SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Vascular Hemostasis Device

Device Trade Name: Perclose ProGlide® Suture-Mediated Closure System

Device Procode: MGB

Applicant's Name and Address: Abbott Vascular
3200 Lakeside Drive
Santa Clara, CA 95054

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P960043/S097

Date of FDA Notice of Approval: February 16, 2018

The original PMA (PMA P960043) was approved on April 30, 1997 and is indicated for the percutaneous delivery of suture for closing the common femoral artery access site of patients who have undergone diagnostic or interventional catheterization procedures using 5 to 8F sheaths. Perclose® ProGlide® 6F Suture-Mediated Closure (SMC) System reduces the time to hemostasis, ambulation (10 feet) and discharge in patients who have undergone diagnostic or interventional catheterization procedures without complicating clinical conditions. The SSED to support the indication is available via FDA's Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852 at (240) 402-7500, by referencing the PMA number or Docket # 97M-0274

The indication was expanded in P960043/S080 to include closing femoral artery access sites using sheaths up to 21F in size. The SSED to support the indication is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf/P960043S080B.pdf) and is incorporated by reference here.

The current supplement was submitted to further expand the indication for the Perclose ProGlide Suture Mediated Closure System to close femoral vein acess sites using sheaths up to 24F.

II. INDICATIONS FOR USE

The Perclose ProGlide SMC System is indicated for the percutaneous delivery of suture for closing the common femoral artery and vein access site of patients who have undergone diagnostic or interventional catheterization procedures. The Perclose ProGlide SMC System is used without or, if required, with adjunctive manual compression:

For access sites in the common femoral artery using 5F to 21F sheaths

For access sites in the common femoral vein using 5F to 24F sheaths.

For arterial and venous sheath sizes greater than 8F, at least two devices and the pre-close technique are required.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Perclose ProGlide SMC device labeling.

V. DEVICE DESCRIPTION

The Perclose ProGlide SMC System (Perclose ProGlide) is designed to deliver a single monofilament polypropylene suture to close femoral arterial and venous puncture sites following diagnostic or interventional catheterization procedures.

The Perclose ProGlide SMC device (Figure 1) is comprised of a plunger, handle, guide, and sheath. The Perclose ProGlide tracks over a standard 0.038" (or smaller) guide wire. A hemostasis valve restricts the blood flow through the sheath with or without the guide wire in place. The guide houses the needles, and the foot, and precisely controls the placement of these needles around the puncture site. The handle is used to stabilize the device during use. The plunger advances the needles and is used to retrieve the suture. A marker lumen is contained within the guide, with the intraluminal port of the lumen positioned at the distal end of the guide. Proximally, the marker lumen exits from the body of the device. The marker lumen allows a pathway for back-bleeding from the femoral artery or vein to ensure proper device positioning.

A knot pusher accessory and suture trimmer accessory are included which are designed to position the pre-tied suture knot to the arteriotomy. The suture trimmer accessory is also designed to trim the trailing limbs of the suture.

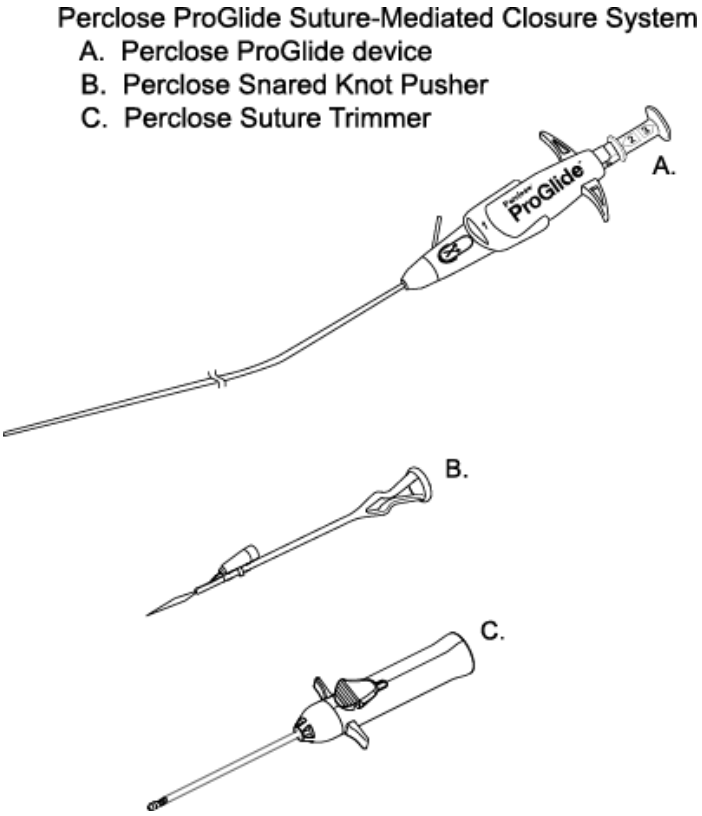

Figure 1. Perclose ProGlide Suture-Mediated Closure System

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives used for achieving femoral vein puncture hemostasis post-catheterization. For small sized punctures up to and including 10F, methods used for hemostasis include manual compression, mechanical compression, other vessel closure devices, and surgical closure. For large sized holes up to 21F in size, surgical cutdown provides an alternative to the subject device. 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 Perclose ProGlide Suture-Mediated Closure System has been commercially available in the United States since May 2004. The Perclose ProGlide is also available for sale in over 50 countries outside of the United States in the European Union, Middle East, Asia Pacific, Latin America and Africa. The Perclose ProGlide has not been withdrawn from marketing in any country for any reason.

VIII. PROBABLE ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the probable adverse effects (e.g., complications) associated with the use of the device.

- Allergic reaction or hypersensitivity to device components
- Anemia
- Arterial stenosis / occlusion
- Arteriovenous fistula
- Bleeding / hemorrhage
- Bruising / hematoma
- Death
- Deep vein thrombosis
- Device entrapment
- Device failure / malfunction / misplacement
- Diminished pulses distal to closure site
- Embolism
- Hypotension / hypertension
- Infection / sepsis
- Inflammation
- Intimal tear / dissection
- Ischemia distal to closure site
- Nerve injury
- Numbness
- Pain
- Perforation
- Pseudoaneurysm
- Pulmonary embolism
- Retroperitoneal hematoma / bleeding
- Thrombus formation
- Vascular injury
- Vasovagal episode
- Vasoconstriction / vasospasm
- Wound dehiscence

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical studies were performed on the Perclose ProGlide SMC device. Testing was referenced from PMA submission P960043 and related supplements for all nonclinical testing. No additional preclinical studies were conducted to support the proposed indication. A summary of previously reported preclinical studies can be found in the Summary of Safety and Effectiveness Data (SSED) for the original PMA (see section I above).

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The applicant performed an analysis using retrospectively collected data to establish a reasonable assurance of safety and effectiveness of the Perclose ProGlide SMC device for

femoral vein access site closure in access sites using up to 24F sheaths in the US. The sponsor analyzed data from the EVEREST II/REALISM Continued Access Registry Study (REALISM IDE #G030064) for the Abbott MitraClip device. The sponsor conducted the analysis on data from subjects in whom Perclose ProGlide was used as the primary method for large bore venous access-site closure during the MitraClip index procedure with a 24F vascular sheath. 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

Patients were treated between August 2009 and October 2013. The database for this Panel Track Supplement reflected a subset of data collected through 30 days post index procedure and included data from 159 patients.

The study was an analysis of data collected retrospectively from the EVEREST II / REALISM Continued Access Study which investigated the Abbott MitraClip device.

The analysis population was derived from a subset of REALISM subjects who were enrolled in the REALISM High Risk (HR) cohort, REALISM Non-High Risk (NHR) cohort, and REALISM Compassionate Use (CU) cohort. REALISM was a continued access study within the EVEREST II trial, which included subjects receiving the MitraClip index procedure with the MitraClip 24Fr sheath. REALISM enrolled 958 subjects, of whom 899 subjects were enrolled per the protocol and 59 as compassionate use.

The ProGlide cohort consists of data from subjects who received at least one ProGlide device as their primary closure method with or without secondary closure methods such as manual compression (MC) or subcutaneous stitch. The ProGlide cohort was selected from subjects enrolled in the seven (7) REALISM sites with high frequency use of vessel closure devices (VCD $\geq$ 15 cases). Of the seven (7) sites, one (1) site did not use ProGlide and another site only used ProGlide for arterial access, and therefore the ProGlide cohort comprised of five (5) sites with a total of 159 subjects.

This study did not include powered comparisons with a control; rather, device success was descriptively compared with patients that received manual compression treatment to achieve hemostasis. The MC cohort included 230 subjects from seven (7) sites that reported high frequency MC usage of $\geq$ 25 cases each without the use of any VCD. Subjects in both cohorts had MitraClip implanted into the mitral valve with access through the common femoral vein.

A Clinical Events Committee (CEC) reviewed and adjudicated the femoral vein access-site related complications.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the ProGlide study was limited to patients who were enrolled in the REALISM study at the selected sites and used either ProGlide or manual compression as the intended method for venous access site hemostasis. Subjects were included with or without a subcutaneous stitch during the index procedure for both ProGlide and manual compression.

Patients were not permitted to enroll in the ProGlide study if they met any of the following exclusion criteria:

- Subjects who were not from the selected 14 sites (7 high frequency sites for MC and 7 high frequency sites for vascular closure device usage)
- Subjects at the selected sites whose venous access closure method was not the ProGlide or MC (with or without subcutaneous stitch)

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days postoperatively.

Preoperatively, investigators collected basline characteristics and comorbidities. Postoperatively, the objective parameters measured during the study included ProGlide usage information, effectiveness of achieving hemostasis (including time to hemostasis) during the index procedure, and adverse events up to 30 days. Adverse events and complications were recorded at all visits.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

The primary endpoint was the rate of freedom from major femoral vein access-site related complications at 30-days post MitraClip index procedure.

Major complication is defined as any event leading to death, life-threatening or major bleeding, surgical intervention, hospitalization, visceral ischemia, or neurological impairment. This list includes development of the following:

- Femoral vein stenosis (> 50%) development at the puncture site related to closure technique;
- Development of deep vein thrombosis in the target limb;
- Significant venous bleeding, retroperitoneal bleeding/hematoma, or hematoma at the access site requiring transfusion or surgical intervention;
- Hematoma that does not require transfusion or surgical intervention;
- Access site-related wound dehiscence or venous access site infection requiring intravenous, intramuscular or oral antibiotics, and/or leading to a prolonged hospitalization;
- Venous access site injury, including vessel laceration, requiring surgical repair, angioplasty, ultrasound-guided compression or thrombin injection;
- Re-bleeding at access site that requires treatment or re-hospitalization;

- AV fistula;
- Pseudoaneurysm;
- Access site-related nerve injury.

With regard to success/failure criteria, the pre-specified acceptance criterion for the rate of freedom from major femoral vein access-site related complications at 30-days post-procedure was ≥ 90%.

B. Accountability of PMA Cohort

At the time of data collection, of 159 patients in the ProGlide cohort, 96% (n = 153) of patients completed their 30 day post-operative visit (**Table 1**).

Table 1. Accountability of patient data at discharge and 30 days post index procedure

Discharge evaluation	30 day post-operative evaluation
159/159 (100%)	153/159 (96%)[1]

[1] Six patients did not reach the 30 day post-operative evaluation due to four patient deaths and two missed visits

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a large bore vascular closure device study performed in the US.

The ProGlide cohort reflected subjects with varying degrees of heart failure. The cohort included elderly subjects with a mean age of 76 years. Male subjects accounted for 52.8%. Subjects presented with multiple comorbidities including high rates of congestive heart failure (CHF) (89.2%), atrial fibrillation (AF) (64.7%), coronary artery disease (CAD) (67.7%), hypertension (84.8%), diabetes (26.4%) moderate to severe renal disease (24.5%), chronic obstructive pulmonary disease (COPD) (23.3%). Patients were predominantly NYHA class III (59.7%) and IV (24.5%). History of prior percutaneous interventions (37.7%) and cardiovascular surgery (42.1%) were common in this cohort.

The MC Cohort also reflected subjects with varying degrees of heart failure. The cohort included 156 (67.8%) subjects from the REALISM High Risk cohort, 58 (25.2%) from the REALISM Non-High Risk cohort, and 16 (7.0%) from the REALISM Compassionate Use cohort. Their mean age was 77 years and subjects in the MC cohort had high rates of CHF (94.8% (218/230), AF (62.9% (134/213), CAD (76.4% (175/229)), diabetes (33.0% (76/230)), moderate to severe renal disease (27.8% (64/230)), COPD (28.4% (65/229)), and prior percutaneous intervention (35.4% (81/229)).

The demographics for both groups are typical for large bore vascular closure device studies given that subjects with these demographics are likely to undergo percutaneous cardiac procedures with large bore sheaths.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the ProGlide cohort of 153 patients/procedures available for the 30 day evaluation. The key safety outcomes for this study are presented below in **Table 2**. Adverse effects are reported in **Table 3**.

The primary endpoint of freedom from major femoral vein access-site related complications through 30 days is presented in **Table 2**. The available information demonstrates that the study device met the acceptance criteria of 90%.

Table 2. Freedom from Major Femoral Vein Access-Site Related Complications through 30 Days (ProGlide Cohort[4]) (subject-based event rate)

Events[1]	**ProGlide (N=159[3])**	**Clinical Acceptance Criteria**
Freedom from Major Femoral Vein Access-Related Complication[2]	98.1% (156/159)	90%

[1] Includes only each subject's first occurrence of each event.
[2] The major femoral vein access-related complication is defined as access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment.
[3] The denominator excludes subjects who withdrew or lost to follow up before the 30-day visit early window (27 days post-procedure) without any femoral vein access-related complication.
[4] ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch).

Adverse effects that occurred in the PMA clinical study:

Major femoral vein access-site related complications through 30 days as adjudicated by the CEC are present in **Table 3.** Five (5) major complications in three (3) subjects were reported within 30 days: one (1) hematoma requiring intervention and one (1) pseudo-aneurysm, one (1) hematoma and one (1) re-bleeding within 48 hours, and one (1) deep vein thrombosis in the target limb 6-days post-procedure.

Table 3. Summary of CEC Adjudicated Major Femoral Vein Access-Site Related Complications Through 30 Days (ProGlide Cohort[3]): Non-Hierarchical by Subject

Non-Hierarchical Major Events[1]	0-48 hours (Subject count)	>48 hours-30 days (Subject count)	0-30 days (Subject count)	Total number of events from 0 to 30 days
Major Femoral Vein Access-Related Complications[2]	1.3% (2/159)	0.6% (1/159)	1.9% (3/159)	5
Femoral vein stenosis (>50% development at the puncture site related to closure technique)	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Development of deep vein thrombosis in the target limb	0.0% (0/159)	0.6% (1/159)	0.6% (1/159)	1
Significant venous bleeding, retroperitoneal bleeding/hematoma, or hematoma at the access site requiring transfusion or surgical intervention	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Hematoma that does not require transfusion or surgical intervention	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Access site-related wound dehiscence or venous access site infection requiring intravenous, intramuscular or oral antibiotics, and/or leading to a prolonged hospitalization	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Venous access site injury, including vessel laceration, requiring surgical repair, angioplasty, ultrasound-guided compression or thrombin injection	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Re-bleeding at access site that requires treatment or re-hospitalization	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
AV Fistula	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0
Pseudoaneurysm	0.6% (1/159)	0.0% (0/159)	0.6% (1/159)	1
Access site-related nerve injury	0.0% (0/159)	0.0% (0/159)	0.0% (0/159)	0

[1] Includes only each subject's first occurrence of each event.
[2] The major femoral vein access-related complication is defined as access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment.
[3]ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch).

A total of 11 minor complications occurred in 10 patients through 30 days including four (4) hematoma events not requiring treatment (2.5%; 4/159) and seven (7) re-bleeds requiring treatment (4.4%; 7/159). All minor complications occurred within 48-hours post-procedure and were resolved by 30 days.

MC cohort results

Thirty-two adjudicated access site complications were reported through 30 days within the MC cohort (10 major (4.4% (10/227)) and 22 minor (9.7% (22/227))). The 30 day major complications were mostly venous bleeding (3.1% (7/227)) with the remaining being development of deep vein thrombosis (0.4% (1/227)), hematoma (0.4% (1/227)), re-bleeding (0.9% (2/227)), venous access site injury (0.9% (2/227)) and pseudo-aneurysm 0.9% (2/227). Minor complications mostly developed within 48-hours post-index procedure and were largely due to hematoma and re-bleeding at the access site that requires treatment.

2. Effectiveness Results

The analysis of effectiveness was based on time to hemostasis (TTH) in the 159 evaluable patients and are presented in **Table 4**.

Table 4. Summary of ProGlide Effectiveness on Hemostasis (ProGlide Cohort[5])

Characteristics	**ProGlide (N=159)**
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	5.92 ± 6.19 (134)
Median (Q1, Q3)	4.50 (1.00, 8.00)
Range (min, max)	(0.00, 30.00)
ProGlide Without Any Adjunctive Closure Method	69.2% (110/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	5.15 ± 6.05 (95)
Median (Q1, Q3)	3.00 (1.00, 7.00)
Range (min, max)	(0.00, 29.00)
ProGlide and Adjunctive Manual Compression (MC) Only	17.6% (28/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	9.3 ± 7.3 (23)
Median (Q1, Q3)	6.0 (5.0, 14.0)
Range (min, max)	(1, 30)
ProGlide and Adjunctive Manual Compression <=5 Minutes[1]	6.3% (10/159)
Time to Achieve Hemostasis (min)	4.0 ± 1.7 (10)
Mean ± SD (n)	5.0 (3.0, 5.0)
Median (Q1, Q3)	(1, 5)
Range (min, max)	
ProGlide and Adjunctive Manual Compression <=10 Minutes[1]	10.1% (16/159)
Time to Achieve Hemostasis (min)	5.1 ± 2.1 (16)
Mean ± SD (n)	5.0 (5.0, 6.0)
Median (Q1, Q3)	(1, 9)
Range (min, max)	
ProGlide and Adjunctive Manual Compression >10 Minutes or Unknown [1,2]	7.5% (12/159)
Time to Achieve Hemostasis (min)	
Mean ± SD (n)	18.7 ± 5.9 (7)
Median (Q1, Q3)	18.0 (14.0, 22.0)
Range (min, max)	(13, 30)
ProGlide and Secondary Vessel Closure Method Only	12.6% (20/159)
Time to Achieve Hemostasis (min)	5.8 ± 3.3 (16)
Mean ± SD (n)	6.0 (3.0, 7.0)
Median (Q1, Q3)	(1, 12)
Range (min, max)	
Type of Secondary Closure Method	
Subcutaneous Stitch	100.0% (20/20)
Other Closure Device	0.0% (0/20)
Surgical Repair	0.0% (0/20)
Data Not Available	0.0% (0/20)

Characteristics	ProGlide (N=159)
Reason to use Secondary Vessel Closure Method	
ProGlide Device Deficiency	0.0% (0/20)
Access Complication (s)	0.0% (0/20)
Failure to Achieve Hemostasis	95.0% (19/20)
Data Not Available[4]	5.0% (1/20)
Hemostasis Achieved by Using ProGlide, Manual Compression and Secondary Vessel Closure Method [3]	0.6% (1/159)

[1] For subjects with missing manual compression time, the non-missing time to achieve hemostasis is used to determine the sub-category.
[2] Subjects with both manual compression time and time to achieve hemostasis missing are also included in this category.
[3] One (1) subject used Angio-seal as the secondary vessel closure method in addition to ProGlide and Manual Compression due to unknown reason. The subject had both manual compression time and time to achieve hemostasis unknown.
[4] Subject who used Secondary closure method with unknown reason was categorized in the Data not available category.
[5] ProGlide group is defined as subjects who had received at least one ProGlide as the primary intended method to close femoral vein access site during the index procedure with or without adjunctive closure methods (manual compression or subcutaneous stitch.

A total of 110/159 (69.2%) subjects achieved hemostasis with ProGlide alone without additional secondary closure methods. In the remaining subjects, adjunctive closure methods including MC (17.6%, 28/159) and subcutaneous stitch (12.6%, 20/159), were required in addition to ProGlide to achieve hemostasis. Within the ProGlide cohort, investigators predominantly used two (2) ProGlide devices to achieve hemostasis (90.6%, 144/159). The remaining 9.4% cases used one ProGlide device for access-site closure.

Within the MC cohort, 50% (115/230) of the subjects received MC alone, 49.6% (114/230) received MC plus a subcutaneous stitch, and 0.4% (1/230) received MC plus other closure device as a secondary method to facilitate hemostasis.

On average, hemostasis was achieved in 5.92 ± 6.19 minutes in the ProGlide cohort. The mean time to achieve hemostasis with ProGlide alone was 5.15 minutes. This time increased to 9.3 minutes when adjunctive MC was used. When a secondary vessel closure method (namely subcutaneous stitch) was used, the mean time to achieve hemostasis was 5.8 minutes. Overall, secondary closures were mostly initiated when there was a failure to achieve hemostasis using ProGlide and MC (95%, 19/20) which occurred in 12.6% of patients. The time required to achieve hemostasis when using the ProGlide was observed to be comparable to that of other vascular closure devices and alternative closure methods.

Within the MC cohort, time to hemostasis measurements were missing for a considerable number of subjects and therefore not reported.

3. Subgroup Analyses

   The following preoperative characteristics were evaluated for potential association with outcomes: ProGlide alone versus ProGlide plus adjunctive closure methods, gender, and the use of one versus two ProGlide devices to achieve hemostasis. All subgroup analyses described in the following sections were limited by sample size and were not powered. For this reason, the following results should be considered descriptive.

ProGlide with minimal MC vs ProGlide with prolonged MC or secondary closure device

The ProGlide with minimal MC (PG) group involved 126 subjects in whom at least one ProGlide was used along with adjunctive MC ≤ 10 minutes. These subjects generally had numerically higher baseline comorbidities, such as atrial fibrillation, coronary artery disease, diabetics, hypocholesteremia, angina, MI and angina, prior percutaneous interventions and cardiovascular surgery, liver disease, and NYHA II compared to the ProGlide with prolonged MC or secondary closure device (PG+) group. The ProGlide Plus group included fewer subjects (n = 33) all of whom required at least one ProGlide with either prolonged MC > 10 minutes or a secondary closure device to achieve hemostasis.

Results:

The observed major complications occurred only in the PG group (2.4% (3/126)) with 1.6% (2/126) complications occurring within the first 48 hours. Minor complications were similar in both groups with approximately 94% freedom from events (PG 6.3% (8/126) and PG+ 6.1% (2/33)).

The PG+ group had a numerically greater time to achieve hemostasis compared to the PG group (9.70 ± 7.34 (23) vs. 5.14 ± 5.65 (111). This result may be due to the requirement of an additional procedure (i.e. MC or secondary closure device).

Gender outcomes

A total of 84 male subjects and 75 female subjects were included in this sub-group analysis. Both groups had a similar mean age (males: 77 years; females: 74 years). Males reported numerically higher baseline incidences of key comorbidities including congestive heart failure, hypercholesteremia, coronary and peripheral vasculardisease (PVD), diabetes, COPD, and NYHA III/IV.

All 30 day major complications were reported in males 3.6% (3/84). However, because the event rates are low, a larger dataset would be needed to confirm a gender difference. Among minor events, men (8.3%, 7/84) had a numerically higher rate compared with women (4.0%, 3/75).

On average, both groups took comparable time to achieve hemostasis (men: 5.69 ± 6.37 (70) vs women: 6.18 ± 6.02 (64)). Males achieved numerically faster hemostasis than

females when adjunctive MC or other secondary closure devices were used (6.9 ± 4.7 (11) vs. 11.4 ± 8.7 (12)).

One ProGlide vs Two ProGlides

Most of the subjects in this study received two (2) ProGlides (n = 144, 90.6%) and only fifteen (n=15, 9.4%) subjects received one (1) ProGlide. Within the Two ProGlides group, 70.8% (102/144) did not require any adjunctive closure methods compared with 53.3% (8/15) in the One ProGlide group.

Both groups were similar in age (one ProGlide: 75 years vs two ProGlides: 76 years). Both groups had approximately the same rates of key risk factors of CHF, atrial fibrillation, angina, and COPD. The One ProGlide subjects had numerically higher rates of CAD, PVD, renal disease, and NYHA III, while the Two ProGlide subjects had numerically higher rates of cardiomyopathy, diabetes, history of CABG, and NYHA IV.

The major complication rates at 30 days were numerically higher in the One ProGlide group at 6.7% (1/15) compared with 1.4% (2/144) in Two ProGlides. The very small sample size of the One ProGlide group must be considered when assessing the 30 day rate. Each group reported only one major access-site complications within 48 hours post-procedure. The 30 day minor complication rate remained unchanged from the 30 day major complication rate for the One ProGlide group and was 6.3% (9/144) for the Two ProGlide group. Given the disproportionate sample sizes of the two groups, the outcomes must be interpreted with caution.

The subjects in the One ProGlide group took numerically longer to achieve hemostasis than those who received two ProGlides (7.93 ± 6.58 (14) vs. 5.69 ± 6.13 (120)). Additionally, the One ProGlide group reported a smaller percentage of subjects achieving hemostasis without any adjunctive methods compared to Two ProGlide (53.3% (8/15) vs. 70.8% (102/144)), a numerically higher percentage of use of adjunctive MC (33.3% (5/15) vs. 16.0% (23/144)) and required a numerically higher percentage of MC ≥ 10 mins compared with the Two ProGlides group (20.0% (3/15) vs. 6.3% (9/144)).

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 clinical study included 64 investigators of which none were full-time or part-

time employees of the sponsor and two had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 1
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. 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 Systems 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 assessment of effectiveness for the Perclose ProGlide SMC device was based on retrospective analysis of time to hemostasis from the EVEREST II / REALISM Continued Access Study. On average, hemostasis was achieved in 5.92 ± 6.19 minutes in the ProGlide cohort (with or without adjunctive closure methods). The mean time to achieve hemostasis with ProGlide with <10 minutes of MC was 5.15 minutes. This duration is comparable to other marketed vascular closure devices.

Effectiveness of the device was also based on the ability to achieve hemostasis. The majority of subjects (69.2%) achieved hemostasis with ProGlide and only <10 minutes of manual compression without additional secondary closure methods. The remaining subjects required adjunctive closure methods including MC (17.6%, 28/159) and subcutaneous stitch (12.6%, 20/159). Overall, secondary closures were mostly initiated when there was a failure to achieve hemostasis using ProGlide and MC (95%, 19/20). Within the ProGlide cohort, two (2) ProGlide devices were used predominantly to achieve hemostasis (90.6%, 144/159), while the remaining 9.4% of cases used a single ProGlide for access-site closure.

Although manual compression or subcutaneous stitch was required for approximately 30% of patients, the use of adjunctive closure methods is a common treatment approach.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and/or animal studies leveraged from the original PMA and related supplements as well as data collected in a clinical study as described above.

The safety assessments for the Perclose ProGlide SMC device were based on the primary endpoint of Freedom from Major Femoral Vein Access-Site Related Complications through 30 Days and overall adverse event rates observed within 30 days. The analysis provided to support this panel track supplement suggests that the device met the primary endpoint success criterion of 90% with an observed rate of 98%. Additionally, adverse events were observed to occur at low and tolerable levels.

The risks associated with the use of the device include access site vascular injury, new onset of lower extremity ischemia, access site related bleeding, infection and nerve injury, as well as mild groin pain or small groin hematoma.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study as described above. The potential benefits of using Perclose ProGlide for closure of 24F venous access site is that the treatment allows for hemostasis to be achieved within a short period of time (5.92 min) to allow for prompt ambulation. The device performance is associated with acceptable major femoral venous access-site complications rate through 30 days of 1.9%.

Additional factors to be considered in determining probable risks and benefits for the Perclose ProGlide device included: major femoral venous access-site complications leading to death, life-threatening or major bleeding, surgical intervention, hospitalization, visceral ischemia, or neurological impairment which may occur up to 30 days. Additional risks include minor femoral venous access-site complications not leading to death, life-threatening or major bleeding, which may require surgical intervention, hospitalization, visceral ischemia, or neurological impairment and may occur up to 30 days. The expected rates for the aforementioned major and minor femoral venous access-site complications are <2% and <10%, respectively.

1. Patient Perspectives
   This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for the percutaneous delivery of suture for closing the common femoral artery and vein

access site of patients who have undergone diagnostic or interventional catheterization procedures, the Perclose ProGlide SMC System used without or, if required, with adjunctive manual compression.

- For access sites in the femoral artery using 5F to 21F sheaths. For sheath sizes greater than 8F, at least two devices and the pre-close technique are required;
- For access sites in the common femoral vein using 5F to 24F sheaths,

the probable benefits outweigh the probable risks.

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. As discussed above the benefits of potential reduced time to hemostasis and shorter time to ambulation coupled with low rates of venous access-site complications suggest that the benefits of using the Perclose ProGlide SMC device outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on February 16, 2018.

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

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.