# DE NOVO CLASSIFICATION REQUEST FOR VASQ

## REGULATORY INFORMATION

FDA identifies this generic type of device as:

**Extravascular support for an arteriovenous fistula for vascular access.** This device is a permanent implant which is surgically placed outside and/or around an artery and/or vein to provide external support to arteriovenous fistulas created for vascular access by means of vascular surgery.

**NEW REGULATION NUMBER:** 21 CFR 870.4600

**CLASSIFICATION:** Class II

**PRODUCT CODE:** QVQ

## BACKGROUND

**DEVICE NAME:** VasQ

**SUBMISSION NUMBER:** DEN220026

**DATE DE NOVO RECEIVED:** April 29, 2022

**SPONSOR INFORMATION:**

Laminate Medical Technologies Ltd.
24 Raoul Wallenberg Street
Tel-Aviv, Israel 6971921

## INDICATIONS FOR USE

VasQ is intended for use as an external support for upper extremity arteriovenous fistulas created for vascular access by means of vascular surgery.

## LIMITATIONS

The sale, distribution, and use of VasQ are restricted to prescription use in accordance with 21 CFR 801.109.

VasQ is contraindicated for use in proximal forearm radial artery based fistulas.

VasQ is contraindicated for patients with target veins <2mm in external diameter, and for patients with target arteries <2mm or >6mm in external diameter.

The safety and effectiveness of VasQ for use in external support of conduits other than arteriovenous upper arm or distal forearm fistulas have not been established.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

## DEVICE DESCRIPTION

VasQ is a nitinol implant that is used to provide external support for arteriovenous fistulas (AVF) created by means of vascular surgery. VasQ is comprised of a braid and a brace that are welded together (Figure 1). The braid is woven nitinol mesh that provides structural support to the segment of the vein that must be mobilized from its natural supporting tissue to allow surgical anastomosis to the artery. The brace is a laser cut nitinol structure intended to maintain geometric properties at the juxta-anastomosis region of the AVF.

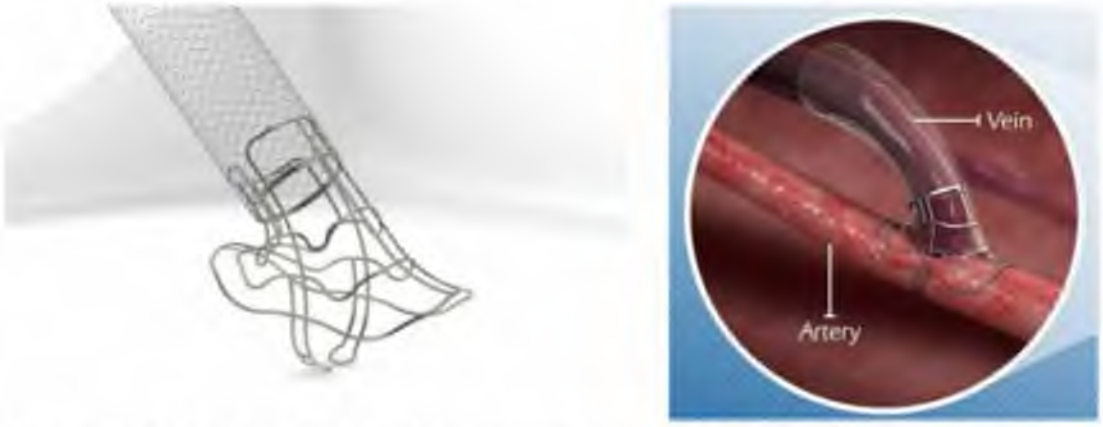


Figure 1: VasQ device (left) and simulated image of VasQ placed on an AVF (right)

VasQ is supplied sterile and implanted over the end-to-side AVF anastomosis during the surgical AVF creation procedure. VasQ is supplied in a range of six dimensional models (VasQ models 1, 2, 3, 4, 5, 6) to support a range of artery and vein diameters 2mm – 6mm (Table 1).

Table 1: VasQ Model Sizes

| VasQ Model | Applicable Vessel Diameter (D), mm |
|---|---|
| **1** | $2.0 \leq D < 3.2$ |
| **2** | $3.2 \leq D < 3.7$ |
| **3** | $3.7 \leq D < 4.1$ |
| **4** | $2.5 \leq D < 4.8$ |
| **5** | $4.8 \leq D < 5.5$ |
| **6** | $5.5 \leq D \leq 6$ |

*Accessories*

Selection of the appropriate VasQ model is facilitated by the VasQ Disposable Laminate Model Selection Tool (DMST), provided sterile for single use (Figure 2). The notches on the DMST are used to gauge the vein and artery, starting with the small notch and progressing one by one to the larger notches, until the vessel fits within the notch. The model is selected to fit the number on the notch which best fits the vessel. The DMST is a class I, 510(k)-exempt device, regulated under 21 CFR 878.4800, Product code FTY.

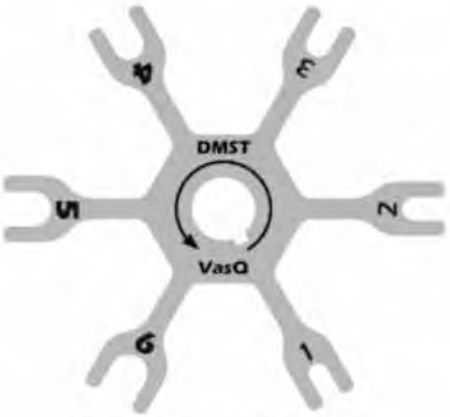


Figure 2: VasQ DMST

## SUMMARY OF NONCLINICAL/BENCH STUDIES

### BIOCOMPATIBILITY

VasQ is a tissue-contacting, permanent (>30 days) implant device. The biocompatibility testing summarized below was performed to demonstrate that the device is biocompatible for its intended use. Testing was conducted in alignment with FDA guidance (*Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process"*). All tests passed.

Table 2: Biocompatibility Testing Summary

| **Test** | **Description** |
|---|---|
| Cytotoxicity | MEM Elution Method with Mouse Fibroblast Assay |
| Sensitization | Guinea Pig Maximization |
| Irritation | Intracutaneous Injection |
| Acute Systemic Toxicity | Acute Systemic Injection |
| Material-Mediated Pyrogenicity | Rabbit Pyrogen Test |
| Implantation | Addressed in animal safety study |
| Subacute/Subchronic Systemic Toxicity | Chemical Characterization<br>Toxicological Risk Assessment |
| Genotoxicity | Chemical Characterization<br>Toxicological Risk Assessment |
| Chronic Toxicity | Chemical Characterization<br>Toxicological Risk Assessment |
| Carcinogenicity | Chemical Characterization<br>Toxicological Risk Assessment |

## STERILITY/ SHELF-LIFE

The shelf-life of VasQ has been established at 5 years based on real time and accelerated aging testing (equivalent to 5 years) on packaging validation testing of the sterile barrier following transit simulation. Test samples underwent environmental conditioning and simulated transportation per ASTM D4169-14 and were visually inspected, dye penetration tested per ASTM 1929, seal strength tested per ASTM F-88, and burst strength tested per ASTM F1140-13. The VasQ device was assessed for susceptibility to aging with consideration of the implant material and the prescribed shelf-life conditions. It was concluded that shelf-life validation testing was not needed on the nitinol implant to support the proposed shelf-life as changes due to age on this material are expected to be negligible.

VasQ is labeled as sterile and has a validated sterility assurance level (SAL) of $10^{-6}$. VasQ is sterilized by gamma irradiation with a dose of 20 kGy. The gamma irradiation sterilization validation was evaluated per AAMI TIR13004:2013 and AAMI 11137-1:2006 (R2010), -2:2013, and -3:2006 (R2010).

## MAGNETIC RESONANCE (MR) COMPATIBILITY

The sponsor conducted MRI compatibility testing on VasQ to verify that it can be used in MRI environments of 1.5, 3, and 7 Tesla. The results demonstrated that the Implant is MR compatible under the conditions specified in the labeling.

## PERFORMANCE TESTING - BENCH

VasQ was subjected to a series of bench tests to assess its functional performance. These tests were performed on final, sterilized product. The engineering bench testing summarized in Table 3 below was performed to demonstrate acceptable mechanical performance of the device for its intended use.

Table 3: Performance Testing (Bench) Summary

| Test | Description/Acceptance Criteria |
|---|---|
| Dimensional Verification | The measured braid length and welding distance should be within the specified engineering tolerances for these dimensions. |
| Flex/Kink Resistance | Devices were flexed around mandrels and kink was defined as a diameter reduction of (b)(4) Devices must demonstrate geometric recovery and a kink radius of (b)(4) mm. |
| Crush Resistance | Devices must demonstrate full geometric recovery following crushing between two plates to (b)(4) of their original diameter. |
| Local Compression | Devices must demonstrate full geometry recovery following (b)(4) geometric displacement due to local compression at various locations of the device. Devices also underwent acute flexion of (b)(4). |

| | |
|---|---|
| Device Integrity | Microscopic visual examination of devices for freedom from surface cracks or scratches |
| Tensile Strength | Joint at the braid-brace welded connection must withstand a tensile force of (b)(4) |
| Corrosion Resistance | Assessment of the VasQ implant's susceptibility to corrosion |
| Durability | Devices tested under cyclic radial loads must demonstrate no breakage after (b)(4) (equivalent to (b)( years real time). |
| Bending Fatigue | Devices shall not have any clinically significant fracture when subjected to (b)( years of simulated in vivo bending (as would result from arm flexion). |

### PERFORMANCE TESTING - ANIMAL

The sponsor conducted an ovine animal study to assess the safety, performance, and integrity of VasQ and to optimize the vessel sizing and appropriate device model selection. In this study, 10 adult sheep underwent bilateral femoral end to side AVF creation. One fistula was randomized to be supported with the VasQ while the other unsupported fistula served as a control. Outflow rates of both fistulas were measured using Doppler ultrasound before closure of the surgical wounds. The animals underwent immediate and late angiography at 1 and 3 months and were then sacrificed for histopathologic evaluation.

The animal study results supported the safety, performance, and integrity of the VasQ. All fistulas were implanted as planned and all animals completed study follow-up duration as planned. Angiography showed that fistulas treated with the device remained patent, without exceptional injury or inflammation to the vessels. The device remained intact without kink or crush deformations, including all welded joints and thin struts, during the follow-up period. The results of the histopathology assessment revealed that fibrous tissue generally surrounded the vein, as well as the device in most histological samples. Results from the animal study also guided vessel sizing and device model selection in clinical use of VasQ.

## SUMMARY OF CLINICAL INFORMATION

VasQ was primarily supported by a pivotal study entitled "a multi-center prospective study to evaluate the safety and effectiveness of the VasQ external support for arteriovenous fistula." The sponsor also conducted two propensity matched comparative studies for the pivotal study results, as well as provided additional information from clinical use outside of the US. Details of the study design and selected clinical results are provided below.

### PIVOTAL CLINICAL STUDY

Objective: The objective of the pivotal study was to provide safety and effectiveness information regarding the use of the VasQ device as an external support for upper extremity AVFs created for vascular access by means of vascular surgery.

Study Design: The study was a prospective, multi-center, single-arm, open-label study in which a total of 144 subjects were enrolled at 15 US sites to undergo creation of an AVF with the VasQ device implanted. The main study cohort consisted of 129 subjects with brachiocephalic fistula (BCF) and the supplementary study cohort consisted of 15 subjects with forearm AVF.

Follow-up visits were scheduled at 1 months, 3 months, 6 months, 9 months, 12 months, and 24 months for doppler ultrasound (except for the 9 month visit), clinical examination (except the 9 month visit), dialysis status, and adverse event follow up. Subjects underwent x-ray imaging of the arm at 12 and 24 months. A core laboratory evaluated the x-ray imaging for device integrity observations, including brace breakage, braid/brace complete detachment, and braid/brace partial detachment. Safety events were reviewed by an independent Clinical Events Committee and Data Safety Monitoring Board.

Patient Selection: Eligible patients were adults aged 18 to 80 years, who were referred for the creation of a new BCF or forearm AVF with vessel diameters meeting criteria outlined below. Baseline vessel diameters were measured according to the study site's standard of care, with (56%) or without (44%) the use of tourniquet distention.

Key inclusion criteria included the following:

- Main study cohort: Patients referred for creation of a new BCF who are not indicated for a more distal fistula per treatment guidelines
- Supplementary study cohort: Patients referred for creation of a new forearm AVF
- Age 18-80 years
- Patients willing and able to attend follow up visits over a period of 24 months

Key exclusion criteria included the following:

- Main study cohort: Target artery <2.5mm or >6mm in inner diameter or target vein <2.5mm in inner diameter by preoperative ultrasound
- Supplementary study cohort: Target artery <2mm or >4.1mm in inner diameter or target vein <2mm in inner diameter by preoperative ultrasound
- Patients with the planned index procedure being a revision surgery of an existing fistula
- Significantly stenotic target vein on the side of surgery (≥50%) as diagnosed on preoperative ultrasound
- Unusual anatomy or vessel dimensions (observed on pre-operative ultrasound or intraoperatively) and which preclude adequate fit of the VasQ
- Patients with central venous stenosis or obstruction on the side of surgery
- Known ipsilateral central venous occlusion
- Depth of vein greater than 8 mm (on ultrasound) on side of surgery
- Prior steal on the side of surgery
- Advanced heart failure (New York Heart Association (NYHA) class 3 or 4)

Primary Effectiveness Endpoint: Primary patency at 6 months post AVF creation. Fistulas are defined as patent if they are free from any intervention (endovascular or surgical) to maintain or restore blood flow. Confirmation of fistula patency is established by meeting one of the following conditions:

1. Artery or vein flow ≥ 500 ml/min determined by Doppler ultrasound
2. Clinical assessment of palpable thrill and audible bruit
3. Patient is receiving dialysis through the fistula

Safety Endpoints: Occurrence of the following non-thrombotic safety events at up to 6 months post AVF creation: steal, infection, aneurysm, and seroma.

Key Secondary Endpoints:

- Assisted primary patency
- Secondary patency
- Time to first successful cannulation
- Time to fistula maturation (physiological)
- Unassisted maturation at 3 months defined as vein diameter ≥ 5mm and blood outflow ≥ 500 ± 50 mL/min by Doppler ultrasound
- Time to first intervention
- Number and rate of interventions (including type and outcome)

Disposition of Subjects

A total of 144 subjects had the VasQ implanted, 129 in the main cohort and 15 in the supplementary cohort. A total of 134 subjects were assessed for the primary endpoint of primary patency at 6 months. The 10 subjects who did not reach the 6 month assessment either died (5), had missing data (2), withdrew consent (1), had the patent fistula abandoned due to vein tortuosity (1), or were excluded from analysis due to major protocol deviation (1).

Demographics

Information on patient characteristics and comorbidities is provided in Table 4. The median age of the pivotal study subjects is younger than the population of newly diagnosed end stage renal disease (ESRD) patients in the US, where according to recent US Renal Data Service data, there is significantly higher incidence of ESRD in patients over the age of 65.[1]

Table 4: Pivotal Study Subject Characteristics and Comorbidities

| Characteristics | | | Comorbidities | |
|---|---|---|---|---|
| Male | | **61% (88/144)** | Diabetic | **69% (100/144)** |
| Hispanic/Latino | | **14% (20/144)** | Hypertension | **94% (136/144)** |
| Black | | **35% (51/144)** | NYHA I or II | **21% (31/144)** |
| White | | **53% (77/144)** | PVD | **6% (8/143)** |
| Other | | **12% (16/144)** | Prior Access | **70% (101/144)** |
| Median-Age | | **60 [22-80]** | Known Malignancy | **15% (21/144)** |
| Median-BMI | | **30.4 [18.1-62.5]** | Current smoker | **15% (21/144)** |
| Active Dialysis | | **66% (95/144)** | Ex-smoker | **35% (51/144)** |
| Artery Diameter (mm) | - Median [min-max] | **4.25 [2.00-6.60]** | | |
| | - Mean [SD] | **4.30 [1.01]** | | |
| Vein Diameter (mm) | - Median [min-max] | **3.95 [2.30-7.80]** | | |
| | - Mean [SD] | **4.13 (1.09)** | | |

PVD = Peripheral Vascular Disease; NYHA = New York Heart Association

Results

Key safety and effectiveness results from the patients in the study are provided below. The primary analysis set was for the main study cohort, which only included BCF patients. The secondary analysis set was for the total study population of the main study cohort and the supplementary study cohort, including patients with BCFs and forearm AVFs.

Primary Effectiveness Endpoint: For the main study cohort, 79 out of 120 evaluable subjects (65.8%) had primary patency at 6 months. For the total study cohort, 88 out of 134 evaluable subjects (65.7%) had primary patency at 6 months. Patency rate and confidence limits (CL) are provided in Table 5. CLs were calculated using Clopper Pearson method. The frequency of interventions required to maintain patency within the first 6 months was 0.97 per patient-year.

Table 5: Primary Patency at 6 Months

| Analysis Set | N | Primary Patency Rate, n (%) | Lower 95% CL | Upper 95% CL |
|---|---|---|---|---|
| Primary Analysis Set | 120 | 79 (65.8) | 56.6 | 74.2 |
| Secondary Analysis Set | 134 | 88 (65.7) | 57.0 | 73.7 |

The primary effectiveness endpoint analysis by VasQ model size with mean and median vessel sizes is provided in Table 6. The study was not designed for subgroup analyses per model size. The majority of the data is obtained from VasQ Models 4-6, which had larger mean and median vessel sizes. Models 5 and 6 are intended for use in vessels larger than 4.8mm (see Table 1 on VasQ model sizes). The primary patency at 6 months was numerically greater for the study subjects that received the larger VasQ model sizes, which generally correlated to subjects with larger vessels having better primary patency.

Table 6: Primary Patency at 6 Months by VasQ Model

| VasQ Model | Artery Diameter (Mean, Median) | Vein Diameter (Mean, Median) | Primary Patency at 6 Months |
|---|---|---|---|
| **1 (n=1)** | (2.7, 2.7) | (3, 3) | 100.00% |
| **2 (n=0)** | NA | NA | NA |
| **3 (n = 6)** | (2.48, 2.3) | (3.17, 3.2) | 50.00% |
| **4 (n = 43)** | (3.84, 3.6) | (3.77, 3.7) | 51.20% |
| **5 (n = 52)** | (4.43, 4.2) | (4.2, 4) | 69.20% |
| **6 (n = 32)** | (5.08, 5.05) | (4.64, 4.35) | 81.20% |
| **Total (n=134)** | (4.3, 4.3) | (4.11, 3.9) | 65.70% |

Safety Endpoints: The rates of safety events up to 6 months are shown in Table 7. Device fractures were observed in 10 devices. Adjacent to one device fracture, there was an observation of juxta-anastomotic stenosis. No clinical sequelae were attributed to an observed fracture. Complete or partial separation of braid from brace was observed in 5/51 devices from an earlier VasQ model: 3/5 were detected during device implantation and 2/5 were observed on study mandated X-ray imaging. No clinical sequelae were attributed to these separations. During the study, a manufacturing change was implemented in the braid to brace welding, which eliminated any further occurrences of these separations in 93 devices implanted after the change.

Table 7: VasQ AVF Safety

| Endpoint | Surgical Site Infection | Seroma | Steal | (Pseudo)aneurysm |
|---|---|---|---|---|
| Upper Arm & forearm | **0.7% [0.0% - 3.8%]** | **0.0% [0.0% - 2.5%]** | **2.1% [0.4% – 6.0%]** | **0.0% [0.0% - 2.5%]** |

[95%-Confidence Interval]; Steal was counted if intervention was required

Secondary Endpoints: Assisted primary patency (freedom from any intervention to restore blood flow for a thrombosed access) and secondary patency (freedom from AVF access abandonment) at 6-, 12- and 24-month follow-up are shown in Table 8.

Table 8: Assisted Primary Patency and Secondary Patency

| Endpoint | 6-month | 12-month | 24-month |
|---|---|---|---|
| Assisted Primary | **85.1% [77.9%-90.1%]** | **78.5% [70.4%-84.7%]** | **70.5% [61.3%-77.9%]** |
| Secondary | **88.8 [82.1%-93.1%]** | **84.7% [77.3%-89.9%]** | **76.6% [67.8%-83.3%]** |

[95%-Confidence Interval]

Results for endpoints associated with AVF functionality over the study duration are provided in Table 9. Maturation is defined as an AVF with a vein diameter ≥5mm and

flow volume ≥500 ± 50 mL/min. First (1st) successful cannulation is defined as the first dialysis via the AVF with 2-needle cannulation for patients on dialysis at study enrollment. Continuous AVF use is defined as the AVF being used for dialysis for ≥30 days in patients on dialysis at each time point. One hundred percent (100%) functional dependency is defined as AVF used with central venous catheter removed for patients on dialysis at study enrollment. Continuous AVF use was not calculated (NC) for the 12 month and 24 month time points.

Table 9: AVF Functionality

| Endpoint (n) | 3-month | 6-month | 12-month | 24-month |
|---|---|---|---|---|
| Maturation (144) | **82.1% [75.2%-88.0%]** | **89.3% [83.3%-93.9%]** | **92.4% [86.7%-96.3%]** | **93.5% [87.9%-97.1%]** |
| 1st Successful Cannulation (95) | **62.8% [52.7%-72.9%]** | **82.9% [74.0%-90.2%]** | **88.3% [80.2%-94.2%]** | **88.3% [80.2%-94.2%]** |
| Continuous AVF Use (91) | **43.3% [32.5%-54.7%]** | **72.5% [62.2%-81.4%]** | **NC** | **NC** |
| 100% Functional Dependency (95) | **30.0% [21.6%-40.9%]** | **68.3% [58.2%-77.9%]** | **78.7% [69.2%-86.9%]** | **80.7% [71.1%-88.7%]** |

[95%-Confidence Interval]

Interventions: The mean time to first intervention in the study was 208 days. Since the beginning of the study, 228 interventions were reported in 88 subjects in the safety analysis set. Out of all subjects who had the device implanted, 39% of subjects did not have any intervention during the study, and 27% had one intervention; 13% of subjects had two interventions and 7% had three. A total of 20 subjects (14%) had more than three interventions during the study. The rate of interventions per patient year was 1.11 and 1.04 for the primary and secondary analysis sets, respectively.

The majority of interventions were for percutaneous transluminal angioplasty (PTA), with 128 PTA interventions conducted over the course of the study. Other common interventions included stenting, percutaneous or surgical thrombectomy, and surgical revisions.

The total post intervention success rate was 90.8% (207/228). The study fistula was abandoned immediately after intervention in 9.2% (21/228) of cases.

Comparators for the Pivotal Study Results

The pivotal study was conducted as a single-arm study without a control group. The sponsor compared the pivotal study results to a performance goal based on literature analysis, a Medicare beneficiary propensity matched cohort, and a retrospective chart review propensity matched cohort. The sponsor calculated a performance goal of 55% for the primary effectiveness endpoint of primary patency at 6 months based on 5 publications including data from 966 patients.[2-6] The publications were selected by the sponsor if they were determined to have 6 months post AVF placement primary patency data for a patient population similar to the one defined in the pivotal study protocol. FDA alignment on the performance goal was not obtained.

*Medicare beneficiary propensity matched comparator*

The sponsor conducted a retrospective study using historical Medicare beneficiary controls treated with standard of care AVFs using data from Centers for Medicare and Medicaid Services (CMS) from the 15 sites of the same performing surgeons that participated in the pivotal study. Patients were selected from a time period just before the pivotal study to avoid bias from selecting from a time window concurrent with the pivotal study, as patients during that time were likely screened and not enrolled into the study and thus would be clinically different from the pivotal study subjects. The covariates for propensity matching were age, race, gender, congestive heart failure, diabetes, hypertension, obesity, and dialysis status at the time of AVF creation as well as each surgeon participating in the pivotal study. CMS data does not include information about the anatomic location of the fistula or vessel size, so these two covariates could not be applied to matching patients.

A total of 782 Medicare beneficiaries were included in the study and outcomes were ascertained through 6 months post AVF creation. For the CMS cohort, primary patency at 6 months was 35.5%, continuous AVF use at 3 months was 43.4%, and continuous AVF use at 6 months was 56.3%. To calculate the primary patency rate at 35.5%, the sponsor original included CMS codes for "Revision, open, arteriovenous fistula" and "Dialysis circuit permanent vascular embolization or occlusion". Given that some but not all these procedures are considered primary patency-ending, a post-hoc worst-case sensitivity analysis removing these two codes from the primary patency ending events was conducted. This resulted in an increase in the weighted primary patency outcome among Medicare patients to 53.4%.

*Retrospective chart review propensity matched comparator*
The sponsor conducted a retrospective chart review of standard of care AVF creation over the 2 years prior to the pivotal study initiation at sites that enrolled ≥6 patients in the pivotal study. At the participating sites, all patients that underwent an AVF creation procedure by a surgeon participating in the pivotal study were consecutively evaluated for inclusion in the retrospective chart review study cohort. Patients were included in the study if they met the inclusion/exclusion criteria of the pivotal study and the data required to evaluate baseline parameters and primary patency outcomes were obtainable. The covariates for propensity matching were age, gender, race, BMI, diabetes, hypertension, previous ipsilateral AVF, dialysis status at the time of AVF creation, fistula location (brachiocephalic vs radiocephalic), artery diameter, and vein diameter.

The weighted propensity score model demonstrated the odds of a treatment effect of VasQ were 1.66 times the odds of those in the control group.

There was additional supplemental clinical data from experience outside US provided for the VasQ device, some of which included comparator information. A summary of this data is available in the VasQ Instructions for Use.

Pediatric Extrapolation
In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

**POSTMARKET SURVEILLANCE**

Postmarket evaluation will be required to collect data on the magnitude and duration of benefit of the VasQ device compared to standard of care. This will be a multi-center prospectively-enrolled controlled study with at least 150 subjects in each arm (AVF creation in patients treated with the VasQ and patients treated per the standard of care) that is designed to demonstrate a clinically meaningful benefit (i.e., superiority) and comparable safety of the VasQ to the standard of care.

This study is intended to address outstanding uncertainty with regard to certain aspects of the effectiveness of the device to provide a clinically meaningful benefit to patients. In particular, there is uncertainty regarding the magnitude of benefit of the device compared to outcomes for similar arteriovenous fistula (AVF) patients who do not receive the device. There is also uncertainty regarding the benefit of the VasQ device in patients with smaller vessel sizes, given that the VasQ pivotal study primarily enrolled patients with larger vessels. The following key questions will be addressed:

- What is the magnitude of benefit of the VasQ device with regard to time to achieving a clinically functional AVF as compared to a comparable contemporary standard of care cohort?
- What is the sustained benefit of the VasQ device, as assessed by primary, assisted primary, and secondary patency, unassisted clinically functional AVF, central venous catheter dwell time, and reinterventions, as compared to the standard of care, over a period of 12 months?
- What is the magnitude and sustained benefit of the VasQ device as a function of vessel sizes as assessed by time to achieving a clinically functional AVF, primary, assisted primary, and secondary patency, unassisted clinically functional AVF maturation success, central venous catheter dwell time, and reinterventions, as compared to standard of care, over a period of 12 months?
- What is the rate of access related complications (including major reintervention related and cannulation related complications) over a period of 12 months for subjects implanted with the VasQ device as compared to a comparable contemporary standard of care cohort?

**LABELING**

VasQ labeling consists of Instructions for Use, packaging labels, and a patient brochure. The Instructions for Use include the indications for use; a description of the device; contraindications, warnings, precautions; a detailed summary of the clinical data collected in support of the device; a list of potential adverse events; a shelf life (expiration date provided on packaging labels); the expertise needed for the safe use of the device; and instructions for the safe use of the device. The labeling satisfies the requirements of 21 CFR 801.109.

Please see the Limitations section above for important contraindications, warnings and precautions presented in the device labeling.

**RISKS TO HEALTH**

The table below identifies the risks to health that may be associated with use of an extravascular support for an arteriovenous fistula for vascular access and the measures necessary to mitigate these risks.

Table 10: Identified Risks to Health and Mitigation Measures

| Risks to Health | Mitigation Measures |
|---|---|
| Vascular or tissue injury or bleeding | Clinical performance testing<br>Animal performance testing<br>Non-clinical performance testing<br>Labeling |
| Adverse effect of hemodynamics of the AVF | Clinical performance testing<br>Animal performance testing |
| Failure to support a durable fistula that is usable for vascular access | Clinical performance testing<br>Animal performance testing |
| Use of the device adversely impacts future vascular access sites | Clinical performance testing<br>Labeling |
| Mechanical device failure/malfunction leading to injury or fistula failure | Clinical performance testing<br>Non-clinical performance testing<br>Labeling |
| Improper size selection | Labeling |
| Improper device placement | Labeling |
| Imaging incompatibility | Non-clinical performance testing<br>Labeling |
| Adverse tissue reaction | Biocompatibility evaluation |
| Infection | Sterilization validation<br>Shelf life testing<br>Labeling |

**SPECIAL CONTROLS**

In combination with the general controls of the FD&C Act, the extravascular support for an arteriovenous fistula for vascular access is subject to the following special controls:

(1) Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. Testing must evaluate:
   (i) The ability to safely implant the device;
   (ii) The ability of the arteriovenous fistula supported by the device to attain a blood flow rate and diameter suitable for hemodialysis;
   (iii) The ability of the fistula to be used for vascular access;
   (iv) The primary, assisted primary, and secondary patency of the fistula;
   (v) The rates and types of device integrity events and any associated clinical sequelae;
   (vi) The rates and types of all adverse events; and
   (vii) The rates and outcomes of reinterventions.

(2) If FDA determines that premarket clinical information is insufficient to evaluate long-term safety and effectiveness of the product, postmarket data must be collected through an adequately designed and powered postmarket study to assess the following:
   (i) The functionality and patency of the fistula through a clinically meaningful timeframe;
   (ii) The rates and types of access-related, reintervention-related, and cannulation-related adverse events; and
   (iii) The reasons for, rates, types, and outcomes of reinterventions.

(3) Animal performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be assessed:
   (i) Implantation of the device;
   (ii) Patency of the fistula; and
   (iii) Gross pathology and histopathology assessing vascular injury and downstream embolization.

(4) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
   (i) Resistance to kinking;
   (ii) Resistance to crush and local compression;
   (iii) Tensile strength of joints and components;
   (iv) Device integrity;
   (v) Corrosion resistance; and
   (vi) Characterization and verification of all dimensions.

(5) Non-clinical testing must evaluate the compatibility of the device in a magnetic resonance (MR) environment.

(6) All patient-contacting components of the device must be demonstrated to be biocompatible.

(7) Performance data must demonstrate sterility of the device components intended to be provided sterile.

(8) Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.

(9) Labeling for the device must include:
   (i) Specific instructions regarding device size selection and device placement;
   (ii) Expertise needed for safe use of the device;
   (iii) A detailed summary of the clinical testing conducted and the patient population studied, including information on effectiveness and device- and procedure-related complications;
   (iv) A detailed summary of the device technical parameters;
   (v) A shelf life and storage conditions; and
   (vi) MR information.

**BENEFIT-RISK DETERMINATION**

The probable benefits of the VasQ device are based on data collected in the clinical study described above, as well as nonclinical laboratory and animal study data. In the pivotal study, the primary patency rate was 65.7% at 6 months. The assisted primary patency rate was 85.1% at 6 months and 78.5% at 12 months. The secondary patency rate was 88.8% at 6 months and

84.7% at 12 months. The 3 month fistula maturation success rate, defined as the rate of access sites with a vein diameter ≥5mm and blood outflow ≥500 ml/min, was 82.1%. Among the 95 patients on dialysis at 6 months, 72.5% of subjects had continuous AVF use, defined as the AVF used for dialysis for ≥30 days. It should be noted that in the main clinical study cohort mean artery diameter was 4.49mm and the mean vein diameter was 4.23mm. Outcomes in terms of both patency and functionality have been shown to be better with larger vessel sizes treated with VasQ, as was seen in the pivotal study (Table 6).

The probable risks of the device are based on data collected in the clinical study described above, as well as nonclinical laboratory and animal study data. The clinical study did not result in any serious adverse events that were attributed to VasQ. Six months after AVF creation, 3/144 subjects (2.1%) experienced steal, 1/144 subjects (0.7%) experienced surgical site infection, and no subjects experienced seromas, aneurysms, or pseudoaneurysms. Fractures were observed in 10 devices out of 144 during study x-ray imaging and complete or partial separation of braid from brace was observed in 5 devices out of 51 with previous manufacturing methods. No clinical sequelae were attributed to an observed fracture or to a braid-brace separation.

Based on the data provided, it has been determined that sufficient information has been provided to demonstrate that the probable benefits outweigh the probable risks for VasQ. Outstanding uncertainty remains with regard to the magnitude and duration of benefit of the device compared to standard of care (i.e., similar AVF patients who do not receive the device). In particular, there is uncertainty regarding the benefit of the device in patients with forearm fistula and smaller vessel sizes, given that the VasQ pivotal study primarily enrolled patients with BCF and larger vessels. Given the remaining uncertainty, additional data postmarket data collection will be required.

Patient Perspectives

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

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

> VasQ is intended for use as an external support for upper extremity arteriovenous fistulas created for vascular access by means of vascular surgery.

The probable benefits outweigh the probable risks for VasQ. The device provides benefits, and the risks can be mitigated by a robust postmarket surveillance study and the use of general controls and the identified special controls.

## CONCLUSION

The De Novo request for VasQ is granted and the device is classified as follows:

> Product Code: QVQ
> Device Type: Extravascular support for an arteriovenous fistula for vascular access
> Regulation Number: 21 CFR 870.4600
> Class: II

References

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4. Field et al. Primary patency rates of AV fistulae and the effect of patient variables. J Vasc Access 2008; 9: 45-50
5. Schinstock et al. Outcomes of Arteriovenous Fistula Creation after the Fistula First Initiative. Clin J Am Soc Nephrol 6: 1996–2002, 2011
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