, for clinical endpoints. An independent clinical research organization was used for site management, data coordination and monitoring.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Scoreflex NC – Scoring PTCA Catheter Clinical study was limited to subjects who met the following inclusion criteria:
Clinical:

- Subject is ≥ 18 years of age
- Subject or a legally authorized representative much provide written informed consent prior to any study related procedures
- Subject must agree not to participate in any other clinical study during hospitalization for the index procedure that would interfere with the endpoints of the study
- Subjects must have a single or double vessel coronary artery disease and clinical evidence of ischemic heart disease, such as CAD, stable/unstable angina, or silent ischemia

Angiographic:

- Subject must have de novo or stenotic lesion(s) in native coronary arteries, including in-stent restenosis suitable for percutaneous coronary intervention
- A maximum of two lesions, including at least one target lesion, in up to two coronary arteries
- Target lesion must have a reference vessel diameter (RVD) between 1.75 and 4.0mm by visual estimation
- Target lesion(s) must have a diameter stenosis of ≥ 70% by visual estimation and may include chronic total occlusions (CTO)
- The non-target lesion must be located in different coronary artery from the Target lesion
- Treatment of non-target lesion, if any, must be completed prior to treatment of target lesion and must be deemed a clinical angiographic success as visually assessed by the physician

Subjects were not permitted to enroll in the Scoreflex NC – Scoring PTCA Catheter Clinical study if they met any of the following exclusion criteria:

Clinical:

- Subject with a known hypersensitivity or contraindication to aspirin, heparin, bivalirudin, anti-platelet medications, or sensitivity to contract media which cannot be adequately pre-medicated
- Subject with known diagnosis of STEMI or NSTEMI at index presentation or within 7 days of study screening
- Subject with known pregnancy or is nursing. Women of child-bearing

potential should have a documented negative pregnancy test within 7 days before index procedure
- Planned or actual target lesions treatment with an unapproved device, atherectomy, laser, cutting balloon or thrombectomy during the index procedure
- A serum creatinine level > 2.0 mg/dl within 7 days prior to index procedure
- Cerebrovascular accident (CVA) within the past 6 months
- Active peptic ulcer or active gastrointestinal (GI) bleeding within the past 6 months
- Subject has a known left ventricular ejection fraction (LVEF) <30%
- Target lesion located within an arterial or saphenous vein graft or graft anastomosis

Angiographic:

- More than two lesions requiring treatment
- Target lesions longer than 30mm by visual estimation
- Extreme angulation (90° or greater) proximal to or within the target lesion
- Previous percutaneous intervention of lesions in a target vessel (including side branches) conducted within 9 months before the study procedure and located within 10 mm from the current target lesion
- Target lesion demonstrating severe dissection prior to planned deployment of the Scoreflex NC device
- Unprotected left main coronary artery disease (greater than 50% diameter stenosis)
- Coronary artery spasm of the target vessel in the absence of a significant stenosis
- Target lesion with angiographic presence of probable or definite thrombus
- Target lesion involves a bifurcation requiring treatment with more than one stent or pre-dilatation of a side branch > 2.0 mm in diameter
- Non-target lesion to be treated during index procedure meets any of the following criteria:
    - Located within a bypass graft (venous or arterial)
    - Left main location
    - Chronic total occlusion
    - Involves a bifurcation (i.e., bifurcation requiring treatment with more than 1 stent)
    - Treatment not deemed a clinical angiographic success

2. Follow-up Schedule

All subjects were followed through hospital discharge. The table below summarizes the schedule of procedures.

Table 3. Schedule of Procedures

	≤ 7 days before procedure	≤ 24 hours before procedure	Procedure	Post-discharge/ Hospital Discharge
Study Eligibility	X			
Informed Consent	X			

Demographics, Medical history including coronary medical history	X			
Physical assessment, including vital signs	X			X
Angina class		X		X
12-lead ECG		X		X
Cardiac Medication review		X	X	X
Pregnancy test (women only)	X			
Laboratory tests				
Serum Creatinine	X			
CBC with platelets	X			
CK Total/CK-MB		X[a]	X[b]	X
Angiographic Assessment			X	
Review of Adverse events and device-related events			X	X

[a] All subjects must have CK/CK-MB drawn within 24 hours before the procedure to determine eligibility; however, if the results are not available, eligibility may be based upon troponin values [b] For three CK-MB draws. The first draw should be performed immediately after the procedure, the second draw should be performed 6-12 hours post-procedure and the third draw should be performed 18-24 hours post-procedure, or prior to discharge, whichever comes first.

3. Clinical Endpoints

Primary safety and efficacy endpoint:

The study primary Device Procedural Success endpoint was defined as consisting of the following:

- Successful delivery, inflation, deflation, and withdrawal of the study balloon
- No evidence of vessel perforation, flow limiting dissection (grade C or higher) or reduction in Thrombolysis in Myocardial Infarction (TIMI) flow from baseline related to the Scoreflex NC study balloon
- Final TIMI flow grade of 3 at the conclusion of the PCI procedure

Secondary endpoint:

- Final diameter stenosis ≤ 50% in at least one of the Scoreflex NC attempted lesions following completion of the interventional procedures, including adjunctive stenting

Secondary clinical endpoints measured through hospital discharge:

- In-hospital Major Adverse Cardiac Events (MACE), a composite of:
  - All death (cardiac and non-cardiac)
  - Myocardial infarction (MI)
  - Target lesion revascularization (TLR), clinically indicated

- In-hospital stent thrombosis (ST) within the target vessel
- Clinically significant arrhythmias (requiring intervention)

Secondary peri-procedural endpoints measured through hospital discharge:

- Occurrence of Scoreflex NC study balloon rupture
- Improvement in Minimum Lumen Diameter (MLD) following use of Scoreflex NC coronary dilatation catheters (measured by QCA)

B. Accountability of PMA Cohort

All 200 subjects enrolled in the PMA study, 100% (n =200) subjects were available for analysis at the completion of the study, which occurred at the time of hospital discharge.

C. Study Population Demographics and Baseline Parameters

A total of two hundred (200) subjects were treated in accordance with the protocol at 12 U.S. investigation sties. All subjects were screened according to the protocol inclusion and exclusion criteria and were followed through hospital discharge. The analyses performed on the intent-to-treat (ITT) population were descriptive.

Table 4. Baseline Patient Demographics -ITT Population

Variables	Patients (N=200)
Age (Years) [1]	
Mean (SD)	67.3 (8.98)
Median	68
Min, Max	40, 89
Gender	
Female	46/200 (23.0%)
Male	154/200 (77.0%)
Race	
Asian	2/200 (1.0%)
Black or African American	18/200 (9.0%)
White or Caucasian	178/200 (89.0%)
Other	2/200 (1%)
BMI (kg/m^2) [2]	
Mean (SD)	31.3 (5.81)
Median	30
Min, Max	20, 52
Left Ventricular Ejection Fraction	
30-40%	28/200 (14.0%)
>40%	170/200 (85.0%)
Not Done	2/200 (1.0%)
Current Cardiac Status	
Asymptomatic	18/200 (9.0%)
Silent Ischemia	8/200 (4.0%)
Stable angina	116/200 (58.0%)
Unstable angina	57/200 (28.5%)

Variables	Patients (N=200)
NSTEMI	0 (0.0%)
STEMI	1/200 (0.5%)
Unknown	0 (0.0%)
Heart failure NYHA class III or IV	4/200 (2.0%)
History of the following	
Diabetes mellitus	88/200 (44.0%)
Prior PCI	106/200 (53.0%)
CABG	26/200 (13.0%)
MI	61/200 (30.5%)
Diagnosis of Heart Failure	18/200 (9.0%)
Hypertension (requiring treatment)	182/200 (91.0%)
Hypercholesterolemia (requiring treatment)	181/200 (90.5%)
Multivessel disease	26/200 (13.0%)
Cigarette smoking (within 30 days)	37/200 (18.5%)

[1] Age is defined as (Enrollment Date – Birth Date + 1)/365.25
[2] BMI is defined as weight (in kg)/height^2 (in meter)
SD: Standard Deviation

Table 5. Baseline Angiographic Characteristics

Parameters	Lesions - 221 (%)
Number of lesions treated per patient	
1 lesion	179/200 (89.5%)
2 lesions	21/200 (10.5%)
Lesion Length, mm (mean ± SD; min, max)	18.37±12.93; 3.45, 83.75
Reference vessel diameter, mm (mean ± SD; min, max)	2.62±0.45; 1.58, 3.95
Minimal luminal diameter, mm (mean ± SD; min, max)	0.84±0.40; 0.00, 2.10
Vessel Location	
LAD	97/221 (43.9%)
LCx	55/221 (24.9%)
RCA	68/221 (30.8%)
N/A	1/221 (0.5%)
Lesion Location	
Ostial	7/221 (3.2%)
Proximal	98/221 (44.3%)
Middle	93/221 (42.1%)
Distal	23/221 (10.4%)
Bifurcation	
Present	83/221 (37.6%)
Absent	137/221 (62.0%)
N/A	1/221 (0.5%)
Calcification, Any	
Moderate	29/221 (13.1%)
Severe	52/221 (23.5%)
None/Mild	123/221 (55.7%)
N/A	17/221 (7.7%)

Parameters	Lesions - 221 (%)
Pre-TIMI	
0	6/221 (2.7%)
1	5/221 (2.3%)
2	6/221 (2.7%)
3	204/221 (92.3%)
Total Occlusion	
Yes	11/221 (5.0%)
No	210/221 (95.0%)

SD: Standard Deviation

Table 6. Investigator-defined Reason for Using the Scoreflex NC

Reason for selecting the Scoreflex NC	Patients (N=200)
Predilatation	127 (63.5%)
Resistant or calcified lesions	17 (8.5%)
Fibrotic lesion	0 (0.0%)
In-stent restenosis	19 (9.5%)
Chronic Total Occlusion (CTO)	5 (2.5%)
Or general use of non-compliant balloon	32 (16.0%)

D. Safety and Effectiveness Results

1. Primary Endpoint Results (Safety and Effectiveness Composite Endpoint)

   Device Procedural Success was site reported as achieved in 187/200 (93.5%) of the subjects, defined as successful delivery, inflation, deflation, and withdrawal of all the study balloons, an absence of device-related vessel injury, and a final TIMI flow grade of 3 at the conclusion of the PCI procedure.

Table 7. Primary Endpoint Summary - ITT Population

Primary Endpoint	Scoreflex NC Scoring PTCA Catheter Subjects (n=200)	Two sided 95% CI Lower Bound using Normal Approximation	Two sided 95% CI Upper Bound using Normal Approximation
Device Procedural Success	187/200 (93.5%)	90.1 %	96.9 %
Success of delivery, inflation/deflation, and withdrawal	191/200 (95.5%)	92.6%	98.4%
Absence of vessel perforation, flow limiting dissection (grade C or higher), or reduction in TIMI flow from baseline related to the study balloon.	196/200 (98.0%)	96.1%	99.9%
Final TIMI flow grade of 3 at the conclusion of the PCI procedure.	198/200 (99.0%)	97.6%	100.0%

Note: The confidence intervals are unadjusted (not accounting for multiplicity).

Details of the nine (9) occurrences where the study balloon was not successfully used are summarized in the table below.

Table 8. Summary of Unsuccessful Uses

Listing of nine (9) instances where the study balloon was not successfully used	**Scoreflex NC Scoring PTCA Catheter** Subjects (n=200)
Physician was able to cross with another device to treat the lesion	4/200 (2.0%)
Physician down-sized to a smaller sized study device and was able to successfully cross to treat the lesion	1/200 (0.5%)
The target lesion was a chronic total occlusion (CTO) that could not be crossed by any device and was left untreated	1/200 (0.5%)
Study device could not exit the guiding catheter, was removed from the patient and returned to the Sponsor for assessment.	1/200 (0.5%)
Study balloon could not be inflated	1/200 (0.5%)
Study balloon burst during the first inflation	1/200 (0.5%)

The freedom from device-related injury, defined as no evidence of vessel perforation; flow limiting dissection; or reduction in TIMI Flow from baseline as related to the use of the Scoreflex NC Scoring PTCA balloon, was achieved in 196/200 subjects (98.0%). Of the four occurrences of device related injuries, there was one (1) case of a vessel perforation caused by the manipulation of the steerable guidewire, one (1) case of flow-limiting dissection associated with the use of the study device, and finally in two (2) cases the angiographic core laboratory determined that a reduction in TIMI flow from baseline was observed after the attempted use of the study device. In each of these cases there were no reports of adverse events or site reported MACE events. There were no unanticipated adverse device effects in the reported data, no reportable events from the enrolling sites and there were zero (0) deaths during the conduct of this study.

TIMI grade flow of 3 at the completion of the PCI procedure, was achieved in 198/200 (99.0%) of the subjects, as evaluated by the angiographic core laboratory. In one (1) subject who presented with a CTO previously presented, the physician could not treat the lesion by any modality including with the Scoreflex NC Scoring PTCA study device, where the subject did not achieve a TIMI grade flow of 3 at the conclusion of the overall PCI procedure. In another case, the Scoreflex NC Scoring PTCA study device was successfully used, however the final TIMI flow at the completion of the procedure was of graded at 2, therefore not meeting the criteria TIMI grade flow of 3 for this endpoint.

FDA has found that the results are consistent with expected results for this device type and are acceptable.

2. Secondary Endpoint Results

The secondary peri-procedural endpoints of the Scoreflex NC Scoring PTCA catheter study device effectiveness are summarized in the table below.

Table 9. Study Device Effectiveness Outcomes

Secondary Endpoint	**Site Reported or Angiographic Central Core Lab Reported (QCA)**	**Overall Population (n=200 subjects)**	Two sided 95% CI Lower Bound using Normal Approximation	Two sided 95% CI Upper Bound using Normal Approximation
Peri-procedural endpoints of study device effectiveness				
Successful balloon delivery to the target lesion	Site Reported	193/200 (96.5%)	94.0%	99.0%
Successful inflation at the target lesion	Site Reported	192/200 (96.0%)	93.3%	98.7%
Successful deflation	Site Reported	193/200 (96.5%)	94.0%	99.0%
Successful withdrawal of the study balloon	Site Reported	199/200 (99.5%)	98.5%	100.0%
Absence of vessel perforation	Site Reported	199/200 (99.5%)	98.5%	100.0%
Absence of flow limiting dissection (Grade C or higher)	Site reported	199/200 (99.5%)	98.5%	100.0%
No reduction in TIMI flow from baseline related to the study balloon*	Core Lab Reported	178/180 (98.9%)	97.4%	100.0%
Final TIMI flow grade of 3 at the conclusion of the PCI procedure	Core Lab Reported	198/200 (99.0%)	97.6%	100.0%
Absence of balloon rupture of the study balloon	Site Reported	198/200 (99.0%)	97.6%	100.0%
Improvement in Minimum Lumen Diameter (measured by QCA) post-use of study device**	Core Lab Reported	161/177 (91.0%)	85.7%	94.7%
Final Diameter Stenosis <=50% at least one of Scoreflex NC study device attempted lesions***	Core Lab Reported	197/200 (98.5%)	96.8%	100.0%

Note: The confidence intervals are unadjusted (not accounting for multiplicity).
*The TIMI flow after study balloon dilation was not analyzable in 20 patients by the Angiographic Core Lab. Therefore, reduction in TIMI flow from baseline related to the study balloon could only be analyzed in 180 patients.
**The Improvement in MLD after use of the study balloon as measured by QCA was not analyzable in 23 patients by the Angiographic Core Lab. Therefore, this value could only be analyzed in 177 patients.
***The percent diameter stenosis was computed by comparing the minimal lumen diameter (MLD) at the stenosis with the corresponding reference diameter (RM) with the formula, [[1-(minimum lumen diameter/reference diameter)]*100]. MLD and RM are the average of MLD and RM at two projections, respectively as provided by the angiographic core laboratory.

A single (1) case of vessel perforation was caused by manipulation of the steerable guidewire and unrelated to the study device. The occurrence of study balloon rupture was reported in two (2) cases: one case where the balloon rupture occurred during the first inflation and prevented successful treatment of the lesion with the Scoreflex NC Scoring PTCA catheter and another case where the balloon burst during the second inflation after the lesion had been treated successfully with the Scoreflex NC Scoring PTCA Catheter. In both occurrences the lesion was successfully treated with the Scoreflex NC Scoring PTCA catheter or another device and there were no dissections or adverse events related to these two incidents or the use of the study device.

The attainment of a final diameter stenosis ≤50% in at least one study device treated lesion following completion of the interventional procedure, as determined by the angiographic core laboratory, was achieved in 197/200 subjects (98.5%). In one (1) subject discussed previously whom presented with a CTO which the physician could not treat by any modality including with the Scoreflex NC Scoring PTCA study device, the procedural angiographic efficacy was not achieved. In one (1) subject who also failed the primary endpoint previously presented above where the physician could not reach the lesion, the physician obtained 64% residual stenosis without adjunctive stenting. The third subject resultant in-segment stenosis was 51% with adjunctive stenting. Adjunctive stenting was not a protocol requirement for inclusion into this study, and there were a total of fifteen (15) subjects treated without the use of adjunctive stenting.

FDA has found that the results are consistent with expected results for this device type and are acceptable.

Adverse effects that occurred in the PMA clinical study

The independent Clinical Events Committee (CEC) positively adjudicated the occurrence of ten (10) major adverse cardiac events (MACE) reported in nine (9) subjects as detailed in the table below.

Table 10. In-hospital Clinical Safety and Efficacy Outcomes

Secondary Endpoint	CEC Adjudication (per protocol)	CEC Adjudication & Subjects without post-procedure enzyme testing*
In-hospital clinical safety and efficacy		
In-hospital MACE (composite of all death, target vessel MI or clinically indicated TLR)	9/200 (4.5%)	14/200 (7.0%)
All Death (cardiac & non-cardiac)	0/200 (0.0%)	0/200 (0.0%)
Myocardial Infarction	8/200+ (4.0%)	13/200 (6.5%)
Clinically indicated TLR	1/200 (0.5%)	1/200 (0.5%)
In-hospital stent thrombosis (ST) within the target vessel	0/200 (0.0%)	0/200 (0.0%)

Clinically significant arrhythmias requiring intervention	1/200 (0.5%)	1/200 (0.5%)

+Eight (8) cases of asymptomatic peri-procedural MIs detected by cardiac enzyme rises
*Worst case calculations for MI and MACE that includes the five (5) patients with missing enzyme data post-procedure and assumes elevated enzymes in these patients.

There were eight (8) incidents of asymptomatic peri-procedural MIs as detected by post-procedure elevations in cardiac enzyme levels which did not require treatment (4.0%), one (1) case with a target lesion revascularization (0.5%), and there were no reports (0) of death in the study. There was one (1) report of a clinically significant arrhythmia requiring intervention (0.5%) and there were no incidents of stent thrombosis.

Device Deficiencies and Protocol Deviations

Investigational sites were instructed to record any observed device deficiencies in the eCRF and report to the Sponsor. Study sites were also instructed to report any AE results from a device deficiency or other device issue as related to the use of the Scoreflex NC study device. There were no UADEs or AEs as a result of the site-reported device deficiencies and no device related complications occurred before discharge in any of the 200 patients. Table 11 below is a summary of the reported device deficiencies.

Table 11. Summary of Site Reported Deficiencies

Device Deficiency Noted	Qty of devices (N)	Resulted in an AE (Y/N)	Returned to Sponsor for Evaluation	Resulted in a MACE event (Y/N)
Unable to cross Lesion	N=8	No (N=8)	N=7	No (N=8)
GW trapped within distal Tip of Balloon, removed intact	N=2	No (N=2)	N=1	No (N=2)
Balloon burst	N=1	No (N=1)	N=1	No (N=1)
Balloon did not inflate	N=1	No (N=1)	N=0	No (N=1)
Balloon inflated to 16 atm for 30 seconds, 16 atm for 20 seconds. Balloon burst during second inflation and was removed	N=1	No (N=1)	N=0	No (N=1)
Balloon slipped off lesion	N=1	No (N=1)	N=1	No (N=1)
Balloon tip bent on itself when removed	N=1	No (N=1)	N=1	No (N=1)
Unable to exit guide with Balloon	N=1	No (N=1)	N=1	No (N=1)

The major and minor protocol deviations are summarized in Table 12 below.

There were nineteen (19) major protocol deviations reported for eighteen (18) subjects.

Table 12. Protocol Deviations

Major deviations	**N=19**
Informed Consent Procedure	0
Pre-procedure Laboratory testing not conducted per protocol	7
Treatment of a target lesion prior to the treatment on a non-target lesion	5
The need to treat more than 2 lesions after the procedure commenced	3
Non-target lesion located in same artery as target lesion.	1
Target lesion located in saphenous vein graft	1
Ejection Fraction value was not known prior to procedure	2
Minor deviations	**N=87**
Scoreflex NC device used on more than one lesion	6
CBC not collected	18
ECG not conducted post procedure	11
Report of at least one laboratory not conducted	34
Report of at least one laboratory collected out of window	16
Medication review not conducted within protocol specified time period	2

FDA has found that the results are consistent with expected results for this device type and are acceptable.

3. Subgroup Analyses

The Device Procedural Success of the Scoreflex NC Scoring PTCA catheter by the investigator specified indication for use in the study is given below in the table below.

Table 13. Device Procedural Success by Investigator Specified Indication for Use of Scoreflex NC

	Subjects	**Device Procedural Success**	**Successful use of Study Balloon**	**Absence of Device-Related Injury**	**Final TIMI flow grade of 3**
Overall	200	187/200 (93.5%)	191/200 (95.5%)	196/200 (98.0%)	198/200 (99.0%)

Pre-dilatation	127	120/127 (94.5%)	121/127 (95.3%)	125/127 (98.4%)	126/127 (99.2%)
Resistant or Calcified Lesions	17	16/17 (94.1%)	16/17 (94.1%)	17/17 (100%)	17/17 (100%)
In-Stent Restenosis	19	19/19 (100%)	19/19 (100%)	19/19 (100%)	19/19 (100%)
Chronic Total Occlusions	5	3/5 (60%)	5/5 (100%)	4/5 (80%)	4/5 (80%)
General Use of NC Balloon	32	29/32 (90.6%)	30/32 (93.8%)	31/32 (96.9%)	32/32 (100%)

4. Pediatric Extrapolation

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal IDE clinical study included twelve (12) investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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 System 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. Effectiveness Conclusions

The Scoreflex NC Scoring PTCA Catheter clinical study was a single arm, prospective, open label, multi-center, observational US study to evaluate the safety and procedural success of the Scoreflex NC Scoring PTCA Catheter for treatment of stenotic coronary arteries in 200 patients. The outcome of the study indicates that the device performs as expected for this device type (93.5% device procedural success; CI 90.1-96.9%), with an acceptable freedom from device-related injury (98.0%; CI 96.1-99.9%).

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. As noted above, the results from the US clinical investigation showed an

acceptable freedom from device-related injury (98.0%; CI 96.1-99.9%). Both the clinical and animal study demonstrates the Scoreflex NC Scoring PTCA catheter is safe with acceptably low rates of complications and adverse events for its intended use. The non-clinical performance data provides further assurance that the Scoreflex NC Scoring PTA catheter is safe when used as indicated and in accordance with the instructions for use.

C. Benefit-Risk Determination

The probable benefits and risks of the device are based on data collected in the in vivo animal and clinical study to support PMA approval. The probable benefit of the Scoreflex NC Scoring Catheter of improving patient symptoms and quality of life outweigh the probably risks associated with use of the device. Additional factors to be considered in determining probable risks and benefits for the Scoreflex NC Scoring Catheter include:

- The clinical study provided adequate acute assessment through hospital discharge to evaluate safety and effectiveness, with updated calculations for MI and MACE to assess the impact of missing data.

- The device is intended for use in subjects with de novo stenotic coronary arteries or in-stent restenosis. The results adequately support general use in the identified population.

- The frequency and types of the adverse events reported throughout the pivotal clinical study are what might be expected in the studied patient population and therapeutic area. No unanticipated adverse device effects were reported in the study.

- Patient risk is minimized by limiting use to operators who have the necessary training to use the device safely and effectively and adhere to recommended peri-procedural medication regimens.

1. Patient Perspectives
   This submission 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.

D. 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. The safety and effectiveness of the Scoreflex NC Scoring PTCA catheter have been demonstrated by results obtained from biocompatibility testing, engineering bench testing, *in vivo* animal testing, sterilization testing, packaging testing, shelf-life testing, and the clinical investigation.

The results of the Scoreflex NC Scoring PTCA Catheter clinical study show that the Scoreflex NC Scoring PTCA Catheter demonstrated device procedural success (93.5%) and an improvement in diameter stenosis to confirm that the Scoreflex NC Scoring PTCA Catheter is appropriate for the treatment of de novo coronary arteries in patients evidencing coronary ischemia for the purpose of improving myocardial perfusion and for in-stent restenosis when used in accordance with the labeling and Directions for Use (DFU).

XIII. CDRH DECISION

CDRH issued an approval order on December 22, 2021. There are no conditions of approval for this device.

XIV. APPROVAL SPECIFICATIONS

Instructions 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: Not applicable

XV. REFERENCES

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3. Jujo K, Saito K, Ishida I, Kim A, Suzuki Y, Furuki Y, Ouchi T, Ishii Y, Sekiguchi H, Yamaguchi J, Ogawa H, Hagiwara N. *Intimal disruption affects drug-eluting cobalt-chromium stent expansion: A randomized trial comparing scoring and conventional balloon predilation.* Int J Cardiology 221:23-31 (2016).