DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

APR 30 1998

Mr. James D. Gustafson
Vice President of Quality Systems
and Regulatory/Clinical Affairs
Possis Medical, Inc.
9055 Evergreen Boulevard, N.W.
Minneapolis, MN 55433-8003

Re: HDE Number: H970005
Perma-Flow® Coronary Graft, Model 2C10
Filed: November 4, 1997
Amended: January 29, February 6, March 12, and March 27, 1998

Dear Mr. Gustafson:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your humanitarian device exemption (HDE) application for the Perma-Flow® Coronary Graft, Model 2C10. This device is indicated for single or multiple vessel coronary artery bypass in patients who are receiving coronary bypass grafting but who have inadequate autologous conduit to complete the required revascularization. CDRH is pleased to inform you that your HDE is approved subject to the enclosed "Conditions of Approval." You may begin commercial distribution of the device after you have submitted an amendment to this HDE with copies of the approved labeling in final printed form.

The sale, distribution, and use of this device are limited to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360j(e)) under the authority of section 515(d)(1)(B)(ii) of the act (21 U.S.C. 360e(d)(1)(B)(ii)). In addition, in order to ensure the safe use of the device, FDA has further restricted the device within the meaning of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act insofar as (1) the labeling shall specify the training requirements for practitioners who may use the device as approved in this order and (2) the sale, distribution, and use must not violate sections 502(q) and (r) of the act (21 U.S.C. 352(q) and (r)).

FDA wishes to remind you that failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

CDRH will notify the public of its decision to approve your HDE by making available a summary of the safety and probable benefit of the device upon which the approval was based. The information can be found on the FDA CDRH Internet HomePage located at http://www.fda.gov/cdrh/hdeinfo.html. Written requests for this information can also be made to the Dockets Management Branch (HFA-305),

Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857. The written request should include the HDE number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Any information to be submitted to FDA regarding this HDE should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above HDE number to facilitate processing:

Document Mail Center (HFZ-401)
Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporated Boulevard
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Dorothy Abel at (301) 443-8262, extension 165.

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

CONDITIONS OF APPROVAL FOR AN HDE

I. APPROVED LABELING

As soon as possible and before commercial distribution of the device, the holder of an HDE should submit three copies of the approved labeling in final printed form as an amendment to the HDE. The supplement should be submitted to the Document Mail Center (HFZ-401), Office of Device Evaluation, Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

II. ADVERTISEMENTS

Advertisements and other descriptive printed materials issued by the HDE holder or private label distributor with respect to this device should not recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360j(e)) under the authority of section 515(d)(1)(B)(ii) of the act (21 U.S.C. 360e(d)(1)(B)(ii)), all advertisements and other descriptive printed material issued by the holder or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and contraindications.

III. HDE SUPPLEMENTS

Before making any change affecting the safety or probable benefit of the device, the HDE holder should submit a supplement for review and approval by FDA unless a "Special HDE Supplement" is permitted as described under 21 CFR 814.39(d)(2) or an alternate submission is permitted as described under 21 CFR 814.39(e). All HDE supplements or alternate submissions must comply with the applicable requirements under 21 CFR 814.39 of the Premarket Approval (PMA) regulation and under 21 CFR 814.108 of the Humanitarian Device Exemption regulation. The review timeframe for HDE supplements is 75 days except for those submitted under 21 CFR 814.39(e).

Since all situations which require an HDE supplement cannot be briefly summarized, please consult the HDE regulation for further guidance. The guidance provided below is only for several key instances. In general, an HDE supplement must be submitted:

1) When unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification; or

2) If the device is to be modified, and animal/laboratory or clinical testing is needed to determine if the modified device remains safe and continues to provide probable benefit.

HDE supplements submitted under 21 CFR 814.39(d)(2) "Special HDE Supplement - Changes Being Effected" are limited to the labeling, quality control, and manufacturing process changes as specified under this section of the regulation. This provision allows for the addition of, but not the replacement of previously approved, quality control specifications

and test methods. These changes may be implemented upon acknowledgment by FDA that the submission is being processed as a "Special HDE Supplement - Changes Being Effected." Please note that this acknowledgment is in addition to that issued by the Document Mail Center for all HDE supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software, or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of an HDE supplement before implementation and include the use of a *30-day HDE supplement* or *periodic postapproval report*. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence to the HDE holder that the alternate submission is permitted for the change. Before this can occur, FDA and the HDE holder must agree upon any needed testing, the testing protocol, the test results, the reporting format, the information to be reported, and the alternate submission to be used.

Please note that unlike the PMA process, a supplement may not be submitted for a new indication for use for a humanitarian use device (HUD). An HDE holder seeking a new indication for use for an HUD approved under the provisions of Subpart H of 21 CFR 814, must obtain a new designation of HUD status for the new indication for use and submit an original HDE application in accordance with §814.104. The application for the new indication for use may incorporate by reference any information or data previously submitted to the agency.

IV. POSTAPPROVAL RECORD KEEPING REQUIREMENTS

An HDE holder is required to maintain records of the names and addresses of the facilities to which the HUD has been shipped, correspondence with reviewing institutional review boards (IRBs), as well as any other information requested by a reviewing IRB or FDA.

V. POSTAPPROVAL REPORTING REQUIREMENTS

Continued approval of the HDE is contingent upon the submission of postapproval reports required under 21 CFR 814.84 and 21 CFR 814.126.

A. ANNUAL REPORT

Annual reports should be submitted at intervals of 1 year from the date of approval of the original HDE. Reports for supplements approved under the original HDE should be included in the next and subsequent periodic reports for the original HDE unless otherwise specified in the approval order for the HDE supplement. Three copies identified as "Annual Report" and bearing the applicable HDE reference number are to be submitted to the HDE Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. Reports should indicate the beginning and ending date of the period covered by the report and include the following information required by 21 CFR 814.126(b)(1):

1. An update of the information required under §814.102(a) in a separately bound volume;

2. An update of the information required under §814.104(c)(2), (c)(3), and (c)(5);

3. The number of devices that have been shipped or sold and, if the number shipped or sold exceeds 4,000, an explanation and estimate of the number of devices used per patient. If a single device is used on multiple patients, an estimate of the number of patients treated or diagnosed using the device together with an explanation of the basis for the estimate;

4. Information describing the applicant's clinical experience with the device. This shall include safety information that is known or reasonably should be known to the applicant, a summary of medical device reports made pursuant to 21 CFR 803, any data generated from postmarketing studies, and information (whether published or unpublished) that is known or reasonably expected to be known by the applicant that may affect an evaluation of the safety of the device or that may affect the statement of contraindications, warnings, precautions, and adverse reactions in the device labeling; and

5. A summary of any changes made to the device in accordance with supplements submitted under §814.108 and any changes required to be reported to FDA under §814.39(b).

B. **ADVERSE REACTION AND DEVICE DEFECT REPORTING**

As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and probable benefit of the device, the holder shall submit three copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the Document Mail Center (HFZ-401), Office of Device Evaluation, Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. Such reports should be submitted within 10 days after the HDE holder receives or has knowledge of information concerning:

(1) A mixup of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device

or any failure of the device to meet the specifications established in the approved HDE that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the HDE holder's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the firm. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the holder shall be included in the "Request for Extension of HDE Approval" described under "Postapproval Reports" above unless otherwise specified in the conditions of approval for this HDE. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of occurrence for each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the HDE holder when determined by FDA to be necessary to provide continued reasonable assurance of the safety and probable benefit of the device for its intended use.

C. **REPORTING UNDER THE MEDICAL DEVICE REPORTING REGULATION**

The Medical Device Reporting regulation (MDR) (21 CFR 803) became effective on April 11, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices:

(1) may have caused or contributed to a death or serious injury; or

(2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Events subject to reporting under the MDR regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements. FDA has determined, however, that such duplicative reporting is unnecessary. Therefore, whenever an event involving a device is subject to reporting under both the MDR regulation and the "Adverse Reaction and Device Defect Reporting" requirements, the report should be submitted in compliance with Part 803 and identified with the HDE reference number to Food and Drug Administration, Center for Devices and Radiological Health, Medical Device Reporting, PO Box 3002, Rockville, Maryland 20847-3002. For questions regarding the MDR regulation, please call (301) 594-2735.

Events included in periodic reports to the HDE that have also been reported under the MDR regulation must be so identified in the periodic report to the HDE to prevent duplicative entry into FDA information systems.

Copies of the MDR regulation and FDA publications, entitled "An Overview of the Medical Device Reporting Regulation" and "Medical Device Reporting for

Manufacturers," are available on the CDRH WWW Home Page (http://www.fda.gov/cdrh), through CDRH's Fact-on-Demand (FOD) at 800-899-0381 (FOD # 336, 1336, 509 and 987) or by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Lane
Rockville, Maryland 20850

SUMMARY OF SAFETY AND PROBABLE BENEFIT

I. GENERAL INFORMATION

Device Generic Name: vascular graft prosthesis of less than 6 millimeters diameter (21 CFR 870.3450).

Device Trade Name: Possis Perma-Flow Coronary Bypass Graft.

Applicant's Name and Address:

Possis Medical, Inc.
9055 Evergreen Blvd. NW
Minneapolis, MN 55433-8003

Humanitarian Device Exemption (HDE) Number: H970005.

Date of Humanitarian Use Device Designation: August 5, 1997.

Date of Panel Recommendation: The HDE was not taken to Panel. Please see Section X of this document for the rationale used in determining that Panel review was unneccesary.

Date of Good Manufacturing Practices (GMP) Inspection: A routine GMP inspection was performed on February 11-13, 17, 19-20, 25-27, and March 2-3, 1998.

Date of Notice of Approval to the Applicant: APR 30 1998

II. INDICATIONS FOR USE

The Perma-Flow Graft is intended for single or multiple vessel coronary artery bypass in patients who are receiving coronary bypass grafting but who have inadequate autologous conduit to complete the required revascularization.

III. DEVICE DESCRIPTION

The Perma-Flow Graft (hereafter called the Graft) is a 5 mm expanded polytetrafluoroethylene (ePTFE) vascular prosthesis 60 cm long with a silicone rubber venturi-shaped flow restriction near the venous end (Figure 1). The Venturi portion has an external sleeve of silicone rubber. The silicone used for the venturi flow control element is a medical grade two-part platinum-catalyzed crosslinked methyl vinyl siloxane elastomer with fumed silica reinforcement. The external sleeve is molded with an arrow as an orientation aid which points towards the venous end, in the direction of blood flow. The venous end of the external sleeve and the venous end of the ePTFE are beveled to approximate the venous anastomosis angle. The Graft has a black orientation line to aid in avoiding twisting during implant.

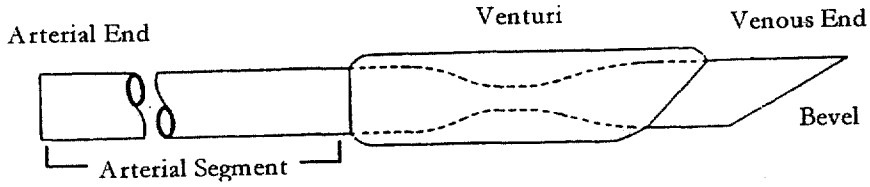


Figure 1. The Perma-Flow Graft

In use, the arterial end of the Graft is attached to the aorta and the venous end is attached to the superior vena cava by standard surgical anastomosis techniques, creating an arteriovenous shunt from the aorta to the vena cava through the Graft. The Venturi is adjacent to the venous anastomosis. Employing standard surgical anastomosis techniques, the Graft is used to bypass a coronary artery by cutting a hole in the arterial segment of the Graft and connecting it to a coronary artery to create a side-to-side anastomosis. Only one Graft is used, but multiple coronary arteries may be bypassed with the Graft by constructing multiple side-to-side anastomoses as needed in sequential fashion.

The Graft is implanted by constructing the vena cava anastomosis first, then completing each coronary anastomosis from distal to proximal to allow proper layout; the Graft can be cut to length as required prior to completing the aortic anastomosis. Figure 2 illustrates a hypothetical layout of the Graft used to bypass two coronary arteries; the direction of blood flow is indicated from the arterial end towards the venous end by arrows.

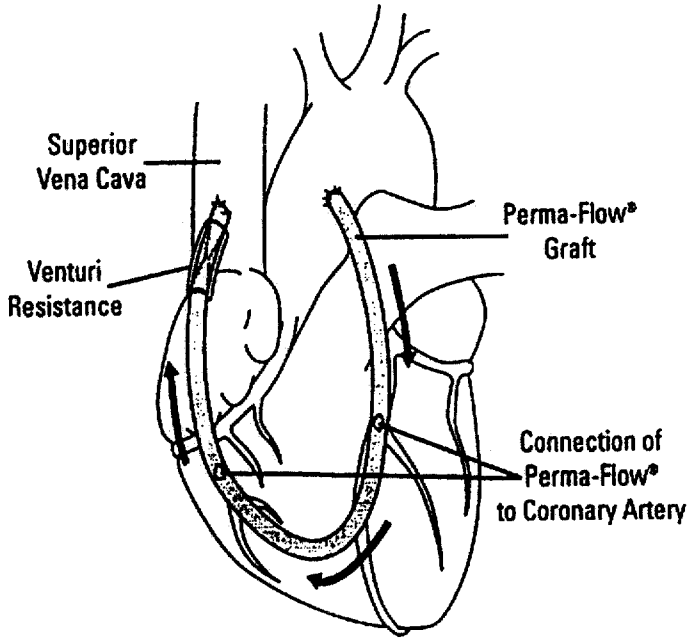


Figure 2. Perma-Flow Graft Layout

IV. CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

A. Contraindications:

None.

B. Warnings:

1. The Graft should not be used when the physician determines that the added arteriovenous shunt may not be tolerated well, possibly due to poor cardiac valves or the presence of a pre-existing arteriovenous shunt.
2. The Graft is not intended for applications as a vascular patch, or for reconstruction purposes.
3. Do not place any object inside the Venturi. Do not place clamps, forceps, dilators, catheters, sheaths, needles, endoscopes, measuring devices, swabs, sponges, or any other object inside the Graft within 1.0cm of the Venturi. Damage of any sort to the Venturi may result in graft thrombosis.
4. The arrow molded into the outer sleeve of the Venturi indicates the direction of blood flow and must always point towards the venous end of the Graft in order for the Graft to properly perfuse the coronary arteries.
5. The layout of the Graft must be carefully determined so that the required anastomoses are constructed without creating sharp bends or stresses in the graft which could cause a permanent kink or lead to mechanical disruptions of the graft, host vessel, and/or suture lines.

C. Precautions:

1. Open the sterile package using standard sterile technique.
2. Do not allow the Graft to come in contact with organic solvents or aqueous solutions; such exposure may cause excessive serum leakage due to wetting. The Graft does not require preclotting. Do not fill with blood before implantation or force irrigating solutions through the Graft wall; attempts to do so may affect the hydrophobic properties of the graft, resulting in possible seroma formation when implanted. Excessive manipulation of the Graft while in contact with tissue fluids or blood should be avoided.
3. The Graft is not elastic. Care should be taken to determine the proper length to allow adequate placement and to eliminate excessive stress on the anastomoses. Cutting the Graft too short may result in anastomotic disruption and excessive bleeding. Leaving the Graft too long may cause the Graft to buckle or to kink.
4. It is recommended that a non-cutting tapered needle be used with the Graft. Do not use a full radius cutting needle as it may damage the Graft at the suture line. Excessive anastomotic bleeding may occur if excessive tension causes suture holes to elongate or tear, if the needle-to-suture diameter is too great, or if gaps occur between the Graft and host vessels.
5. It is recommended that only smooth jawed or rubber shod clamps be used during implantation to avoid damage to the Graft wall. Do not clamp the Graft within 3.0cm of the Venturi and minimize the use of repeated clamping.

6. Do not bend the Graft in the Venturi outer sleeve region or within 1.5cm of the Venturi region as increased tendency to kink may result. The Venturi should be kept straight and the Graft not implanted if the Venturi has a kink or bend.
7. Twisting of the Graft must be avoided. Twisting may be detected by observing the longitudinal black orientation line on the Graft.
8. It is important to use proper cutting technique when implanting the Graft. Failure to do so may cause damage to the Graft or reduce the suture retention strength. When cutting, gently pull the Graft taut to determine the correct length and cut with a sharp surgical instrument. Excessive tension on the Graft during cutting or punching can cause damage or tearing to the Graft. An uneven edge should be carefully trimmed.
9. A topical hemostatic agent applied to completed arterial anastomoses may be helpful in minimizing any bleeding that may occur.
10. It is recommended that patients receive daily aspirin or other antiplatelet therapy as a deterrent to clot formation in the Graft. As with any synthetic implant, patients should be instructed to obtain and use prophylactic antibiotics prior to dental work or other surgery.

V. Adverse Effects of the Device on Health

In the Phase 1 feasibility clinical trial comprising 32 patients, the following complications were observed (listed in decreasing order of frequency): death, congestive heart failure, pleural effusions, ventricular tachycardia, coronary steal, sternal infection, pulmonary edema, renal failure, and graft weeping.

In the ongoing Phase 2 trial, these additional complication types have been observed: anastomotic disruption or obstruction, atrial fibrillation, atelectasis, bleeding, cardiac ischemia, congestive heart failure, cerebrovascular accident, ectasia, embolism, hypotension, infection, kinking, pneumothorax, prosthesis obstruction, and respiratory failure. Only three of these events (anastomotic disruption, cardiac ischemia, and prosthesis obstruction) were reported to be Graft related.

In addition to complications associated with open heart surgery, complications which may occur in conjunction with the use of the Graft include, but are not limited to: infection, perigraft seroma, thrombosis, stenosis, excessive suture hole bleeding, aneurysm, or mechanical disruptions or tearing of the suture line, graft, and/or host vessels and the resulting hemorrhage.

VI. Alternative Practices and Procedures

The Graft is indicated for patients who require coronary bypass grafting surgery but who have inadequate autologous conduit with which to complete the needed bypasses. Medical management and percutaneous intervention such as balloon angioplasty have already been considered for such patients, and been rejected.

Without sufficient autologous conduit, the treatment options for such patients are incomplete surgical revascularization, use of non-autologous conduit, incomplete revascularization followed by subsequent percutaneous interventions, or continuing medical management. Incomplete surgical revascularization entails performing the coronary bypasses possible with available autologous conduit, accepting fewer bypasses than needed. Available non-autologous conduits include cryopreserved saphenous vein homografts.

VII. MARKETING HISTORY

From 1993 to the present a total of 204 Grafts were shipped to Holland, Germany, Belgium, France, Switzerland, Austria, the United Kingdom, Italy, Greece, Norway, Canada, and Japan.

A Graft Implant Registration Form is included in each Perma-Flow package. Users are encouraged to complete the form and return it to Possis Medical to allow device tracking. To date, the only forms received have been from domestic and international IDE clinical trial sites.

Possis Medical estimates that the current total of Grafts implanted throughout the world is less than 200. The Graft has not been removed from any international market for any reason.

The Perma-Flow Graft has displayed the CE Mark since July 1997.

VIII. SUMMARY OF STUDIES

A. Pre-Clinical Testing

In the concept development phase, testing established the design features of the device, including the feasibility of the shunt concept, dimensions for the venturi, and Graft materials. With these established, more focused pre-clincial testing was performed on the device, as described below. The ANSI/AAMI VP20-1994 Cardiovascular Implants-Vascular Prosthesis (AAMI) standard was followed for testing the Graft.

1. Functional, Mechanical, and Physical Testing
Summaries of the functional and mechanical tests performed and the results obtained appear below in Table 1.

Table 1. Graft Mechanical and Functional Testing.

TEST PROTOCOL	SAMPLES	RESULTS
Hemolysis by Venturi: Plasma-free Hgb levels every 30m for 5h in a test apparatus pulsing fresh bovine blood at 120 mmHg through polyurethane grafts with and without venturis.	5 test grafts 5 controls	Test grafts: avg 0.285 mg Hgb/min*. Controls: avg 0.036 mg Hgb/min.
Platelet Activation by Venturi: Physical examination of grafts after 2h exposure to primate blood flow at physiological pressure and flow rates in polyurethane grafts with and without venturis.	4 test grafts 8 controls	No significant differences in platelet activation, CBC, plasma fibrinogen, or plasma hemoglobin.
Fatigue: In vitro test fixture sustaining 140/90 mmHg at 14 Hz for 90 days, simulating 36 months exposure to physiological conditions.	8 test grafts 8 controls	No significant differences in ePTFE tubing dimensions, internodal distance, balloon or tensile strength, or suture retention, or in venturi throat diameter or tensile strength.

*Hemolysis caused by venturi similar to that reported for heart valves (Indeglia et al, "Erythrocyte destruction by prosthetic heart valves, Circ. Supp II, April 1968, p. II - 86.)

Physical testing compared Graft ePTFE tubing to commercially available ePTFE vascular graft tubing, as summarized in Table 2.

Table 2. Physical Tests Comparing Graft and Commercially Available ePTFE Tubing (average/n).

TEST AND METHOD	PERMA-FLOW	CONTROL
Inner Diameter (mm), adapted* from AAMI section 8.5	5.17 (410)	5.01 (547)
Wall Thickness (mm), adapted* from AAMI section 8.5	0.42 (410)	0.45 (547)
Concentricity (mm), adapted* from AAMI section 8.5	0.043 (410)	0.041 (22)
Kink Diameter (mm), adapted** from AAMI section 8.9	12.6 (123)	14.4 (14)
Water Entry Pressure (mmHg), per AAMI section 8.2.4	309 (123)	276 (547)
Polymer Density (g/cu. cm); sample weight in air by volume displaced in a fluid of known density	2.2 (123)	2.2 (22)
Balloon Strength (kPa), per AAMI section 8.3.3.3	381 (123)	325(547)
Circ. Suture Retention*** (g); a simulated suture is pulled through the sample at a constant rate, similar to AAMI section 8.8	889 (123)	1205 (84)
Circ. Tensile Strength (N/mm), per AAMI section 8.3.1	3.5 (410)	3.1 (537)
Longitudinal Suture Retention*** (g); a simulated suture is pulled through the sample at a constant rate, similar to AAMI section 8.8	535 (408)	283 (115)
Longitudinal Tensile Strength (N), per AAMI section 8.3.2	121 (123)	126 (26)
Internodal Distance (ID) (microns), per AAMI section 8.2.1.3	21 (123)	21 (10)
Internodal Distance (OD) (microns), per AAMI section 8.2.1.3	32 (123)	33 (10)
Pore Volume (%), per AAMI section 8.2.1.2	0.67 (123)	0.69 (22)

*Adaptation involved the use of an optical scope on an x-y stage to minimize operator variability.
**Test sample was unsupported by a rod or radius gage, to avoid artifactual kink resistance.
***The test was developed and performed prior to availability of the AAMI Standard.

2. Biocompatibility Testing

Biocompatibility testing was performed on Graft materials after exposure to manufacturing conditions, as summarized in Table 3.

Table 3. Biocompatibility Testing for Perma-Flow Graft Materials

TEST PROTOCOL	TEST SAMPLES	RESULT
Cytotoxicity: Cultured mouse L929 fibroblast cells exposed to MEM media Graft material extract*.	1 Graft; USP designated plastic control	Passed
Hemolysis: Fresh rabbit blood incubated with 10 ml of Graft material extract*, using 0.9% saline media. Adapted from ASTM 756-82 and ASTM 619.	1 Graft; extraction media Graft exposure as control	Passed
Physio/Chemical: Buffering capacity, heavy metals, nonvolatile residue, and residue on ignition, per USP XXII, pp. 1572-3.	3 Grafts	Passed
Systemic Toxicity: Mice injected with Graft material extracts* using 0.9% saline, USP alcohol, polyethylene glycol, and cotttonseed oil media, per USP XXII, pp. 1497-9 and USP -NF, pp. 2703-4 (supp. 5).	20 mice; saline control	Passed
Intracutaneous Toxicity: Rabbits injected with Graft material extracts* using 0.9% saline, USP alcohol, polyethylene glycol, and cotttonseed oil media, per USP XXII, pp. 1497-9 and USP -NF, pp. 2703-4 (supp. 5).	8 rabbits; saline control	Passed
Carcinogenicity/Genotoxicity: *Salmonella typhimurium* and mouse L5178Y/TK lymphoma cells exposed to Graft material extracts using 0.9% saline and DMSO media per Ames Salmonella Mutagenicity Assay, and "Health Effects Guideline 476 (Genetic Toxicology: in vitro mammalian cell gene mutation tests), April 1984, published by OECD, respectively.	1 Graft; extraction media without Graft exposure as control	Passed
Dermal Sensitization: Guinea pigs intradermally injected with Graft material extract using Freund's complete adjuvant media, per Magnusson and Klingman, Allergic Contact Dermatitis, Identification of Contact Allergens, 1970, and USP XXII, pp. 1497-9.	15 Guinea pigs; extraction media without Graft exposure as control	Passed
Subchronic Toxicity: Mice dosed 5 days with daily hematology and homeostatic evaluations, and gross necropsy at 14 days, per Page and Sawhney, Proceedings of the Workshop on Subchronic Toxicity Testing, 1980.	24 mice extraction media without Graft exposure as control Graft materials.	Passed
Intramuscular Irritant Implant: 90 day intramuscular Graft material implant in rabbits.	3 rabbits; USP plastic control	Slight irritation**
Pyrogens: Material mediated pyrogen testing per USP biological test <151>.	3 rabbits	Passed

*Extraction methods per USP <87>, XXII, as recognized by TC 194 (ISO 10993-12).
**Findings not remarkable.

3. Functional Testing in Animals

Grafts were implanted in 53 canines (20-30kg) via standard left lateral thoracotomy. The Graft connected the left subclavian artery to the superior vena cava via end-to-side anastomoses, bypassing a ligated coronary artery via a side-to-side anastomosis. Nine of the animals had double coronary bypasses. Anastomosed coronary vessels were 1.5-2.0 mm in diameter. Animals were maintained on aspirin and dipyridimole. Follow-up was performed at 14 days, and two and six months, including periodic angiograms. There were three perioperative deaths, and two perioperative infections causing graft occlusions. A patency rate of 74% was observed out to 12 months, with 62% patency at three years. Explanted patent Grafts showed the coronary anastomoses to be stable, with no significant tissue build-up; there was no gross mural thrombi projecting into the Graft lumen, and no mural thrombus adherent to the silicone flow surface of the venturi. Histological study showed a healing reaction typical of ePTFE vascular grafts, with variable pseudointima and proteinaceous material coating the flow surface. The flow surfaces of explanted venturis were smooth and free of gross deposits, with a thin coating of proteinaceous material.

4. Process Validation

As part of design development, process validation testing verified that acceptable Grafts are obtained when the process is operated at the limits of critical parameters, and that nominal processing conditions will produce acceptable Grafts over several consecutive manufacturing lots, as summarized in Table 4. These results demonstrated that the Graft manufacturing process is robust to material lot changes and has minimal variability from one manufacturing lot to the next.

Table 4. Process Validation Testing Against Specifications (Graft Venturi and ePTFE Tubing)

TEST AND METHOD	SPEC	RESULT
VENTURI:		
Kink Diameter, adapted* from AAMI section 8.9	≤ 20 mm	Passed
Tensile Strength; a venturi cut in half longitudinally is pulled at a constant rate to failure	≥ 44.5 N	Passed
Throat ID, measured optically at the narrowest point	[proprietary]	Passed
ePTFE TUBING:		
Inner Diameter, adapted** from AAMI section 8.5	4.93-5.29 mm	Passed
Wall Thickness, adapted** from AAMI section 8.5	0.38-0.46 mm	Passed
Concentricity, adapted** from AAMI section 8.5	≤ 0.089 mm	Passed
Kink Diameter, adapted**** from AAMI section 8.9	≤ 20 mm	Passed
Water Entry Pressure, per AAMI section 8.2.4	≥ 181 mmHg	Passed
Differential Scanning Calorimeter; thermal cycling	100% sintered	Passed
Balloon Stength, per AAMI section 8.3.3.3	≥ 207 kPa	Passed
Circumferential Suture Retention***; a simulated suture is pulled	≥ 600 g	Passed

through the sample at a constant rate, similar to AAMI section 8.8		
Circumferential Tensile Strenth, per AAMI section 8.3.1	≥ 1.41 N/mm	Passed
Longitudinal Suture Retention***; a simulated suture is pulled through the sample at a constant rate, similar to AAMI section 8.8	≥ 200 g	Passed
Longitudinal Tensile Strength, per AAMI section 8.3.2	≥ 86 N	Passed
Internodal Distance (ID), per AAMI 8.2.1.3	8-40 microns	Passed
Internodal Distance (OD), per AAMI 8.2.1.3	8-40 microns	Passed
Pore Volume, per AAMI section 8.2.1.2	65-75 %	Passed

*Adaptation needed for unique features of venturi not accomodated by Standard.
** Adaptation involved the use of an optical scope on an x-y stage to minimize operator variability.
***The test was developed prior to the availability of the AAMI Standard.
****Test sample was unsupported by a rod or radius gage, to avoid artifactual kink resistance.

B. Clinical Experience

A Phase 1 feasibility trial of the Graft was conducted under IDE G910121. A total of 32 patients received Graft implants from November 1992 through December 1995. The protocol required 12 month follow-up. A total of 424 months were reported, for an average of over 13 months (range 0-38 months). A total of nine patients died; five of the deaths were prior to discharge. None of the deaths were reported as device-related by the investigators. Ten other complications were also reported, including one coronary steal with angina, two pleural effusions, two congestive heart failures, one ventricular tachycardia, one sternal infection, one case of graft weeping, one pulmonary edema, and one renal failure. This total of 19 complications were reported in 17 patients. Fifteen patients reported no complications. Only the graft weeping (serous fluid oozing through the graft wall) and coronary steal (angina secondary to coronary ischemia caused by the volume of blood shunted through the Graft) were reported to be Graft related. Neither required treatment. Probable clinical benefit of Graft treatment is suggested by the improvement in New York Heart Association functional classification: The number of patients in classes I and II, the higher ratings, improved from 28% pre-operative to 73% at six months, while the number of patients in classes III and IV, the lowest ratings, decreased from 66% to 5%.

The Phase 2 trial began in January 1996, and through September 1997, 62 patients have been enrolled in Phase 2. The results currently available are insufficient to support statistically valid conclusions. However, the Phase 1 and 2 results taken together suggest that the Graft is safe for use in seriously compromised patients who require coronary bypass surgery but lack the autologous conduit with which to perform it. The complications seen thus far are not different from those seen in conventional coronary artery bypass grafting. They include anastomotic disruption or obstruction, atrial fibrillation, atelectasis, bleeding, cardiac ischemia, congestive heart failure, cerebrovascular accident, ectasia, embolism, hypotension, infection, kinking, pneumothorax, prosthesis obstruction, and respiratory failure. Only three of these events (anastomotic disruption, cardiac ischemia, and prosthesis obstruction) were reported to be Graft related. The probable clinical benefit is suggested in the improved New York Heart Association functional class reported

postoperatively. The results to date therefore support the conclusion that the Graft is safe and has probable clinical benefit when used as intended.

XI. Conclusions Drawn from Studies

The results of biocompatibility testing provide adequate assurance that the materials used in the device are biocompatable for the proposed intended use. Performance testing to assess mechanical properties and flow performance of the Graft demonstrate that the design is appropaite for the proposed intended use.

The clinical data available show that the risk of illness or injury from the device is comparable to that seen in conventional coronary artery bypass grafting surgery. The improved postoperative NYHA functional classification scores suggest probable benefit to health from use of the device.

In conclusion, the preclincial studies provide reasonable assurance that the device materials and design are appropriate for the proposed intended use. The limited clinical data suggest that the device will not expose patients to an unreasonable or significant risk of illness or injury, and that the probable benefit to health from use of the device outweighs the risk of injury or illness, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

X. Panel Recommendation

This HDE was not taken to an Advisory Panel, as the data suggest reasonable patency of the device at one month (92%) and reduced patency at one year (67%). In addition, there have been no unexpected safety concerns with the device. Therefore, based on the extensive pre-clinical testing which has been performed on this device, and the fact that no safety concerns have been identified at this time, Panel review is not needed.

XI. CDRH Decision

CDRH determined that, based on the data submitted in the HDE, the Possis Perma-Flow Coronary Bypass Graft will not expose patients to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the device outweighs the risk of illness or injury, and issued an approval order on APR 30 1998

XII. Approval Specifications

Indications For Use: See the Instructions for Use and Patient Education and Product Information

Hazards to Health from Use of the Device: See Sections IV and V above.

XIII. Publications and Other Outside Information

1. Drasler WJ, Jenson ML, George SA, et al: A Unique Vascular Graft Concept for Coronary and Peripheral Applications. Transactions of the American Society of Artificial Internal Organs 34(3):769-772, 1988.

2. Emery RW, Petersen RJ, Baumgard C, Nicoloff DM. First clinical use of the Possis synthetic coronary graft. J Cardiac Surg 8:439-42, 1993.

3. Emery RW, Joyce LD, Arom KV, King RM, Nicoloff DM. Operative considerations in implantation of the Perma-Flow Graft. Ann Thorac Surg 58:1770-73, 1994.

4. Kerber S, Baumbach M, Rahmel A, Weyand M, Scheld HH, Breithardt G. Clinical and invasive 7-month follow-up of a patient with a synthetic coronary graft. Int. J Cardiol 51:143-148, 1995.

5. Emery RW, Mills NL, Teijeira FJ, Arom KV, Baldwin P, Petersen RJ, Joyce LD, Grinnan GLB, Sussman MS, Copeland JG, Ochsner JL, Boyce SW, Nicoloff DM. North American Experience with the Perma-Flow Prosthetic Coronary Graft. Ann Thorac Surg 62:691-6, 1996.

6. Schmid C, Weyand M, Derber S, Breithardt G, Scheld HH. The use of a Perma-Flow Graft for coronary artery bypass surgery. Eur J Cardio-thorac Surg 10:284-286, 1996.

7. Mooney MJ, Emery RW, Kern MJ. Coronary Flow in a Prosthetic Aorta-Coronary Bypass Graft: First Report of Possis Perma-Flow® Graft Physiology in a Patient. Cathet. Cardiovasc. Diagn. 40:315-318, 1997.

8. Vogt S, Vanoucchi A, Rybinsk L, Froelich JJ, Waldhans S, Wolter F, Moosdorf R. Alternative aortocoronary bypass-grafting with the Perma-Flow Prosthesis: first experience with a new concept. (abstract) Presented at the 7th World Congress, International Society of Cardio-Thoracic Surgeons (ISCTS), 2-5 Sep 97, Dusseldorf.

9. General Program Memorandum #G91-1: Device Labeling Guidance.

Perma-Flow Coronary Bypass Graft
Instructions for Use

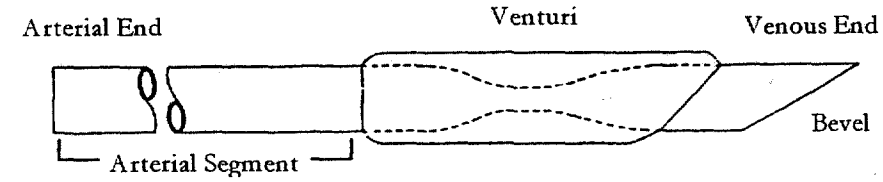
Humanitarian Device.
Authorized by Federal law for use in the treatment of coronary artery occlusive disease in patients who require surgical revascularization but lack sufficient autologous vessel conduit. The effectiveness of this device for this use has not been demonstrated.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

CAUTION: This device should be used only by physicians trained in coronary bypass surgical techniques, who have training or experience in the use of this device, at facilities adequate for the conduct of such surgery. The device should be used only by physicians prepared to provide long-term follow-up patient monitoring.

REF Reference Number 15664

Product Description
The Perma-Flow® Coronary Bypass Graft (Graft) is a vascular graft designed to bypass occluded coronary arteries. The Graft is made of expanded PTFE (ePTFE) and incorporates a silicone elastomer Venturi constriction near the distal (venous) end. The distal Venturi controls the flow rate (approximately 10% of cardiac output) in the Graft and maintains arterial pressure at the side-to-side anastomoses to support coronary perfusions. The Graft has an internal diameter of 5mm and is supplied with a length of 60cm. It features a longitudinal black orientation line to aid in implant.



Single Use Only

STERILE EO Sterilized with Ethylene Oxide

Do not use if sterile package is opened or damaged. Do not resterilize.

Indications for Use
The Perma-Flow® Coronary Bypass Graft is indicated for single or multiple vessel coronary artery bypass in patients who are receiving coronary bypass grafting but who have inadequate autologous conduit to complete the required revascularization.

Contraindications
None

WARNINGS

1. **The Graft should not be used when the physician determines that the added arteriovenous shunt may not be tolerated well, possibly due to poor cardiac valves or the presence of a pre-existing arteriovenous shunt.**
2. The Graft is not intended for applications as a vascular patch, or for reconstruction purposes.
3. Do not place any object inside the Venturi. Do not place clamps, forceps, dilators, catheters, sheaths, needles, endoscopes, measuring devices, swabs, sponges, or any other object inside the Graft within 1.0cm of the Venturi. Damage of any sort to the Venturi may result in graft thrombosis.
4. The arrow molded into the outer sleeve of the Venturi indicates the direction of blood flow and must always point towards the venous end of the Graft in order for the Graft to properly perfuse the coronary arteries.
5. The layout of the Graft must be carefully determined so that the required anastomoses are constructed without creating sharp bends or stresses in the graft which could cause a permanent kink or lead to mechanical disruptions of the graft, host vessel, and/or suture lines.

Precautions

1. Open the sterile package using standard sterile technique.
2. Do not allow the Graft to come in contact with organic solvents or aqueous solutions; such exposure may cause excessive serum leakage due to wetting. The Graft does not require preclotting. Do not fill with blood before implantation or force irrigating solutions through the Graft wall; attempts to do so may affect the hydrophobic properties of the graft, resulting in possible seroma formation when implanted. Excessive manipulation of the Graft while in contact with tissue fluids or blood should be avoided.
3. The Graft is not elastic. Care should be taken to determine the proper length to allow adequate placement and to eliminate excessive stress on the anastomoses. Cutting the Graft too short may result in anastomotic disruption and excessive bleeding. Leaving the Graft too long may cause the Graft to buckle or to kink.
4. It is recommended that a non-cutting tapered needle be used with the Graft. Do not use a full radius cutting needle as it may damage the Graft at the suture line. Excessive anastomotic bleeding may occur if excessive tension causes suture holes to elongate or tear, if the needle-to-suture diameter is too great, or if gaps occur between the Graft and host vessels.
5. It is recommended that only smooth jawed or rubber shod clamps be used during implantation to avoid damage to the Graft wall. Do not clamp the Graft within 3.0cm of the Venturi and minimize the use of repeated clamping.

6. Do not bend the Graft in the Venturi outer sleeve region or within 1.5cm of the Venturi region as increased tendency to kink may result. The Venturi should be kept straight and the Graft not implanted if the Venturi has a kink or bend.
7. Twisting of the Graft must be avoided. Twisting may be detected by observing the longitudinal black orientation line on the Graft.
8. It is important to use proper cutting technique when implanting the Graft. Failure to do so may cause damage to the Graft or reduce the suture retention strength. When cutting, gently pull the Graft taut to determine the correct length and cut with a sharp surgical instrument. Excessive tension on the Graft during cutting or punching can cause damage or tearing to the Graft. An uneven edge should be carefully trimmed.
9. A topical hemostatic agent applied to completed arterial anastomoses may be helpful in minimizing any bleeding that may occur.
10. It is recommended that patients receive daily aspirin or other antiplatelet therapy as a deterrent to clot formation in the Graft. As with any synthetic implant, patients should be instructed to obtain and use prophylactic antibiotics prior to dental work or other surgery.

Adverse Events and Possible Complications

In the Phase 1 feasibility clinical trial comprising 32 patients, the following complications were observed (listed in decreasing order of frequency): death, congestive heart failure, pleural effusions, ventricular tachycardia, coronary steal, sternal infection, pulmonary edema, renal failure, and graft weeping. Only the graft weeping was reported to be Graft related.

In the ongoing Phase 2 trial, these additional complication types have been observed: anastomotic disruption or obstruction, atrial fibrillation, atelectasis, bleeding, cardiac ischemia, congestive heart failure, cerebrovascular accident, ectasia, embolism, hypotension, infection, kinking, pneumothorax, prosthesis obstruction, and respiratory failure. Only three of these events (anastomotic disruption, cardiac ischemia, and prosthesis obstruction) were reported to be Graft related.

In addition to complications associated with open heart surgery, complications which may occur in conjunction with the use of the Graft include, but are not limited to: infection, perigraft seroma, thrombosis, stenosis, excessive suture hole bleeding, aneurysm, or mechanical disruptions or tearing of the suture line, graft, and/or host vessels and the resulting hemorrhage.

Patient Care and Follow-Up

The patient and follow-up physician should be notified of the high flow (approximately 10% of cardiac output) in the Graft resulting from the arteriovenous shunt. As with any synthetic implant, patients should be instructed to:

- inform physicians of the Graft implant;
- obtain and use prophylactic antibiotics prior to dental work or other surgery;
- receive daily aspirin or other antiplatelet therapy as a deterrent to clot formation in the Graft.

Standard angiographic techniques may be used to evaluate patency of both the Graft and its coronary anastomoses. Care should be taken to administer the appropriate amount of contrast agent in order to provide the greatest image clarity of the coronary anastomosis. The high flow of blood (approximately 10cc/second) through the Graft requires a greater rate of infusion of contrast agent to achieve an image that indicates anastomotic patency.

Ultrasound imaging may be useful in observing the high velocity flow through the Graft.

Directions For Use

The Graft is used in conjunction with common coronary bypass methods to create an arteriovenous shunt from the ascending aorta to the superior vena cava (SVC). Side-to-side anastomoses proximal to the Venturi are created to coronary arteries requiring bypass. The high flow in the Graft resulting from the arteriovenous shunt, aids in maintaining graft patency.

1. Graft anastomoses are created in reverse order of blood flow through the Graft. **The arrow molded into the outer sleeve of the Venturi indicates the direction of blood flow and must always point towards the venous end of the Graft.**
2. Judgment of the normal position of the heart and greater vessels should be used in determining the proper layout and Graft length, even though the heart may not be positioned or inflated normally during the surgery. Use of the pericardial margin may aid in determining distances and layouts. **The layout of the Graft must be carefully determined so that the required anastomoses are constructed without creating sharp bends or stresses in the Graft which could cause a permanent kink or lead to mechanical disruptions of the graft, host vessel, and/or suture lines.** Noting the normal positions prior to manipulation may be helpful.
3. The construction of the SVC anastomosis is undertaken first, before any other anastomoses are constructed. The Graft may be implanted so that the Venturi lays on the anterior surface of the SVC (Figure a) or from the left side of the SVC via the transverse sinus (Figure b) depending on the coronary arteries requiring bypass.

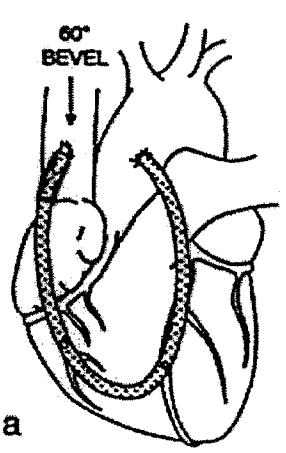


Figure a

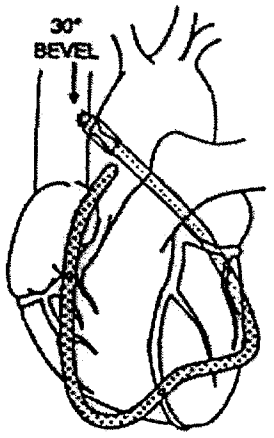


Figure b

4. The venous end of the Graft as supplied is cut at a 60° bevel. For anterior placement of the Venturi, the 60° bevel should be maintained so that the Venturi portion can lay properly on the anterior surface of the SVC (Figure a). This will allow the Graft to lie adjacent to the heart without distortion of the anastomosis and provides an external stent for the SVC (Figure c).

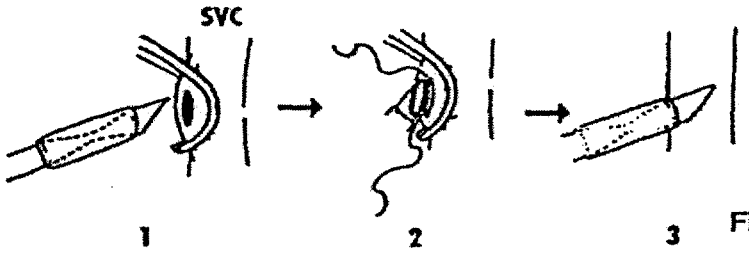


Figure c

5. For Graft placement through the transverse sinus, the bevel should be trimmed to 30° as close to the Venturi as possible to allow appropriate construction of the anastomosis (Figure b).
6. The SVC anastomosis is constructed using a nonabsorbable monofilament suture suitable for vascular anastomosis on a small non-cutting needle to minimize needle hole size and suture hole bleeding (for example, 6-0 Prolene* suture on a C-1* taper needle). Following construction of the SVC anastomosis, the Graft is de-aired by retrograde filling with venous blood until the air in the Graft is removed. An atraumatic clip is placed a minimum of 3.0cm from the Venturi to act as an occluder.
7. Next, measurement is made to the coronary artery anastomosis site, which is closest to the Venturi. The inter-anastomotic length must be precise since ePTFE is not elastic. The anastomosis must be done without tension, using the pericardial margin as a reference. Twisting of the graft must be avoided. Twisting may be detected by observing the longitudinal black orientation line on the Graft and should be used throughout construction of anastomoses to avoid twisting or torquing of the Graft.
8. After the Graft is measured to the appropriate coronary artery, an arteriotomy and an incision along the longitudinal black line are made. A 2.0mm x 4.0mm elliptical punch may be used to create a longitudinal elliptical hole in the ePTFE conduit that will approximate the length of the arteriotomy in the coronary artery and allow anastomotic construction without distortion. The anastomosis is constructed using a running technique (Figure d) with a nonabsorbable monofilament suture suitable for vascular anastomosis on a small non-cutting needle to minimize needle hole size and suture hole bleeding (for example, 7-0 Prolene* suture on a C-1* taper needle). Each suture bite should capture a small piece of epicardium to lie between the ePTFE and the coronary artery wall. This will add strength and hemostatic security to the anastomosis. After construction of the anastomosis, the Graft should be de-aired and the anastomosis is checked using a syringe with a tapered connector. When injecting any solution into the Graft, use minimum syringe pressure to avoid forcing solution into the graft wall, which could lead to leakage or seroma formation.

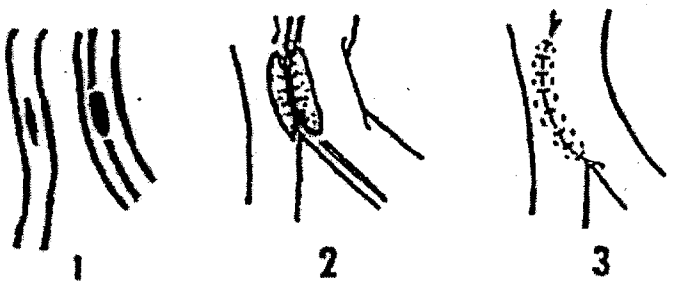


Figure d

9. The process of laying, measuring, constructing the coronary anastomosis and de-airing the Graft is repeated for each coronary anastomosis, working from the venous end towards the aortic end of the Graft. At each anastomosis, the Graft should be aligned as parallel as possible to the coronary artery being bypassed, while avoiding sharp bends or excessive length. The Graft should be laid out in a gentle curve to approximate the vessel and allow for expansion and contraction of the inter-anastomotic loops of the Graft between cardiac systole and diastole (Figure e).

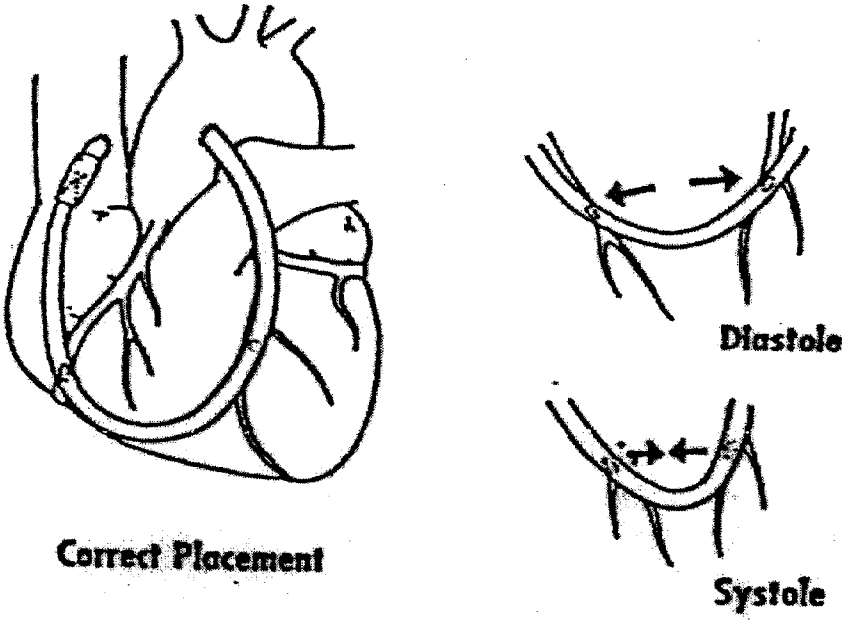


Figure e

10. Prior to release of the aortic clamp, ensure that the Graft is de-aired completely by retrograde venous filling and aspirating all air. The administration of retrograde cardioplegia solution at this time will assist in removing all air from the coronary system. Testing of the Graft with a cardioplegia infusion between anastomoses will allow evaluation of anastomotic hemostasis and the configuration of the Graft between coronary anastomoses.

11. The length of the Graft between the last coronary anastomosis created and the aorta must be precisely measured following clamp release using the pericardial margin as a reference.

12. Construction of the anastomosis of the Graft to the aorta should be done with partial aorta occlusion and with a 5.0mm aortic punch using a nonabsorbable monofilament suture suitable for vascular anastomosis on a small non-cutting needle to minimize suture hole bleeding (for example, 6-0 or 7-0 Prolene* suture on a C-1* taper needle).

Labels

Labels have been supplied for patient records. Please take time to fill out the Graft Implant Registration Form completely and return it to Possis Medical, Inc. ("PMI").

Clinical Experience

In a Phase 1 feasibility trial, a total of 32 patients received Perma-Flow Graft implants. The protocol required 12 month follow-up. A total of 424 months were reported, for an average of over 13 months (range 0-38 months). A total of nine patients died, of which five were in-hospital deaths. None of the deaths were device-related. Other reported complications included on coronary steal with angina, two pleural effusions, tow congestive heart failures, one ventricular tachycardia, one sternal infection, one case of graft weeping, one pulmonary edema, and one renal failure. Only the graft weeping (serous fluid oozing through the graft wall) and coronary steal (angina secondary to coronary ischemia caused by the volume of blood shunted through the Graft) were reported to be Graft related. Neither required treatment. Fifteen patients reported no complications. The number of patients in New York Heart Association functional classes I and II improved from 28% preoperative to 73% at six months, while the number of patients in classes III and IV decreased from 66% to 5%. A Phase 2 study is underway.

References

1. Emery RW, Joyce LD, Arom KV, King RM, Nicoloff DM. Operative considerations in implantation of the Perma-Flow Graft. Ann Thorac Surg 58:1770-73, 1994.
2. Mooney MJ, Emery R, Kern MJ. Coronary Flow in a Prosthetic Aorto-Coronary Bypass Graft: First Report of Possis Perma-Flow® Graft Physiology in a Patient. Cathet. Cardiovasc. Diagn. 40:315-318, 1997.
3. Vogt S, Vanoucchi A, Rybinsk L, Froelich JJ, Waldhans S, Wolter F, Moosdorf R. Alternative aortocoronary bypass-grafting with the Perma-Flow Prosthesis: first experience with a new concept. (abstract) Presented at the 7th World Congress, International Society of Cardio-Thoracic Surgeons (ISCTS), 2-5 Sep 97, Dusseldorf.

Limited Warranty and Disclaimer

PMI hereby warrants that if the Perma-Flow® Coronary Bypass Graft fails to perform within normal tolerance due to a defect in materials or workmanship, PMI will provide, at no charge, a replacement to the failed product.

This limited warranty applies only if:

1. PMI packaged and labeled the product;
2. The sterile package was unopened and undamaged before product use;
3. The failed product is returned to PMI; and
4. The product has not been mishandled, reprocessed or altered.

PMI MAKES NO REPRESENTATION OR WARRANTY THAT A PMI PRODUCT WILL NOT FAIL. PMI IS NOT RESPONSIBLE FOR ANY MEDICAL COMPLICATIONS RESULTING FROM THE USE OF ITS PRODUCTS. EXCEPT AS EXPRESSLY PROVIDED HEREIN, PMI IS NOT RESPONSIBLE FOR ANY DIRECT, INCIDENTAL, OR CONSEQUENTIAL DAMAGES BASED ON ANY DEFECT, FAILURE, OR MALFUNCTION OF ITS PRODUCTS, WHETHER THE CLAIM IS BASED ON WARRANTY, CONTRACT, TORT, OR OTHERWISE. FURTHERMORE, EXCEPT AS EXPRESSLY PROVIDED BY THE LIMITED WARRANTY, PMI MAKES NO WARRANTY, EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE.

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INNOVATIONS FOR LIFE™

CE 0123

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Manufacturer's Official EU Representative:
Possis Medical Europe b.v. • Keizergracht 62-64• 1015 CS Amsterdam • The Netherlands
Phone: 31(0)-20-520-75-35 • Fax: 31(0)-20-520-75-10

Your physician has determined that you may benefit from receiving the Perma-Flow®. This pamphlet is intended to help you. It is important that you and your doctors understand this information. If you have any questions, write them down and ask your doctor or nurse.

Components of Possis Medical, Inc.

Possis Medical, Inc. would like to thank Pam Baldwin, RN, study coordinator for the Perma-Flow® Clinical Study at the Minneapolis Heart Institute, for her authorship of this patient education brochure.

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Phone: 31(0)-20-520-75-35 • Fax: 31(0)-20-520-75-10

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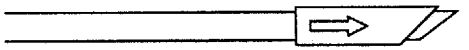
Designed to Exceed

PERMA-FLOW®

Coronary Bypass Graft



Patient Education and Product Information

From:
Possis MEDICAL INC
INNOVATIONS FOR LIFE™

POSSIS

PERMA-FLOW®

CORONARY BYPASS

GRAFT

Humanitarian Device.

Authorized by Federal law for use in the treatment of coronary artery occlusive disease in patients who require surgical revascularization but lack sufficient autologous vessel conduit. The effectiveness of this device for this use has not been demonstrated.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Many patients are in need of coronary bypass grafting yet lack the appropriate veins from their own body to be used for the procedure. With the development of an artificial blood vessel, patients who lack usable veins may still be considered candidates to receive coronary bypass surgery.

The Possis Perma-Flow® Coronary Bypass Graft is constructed of materials similar to those that have been successfully used in other artificial blood vessels. The Possis graft is designed to keep a controlled amount of blood continuously flowing through the graft to help keep it open. This flow is obtained by a narrowing (a venturi) placed inside the graft. It is designed to create a resistance which increases the speed of bloodflow yet maintains an appropriate blood pressure for effective coronary circulation.

Your doctor may choose to use the Possis Perma-Flow® Coronary Bypass Graft because your veins are too small, short or diseased to be used as bypasses to your coronary arteries. The Possis graft can be sewn to as many coronary arteries as your doctor feels are necessary. This artificial blood vessel will be sewn from the aorta to the coronary artery (to supply blood past a narrowed region of the coronary artery) and then to a large vein called the vena cava (see Figure 1).

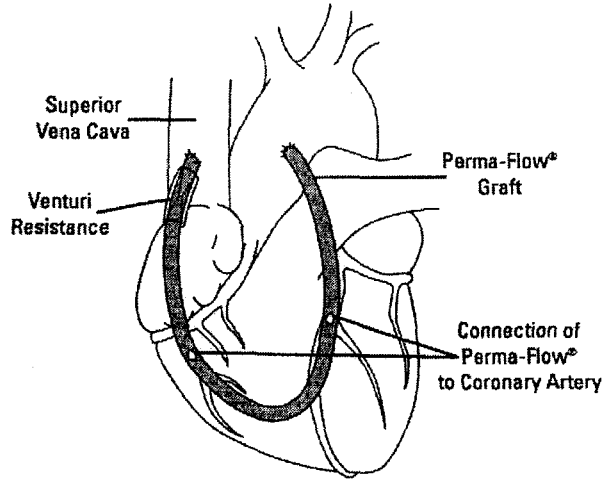


Figure 1. *Placement of Perma-Flow on the heart with arrows representing direction of blood flow.*

If you receive the graft you will need to take medicine such as aspirin every day to help keep the blood swiftly flowing through the graft without clotting. Your doctor will start giving you this medicine shortly after your surgery is completed. You may need to take preventative antibiotics whenever having any dental work, or after surgery or trauma to avoid infection which may occur with any artificial material (artificial heart valves, knees and hips are other examples). Your doctor will give you special instructions for your particular medical condition. If something in this pamphlet differs from the instructions of your doctor, always follow your doctor's special instructions.

Routine care is not affected by receiving the Possis Perma-Flow® Coronary Bypass Graft. However, you will be responsible to inform healthcare personnel of your artificial coronary graft during any medical visit. With medical personnel unfamiliar with this graft, you may also need to explain why you are taking an aspirin every day and why you may need preventative antibiotics.

Your physician has determined that you may benefit from receiving the Possis Perma-Flow® Coronary Bypass Graft and this pamphlet is intended to help you better understand what the Possis graft is and how it may help you. If you have any questions, write them down and ask your doctor or nurse.