February 7, 2025

Medical Microinstruments, Inc.
Zainab Amini
Sr. Regulatory Affairs Specialist
Via Egidio Giannessi 54
Pisa, Italy 56121
Italy

Re: K242368
Trade/Device Name: Symani Surgical System
Regulation Number: 21 CFR 878.4963
Regulation Name: Electromechanical System For Open Microsurgery
Regulatory Class: Class II
Product Code: SAQ,
Dated: January 8, 2025
Received: January 8, 2025

Dear Zainab Amini:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898, and the April 5, 2024 De Novo classification order for this

type of device. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Per the April 5, 2024 De Novo classification order for this device type, you must demonstrate that the device performs as intended under anticipated conditions of use in the intended patient population and anatomical location. The special control requirements set forth in that order include initiation, enrollment, completion, and reporting requirements associated with any required postmarket surveillance. Within 30 days of receipt of this letter, you must submit a complete study protocol for a postmarket surveillance study consistent with the special control requirements. FDA expects to work with you to approve your study protocols within 60 days of this letter. Your submission should be clearly labeled as "Postmarket Study Protocol" and submitted to the Agency as specified below. Please reference the 510(k) number above to facilitate processing. If there are multiple protocols being finalized after clearance of this 510(k) submission, please submit each protocol as a separate submission, identified by their unique study name(s).

From the date of study protocol approval, you must meet the following timelines:

- First subject enrolled within 12 months
- 20% of subjects enrolled within 24 months
- 50% of subjects enrolled within 36 months
- 100% of subjects enrolled within 48 months

In addition, you must submit separate periodic reports on the progress of the study as follows:

- Postmarket surveillance progress reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the protocol approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting enrollment status reports every three (3) months in addition to your annual postmarket study progress reports, until enrollment has been completed, or FDA notifies you otherwise.
- Submit the final postmarket study report three (3) months from study completion (i.e., last subject's last follow-up date).

Each postmarket surveillance report should be submitted to the Agency as specified below, identified as a "Postmarket Surveillance Report" in accordance with how the study is identified above, and bearing the applicable 510(k) reference number.

Be advised that failure to comply with any special control requirement, including the initiation, enrollment, completion, and reporting per the postmarket surveillance data requirements outlined above, may result in the adulteration and misbranding of your device.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming

product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above 510(k) number to facilitate processing.

Postmarket Mandated Studies Program
U.S. Food and Drug Administration
Center for Devices and Radiological Health

Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Alternatively, documents can be submitted electronically through the CDRH Portal. For more information on the CDRH Portal, please visit https://www.fda.gov/medical-devices/industry-medical-devices/send-and-track-medical-device-premarket-submissions-online-cdrh-portal.

Sincerely,

Mark Trumbore -S

Digitally signed by Mark Trumbore -S
Date: 2025.02.07 14:17:23 -05'00'

Mark Trumbore, Ph.D.
Assistant Director
DHT4A: Division of General Surgery Devices
OHT4: Office of Surgical and Infection Control Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K242368

Device Name
Symani Surgical System

Indications for Use *(Describe)*
The Symani® Surgical System is intended for soft tissue manipulation to perform anastomosis, suturing, and ligation microsurgery techniques on small blood vessels and lymphatic ducts between 0.1 and 2.5 mm in open free-flap surgery of the breast, mouth, scalp, extremities, and in open lymphatic surgery of the extremities.
The Symani® Surgical System is indicated for use during microsurgical procedures when use of a motion scaling function is deemed appropriate by the surgeon. The System is indicated for use in adults. It is intended to be used by trained physicians in an appropriate operating environment in accordance with the Instructions for Use.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary

I. SUBMITTER INFORMATION

Submitter: MEDICAL MICROINSTRUMENTS, INC.
Via Egidio Giannessi 54
Pisa, IT 56121

Contact: Zainab Amini
(904) 896-6812
Zainab.amini@mmimicro.com

Date: 4 February 2025

II. SUBJECT DEVICE INFORMATION

Device Trade Name: Symani® Surgical System
Classification Name: Electromechanical System For Open Microsurgery (21CFR §878.4963)
Regulatory Class: II
Product Code: SAQ
Submission Type: Traditional 510(k)

III. PREDICATE DEVICE INFORMATION:

Predicate Device: Symani Surgical System, DEN230032

IV. DEVICE DESCRIPTION:

This 510(k) is for a labeling modification only, the addition of the mouth and scalp to the indication for use among the existing open free-flap surgery. The technological characteristics remain identical as the predicate device, Symani Surgical System in DEN230023.

Symani is designed to provide surgeons with increased precision while leveraging the surgeon's own surgical experiences. The Symani Surgical System consists of three components, the CMM, Console, and Instruments, with selectable scaling factors (between 7x to 20x) to improve motion control and scale down any physiological tremor of the operator in a similar fashion to conventional robotic-assisted surgical device (RASD) systems, and the instruments with wristed end-effectors to improve dexterity for tissue manipulation and suturing.

V. INDICATIONS FOR USE

The Symani® Surgical System is intended for soft tissue manipulation to perform anastomosis, suturing, and ligation microsurgery techniques on small blood vessels and lymphatic ducts between 0.1 and 2.5 mm in open free-flap surgery of the breast, mouth, scalp, extremities, and in open lymphatic surgery of the extremities. The Symani® Surgical System is indicated for use during microsurgical procedures when use of a motion scaling function is deemed appropriate by the surgeon. The System is indicated for use in adults. It is intended to be used by trained physicians in an appropriate operating environment in accordance with the Instructions for Use.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The technological characteristics of the subject and predicate devices remain the same in this submission.

VII. PERFORMANCE DATA

The data used for this 510(k) comes from a prospective, non-randomized, single-arm, multicenter, post-market clinical follow-up (PMCF) study designed to evaluate the safety and effectiveness of the Symani System when used to assist microsurgical anastomoses in the real-world setting.

For this 510(k), a subset of patients has been analyzed, specifically the free tissue transfer procedures performed using Symani with mouth or scalp as the recipient sites. The endpoints considered and analysis performed follow a robust Statistical Analysis Plan from the predicate device.

Sixty-two patients were identified, of which 55 are prospective enrollments and 7 are retrospective enrollments.

Clinical Study Demographics

Table 1. Free-Flap Clinical Study Demographics in the Mouth and Scalp.

Characteristic	Statistics	Mouth	Scalp
Demographics			
Age (years)	Mean (SD); N	62.1 (12.03); 40	63.5 (12.77); 20
Gender	-	-	-
Male	n (%); N	25 (62.5%); 40	14 (70.0%); 20
Female	n (%); N	15 (37.5%); 40	6 (30.0%); 20
Race	-	-	-
Caucasian	n (%); N	40 (100.0%); 40	20 (100.0%); 20
Black	n (%); N	0 (0.0%); 40	0 (0.0%); 20
Asian	n (%); N	0 (0.0%); 40	0 (0.0%); 20
Other	n (%); N	0 (0.0%); 40	0 (0.0%); 20
Height (cm)	Mean (SD); N	173.1 (9.92); 39	173.2 (10.34); 20
Weight (kg)	Mean (SD); N	75.4 (16.05); 39	71.0 (17.33); 20
BMI	Mean (SD); N	25.22 (5.292); 39	23.34 (4.001); 20
Pre-operative co-existing conditions/disease			
Pre-operative radiotherapy	n (%); N	8 (20.0%); 40	3 (15.0%); 20
Pre-operative chemotherapy	n (%); N	5 (12.8%); 39	4 (20.0%); 20
Smoking now/past	n (%); N	18 (45.0%); 40	11 (55.0%); 20
Hypertension	n (%); N	14 (35.0%); 40	11 (55.0%); 20
Pulmonary disease	n (%); N	7 (17.5%); 40	5 (25.0%); 20
Diabetes	n (%); N	4 (10.0%); 40	1 (5.0%); 20
Ischaemic heart disease	n (%); N	4 (10.0%); 40	1 (5.0%); 20
Alcohol consumption over limits	n (%); N	10 (25.0%); 40	5 (25.0%); 20
Steroids	n (%); N	1 (2.5%); 40	0 (0.0%); 20
Extra-cardiac arteriopathy	n (%); N	4 (10.0%); 40	2 (10.0%); 20
BMI	-	-	-
<20	n (%); N	5 (12.8%); 39	5 (25.0%); 20
20-<25	n (%); N	19 (48.7%); 39	9 (45.0%); 20
25 to <30	n (%); N	9 (23.1%); 39	5 (25.0%); 20
30 to <35	n (%); N	4 (10.3%); 39	1 (5.0%); 20
≥ 35	n (%); N	2 (5.1%); 39	0 (0.0%); 20

American Society of Anesthesiologist Score (ASA)	-	-	-
1	n (%); N	18 (45.0%); 40	7 (35.0%); 20
2	n (%); N	13 (32.5%); 40	10 (50.0%); 20
3	n (%); N	9 (22.5%); 40	3 (15.0%); 20
4	n (%); N	0 (0.0%); 40	0 (0.0%); 20

Analysis results – Effectiveness Endpoints:

Intraoperative patency at first attempt

The subset of data used for this effectiveness endpoint were anastomoses that were marked as first attempt using the robotic approach. The patency of all anastomoses (100%) was confirmed prior to closure. Results reported by site for intraoperative patency at first attempt are as follows:

Table 2. Intra-operative Anastomosis Patency at First Attempt

Site	Number of anastomoses	Number patent	Patency estimate	95% CI
Mouth	66	60	90.9%	[81.3%, 96.6%]
Scalp	26	18	69.2%	[48.2%, 85.7%]

Operative time and suturing time

The average procedure time and average suturing time for robotic, manual, and hybrid anastomoses were analyzed and are summarized as follows:

Table 3. Operative Time and Suturing Time

Site	Average Operative time (hours)	Average suturing time (minutes)		
		Robotic	Manual	Hybrid
Mouth	11.66	37.4	27.0	48.7
Scalp	12.30	41.2	26.0	38.5

Rate of intra-operative change from robotic to manual suturing:

The subset of data used for this effectiveness endpoint were anastomoses that used the robotic approach. There were five changes in the intraoperative suturing approach with the estimated change rate being 5.1% (5/98). Results reported by site for rate of intra-operative approach change from robotic to manual suturing are as follows:

Table 4. Rate of intra-operative change

Site	Intraoperative changes	Intraoperative Change Rate	95% Confidence Interval
Mouth	3/72	4.2%	[0.9%, 11.7%]
Scalp	2/26	7.7%	[0.9%, 25.1%]

Analysis results – Safety Endpoints:

The safety endpoint in the study was freedom from Serious Adverse Device Effects (SADE), which was 100.0%. The freedom from SADE rate is the complement of the estimated SADE rate. The Serious Adverse Device Effect Rate is presented in Table 5 below.

Table 5. Serious Adverse Device Effect Rate

Site	SADE/Total patients	SADE Rate	95% Confidence Interval
Mouth	0/41	0.0%	[0.0%, 8.6%]
Scalp	0/20	0.0%	[0.0%, 16.8%]

Adverse events

There were a total of 27 adverse events (from 25 patients). The incidents of AE was 41.0%(25/61 patients). A literature search showed a high variability in AE reporting, leading to the conclusion that for head & neck recipient sites, the AE rate ranges between 21.5% and 61.3% (KM Estimate 54.2 % [95% CI: 38.6%, 69.1%]). The incidence of AE from the head & neck procedures of the subject device study at the time of this interim analysis is consistent with the range identified in the literature search.

There was a total of 5 (5/41; 12.2%) and 2 (2/20; 10%) serious adverse events for the mouth and scalp, respectively. This was lower than the predicate device. The rate of adverse events resulting in anastomosis revision of the mouth was 5% (2/40). The were no adverse events resulting in anastomosis revision for the scalp.

3-Day Reoperation Rate

The 3-day anastomosis specific reoperation rate is a clinical risk to the anastomosis in free flap surgery (Table 6). This is the timeframe the anastomosis typically fails and needs a revision. In the mouth cohort, there were two reoperations (2/40; 5.00%) done within 3 days to revise the anastomosis.

Table 6. 3-day Reoperation Rate

Site	Count/Total	Percentage	95% CI
Mouth	2/40	5.00%	[0.61% - 16.92%]
Scalp	0/20	0.00%	[0.00% - 16.84%]

VIII. Postmarket Surveillance

In summary, the premarket data demonstrates several probable benefits and risks when used in the creation of vascular anastomoses. The risks of the Symani Surgical System and clinical study limitations are mitigated by the special controls and labeling. Outstanding uncertainty regarding the generalizability of effectiveness of device use in the target U.S. patient population will be addressed by postmarket data collection associated with special controls requirements. Medical Microinstruments, Inc. will meet defined enrollment milestones following device clearance and will submit periodic postmarket surveillance progress reports until enrollment is complete, followed by annual updates.

IX. CONCLUSION

Based on the information provided within this submission, and comparison of the subject vs. predicate device, the subject device Symani Surgical System has the same intended use and technological characteristics as the predicate device.

The clinical evidence provided relating to free flap procedures in the mouth and scalp anatomical regions demonstrated that use of the Symani Surgical System in these indications is as safe and effective as the predicate device. For the mouth, the patency at first attempt rate and 3-day reoperation rate are similar to the predicate device. The patency at first attempt rate for the scalp was lower than the predicate device. This may be a result of unique challenges in the anatomy. If the first attempt at creating an anastomosis is not be successful, the anastomosis may be redone intraoperatively. The patency of all anastomoses (100%) was confirmed prior to closure. There were no device related adverse events resulting in anastomosis revision.

Therefore, the subject device is deemed to be substantially equivalent to the legally commercialized predicate device.