SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Neurovascular Liquid Embolic Agent

Device Trade Name: SQUID Liquid Embolic Agent (LEA)

Device Procode: SGU

Applicant's Name and Address: Balt USA, LLC
29 Parker
Irvine, California 92618

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P250009

Date of FDA Notice of Approval: January 30, 2026

II. INDICATIONS FOR USE

The SQUID Liquid Embolic Agent (LEA) is indicated for the embolization of the middle meningeal artery (MMA) as an adjunct to usual care treatment in patients with symptomatic chronic subdural hematoma(s) (SDH) measuring 10 mm or greater in thickness in whom an intervention is deemed necessary as determined by a neurosurgeon.

III. CONTRAINDICATIONS

The use of the SQUID LEA is contraindicated under the following circumstances:

- When optimal catheter placement is not possible
- When vasospasm stops blood flow

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the SQUID LEA labeling.

V. DEVICE DESCRIPTION

The SQUID LEA is a non-adhesive, liquid embolic agent consisting of an ethylene vinyl alcohol (EVOH) copolymer dissolved in dimethyl sulfoxide (DMSO) and suspended micronized tantalum powder to provide contrast for visualization under fluoroscopy.

The SQUID LEA consists of the following components:

- 1 vial of SQUID
- 1 vial of DMSO

- SQUID delivery syringe(s)
- 1 DMSO delivery syringe
- Syringe adapter(s)
- Stickers to identify the vials of SQUID

Figure 1: SQUID LEA

A DMSO-compatible delivery micro-catheter is used to access the embolization site and deliver SQUID LEA; a delivery micro-catheter is not included with SQUID LEA. The syringe adapter is an interface between the SQUID delivery syringe and the delivery catheter.

SQUID LEA is available in six product formulations corresponding to different viscosities with SQUID 12 having the lowest viscosity. Low density (LD) versions include a smaller amount of tantalum powder, which decreases opacity under fluoroscopy.

- SQUID12/12LD (4% EVOH),
- SQUID18/18LD (5.3% EVOH),
- SQUID34/34LD (7% EVOH)

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of chronic subdural hematoma including non-surgical and surgical approaches. Non-surgical approaches include medication to limit or eliminate further bleeding by modifying blood coagulation and clotting and to withhold blood thinning medications. Alternatively, surgical approaches may include procedures to remove/drain blood from areas within the hematoma and to repair or remove abnormal areas of the neurovasculature that are causing the hematoma and may be conducted during a craniotomy, burr hole surgery, or twist drill craniotomy. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The SQUID LEA is marketed for middle meningeal artery embolization (MMAE) in the following regions: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Monaco, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Australia, Brazil, Canada, Albania, Algeria, Argentina, Armenia, Chile, Colombia, Costa Rica, Ecuador, Egypt, El Salvador, Guatemala, Georgia, Honduras, Hong-Kong, Iceland, India, Indonesia, Israel, Jordan, Kazakhstan, Kyrgyzstan, Kurdistan (Iraq), Kuwait, Macedonia, Malaysia, Mexico, Moldavia, Mongolia, Morocco, Nepal, New Zealand, Panama, Paraguay, Peru, Russia, Saudi Arabia, Serbia, South Africa, Switzerland, Taiwan, Thailand, Turkey, United Kingdom, United Arab Emirates, and Uruguay.

The SQUID LEA has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

- Access site complications such as radial artery spasm, radial artery perforation, infection, necrosis, pain and tenderness, compartment syndrome, limb amputation, radial artery occlusion, hematoma or hemorrhage, sterile inflammation, granulomas, hand dysfunction, and pathological hand cold intolerance
- Allergic reaction
- Artery occlusion / stenosis
- Cardiac disorder (such as arrythmia, myocardial infarction)
- Catheter entrapment
- Cerebral infarction
- Death
- Fluoroscopy-related risks to physicians and patients associated with x-ray exposure may include, but are not limited to, alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, delayed neoplasia
- Headache
- Hemorrhage / rupture
- Hydrocephalus
- Infection
- Inflammatory response
- Neurological deficit
- Non-target embolization (passage of embolic material into unintended vessels adjacent to the target) which may cause but is not limited to: blindness, dysesthesias of the face (increased or decreased sensitivity), facial weakness, or deafness
- Organ Disorders
- Puncture Site Injury

- Renal Failure
- Respiratory Failure
- Seizure
- Thromboembolic Events and Ischemic Events (transient ischemic attack (TIA)/stroke)
- Vascular complications including but not limited to dissection, perforation, rupture, occlusion, vasospasm, hypotension
- Vasospasm

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

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Laboratory Studies

Performance Testing

The sponsor conducted performance testing to verify that the SQUID LEA functions as intended, and all system level design and functional specifications are met. **Table 1** summarizes performance testing which demonstrates the SQUID LEA functions as intended.

Table 1: Summary of SQUID LEA Performance Testing

Test	Objective	Acceptance Criteria	Results
Viscosity	Evaluate the viscosity of the SQUID LEA using Cone-Plate method.	SQUID viscosities shall be: SQUID12KIT = 12±5 cP SQUID12LDKIT = 12±5 cP SQUID18KIT = 18±5 cP SQUID18LDKIT = 18±5 cP SQUID34KIT = 34±5 cP SQUID34LDKIT = 34±5 cP	Pass
Solidification	Evaluate the solidification time of SQUID LEA in Phosphate Buffered Saline (PBS).	Device solidification time shall be ≤ 3 min.	Pass
Material Expansion (Dimensional and Tensile)	Measure the peak tensile force and perform dimensional testing of the SQUID LEA.	Dimensions and tensile properties of rod-shaped device precipitates shall not change substantially and shall show statistical equivalence across 1, 3, and 7 days of solidification.	Pass
Infusion Pressure	Characterize the injection pressure of SQUID LEA and verify if this injection pressure is within the typical burst pressure limits of recommended DMSO-compatible microcatheters.	Infusion pressure of the device shall be within the typical burst pressure limits of DMSO-compatible microcatheters at the recommended flow rate.	Pass

Test	Objective	Acceptance Criteria	Results
Material Adhesion	Verify that the force to remove an entrapped catheter from the SQUID cast is less than the tensile strength of the catheter.	Extraction force of commercially available DMSO compatible microcatheters shall be less than the tensile strength of a commercially available DMSO-compatible catheter.	Pass
Particulate Matter	Evaluated embolic for particulate matter generation.	Device shall release no more than clinically acceptable number of particulates of sizes ≥10 µm and ≥25 µm as compared to historically meaningful limit.	Pass
Radiopacity	Verify radiopacity of the SQUID LEA as per standard ASTM F640-20.	The measured mean pixel intensities of within the liquid filled area of the device provides adequate radiopacity relative to background that allow for acceptable visibility with in vivo procedural use as evaluated by animal studies.	Pass
Tantalum Powder Suspension	Verify the homogeneity of tantalum suspension in SQUID LEA.	The difference in the mean pixel intensities of the top half and bottom half of the vial as characterized provides acceptable homogeneity as confirmed by usability in animal studies when prepared per the Instructions for Use.	Pass
Magnetic Resonance Imaging (MRI) Safety Testing	Evaluate the MRI safety of SQUID LEA in accordance with the applicable requirements of ASTM F2052, ASTM F2113, ASTM F2119, and ASTM F2503.	There is no greater magnetically-induced torque or displacement force than those induced by gravity. MR image artifact is not considered a harmful interaction or performance issue (characterization only). Conductivity for RF heating evaluation is characterized.	Pass
Adjunctive Device Compatibility (Coils and Glues)	Assess SQUID LEA compatibility with adjunctive embolization devices.	The physical, chemical stability, and performance impacts of the precipitated test devices following incubation in a DMSO solvent are characterized.	Pass, compatible
Effects of Radiation and Stability of SQUID Precipitates	Evaluate the stability of SQUID LEA material after the exposure of radiation	The behavior of the precipitated SQUID LEA when exposed to a conservative lifetime radiation dose is characterized.	Pass, comparable to comparator device

Biocompatibility Studies

The sponsor conducted biocompatibility studies on the SQUID LEA, syringe, and adapter in accordance with ISO 10993-1, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing." Summaries of the results of this testing are provided in **Table 2** and **Table 3**.

Table 2: Summary of Biocompatibility Testing of the SQUID LEA

Test	Test Description	Results
Cytotoxicity	Evaluate the potential for substances that may leach or be extracted from the test article to cause cytotoxicity per ISO 10993-5.	Non-cytotoxic
Sensitization	Evaluate the potential for substances that may leach or be extracted from the test article to cause skin	Non-sensitizing

Test	Test Description	Results
	sensitization per ISO 10993-10.	
Irritation or Intracutaneous reactivity	Evaluate the potential for substances that may leach or be extracted from the test article to cause local irritation in the dermal tissues of rabbits per ISO 10993-10.	Non-irritating
Acute systemic toxicity	Evaluate the potential acute systemic toxicity of a test article by chemical characterization (CC) and toxicological risk assessment (TRA).	Compounds detected and identified in extracts of the test articles were present at levels that would not be expected to pose any significant risk of adverse systemic toxicological effects
Acute systemic toxicity: Intramuscular implantation (4-week Rabbit)	Evaluate the potential acute systemic toxicity and provide general information on the health hazards likely to arise from continuous exposure to the device under investigation for systemic toxicity per ISO 10993-6.	Non-toxic
Material-mediated pyrogenicity	Evaluate the potential for saline extracts of the test article to cause a febrile response in rabbits per USP <151>.	Non-pyrogenic
Subchronic toxicity	Evaluate the potential subchronic toxicity of a test article by CC and TRA.	Compounds detected and identified in extracts of the test articles were present at levels that would not be expected to pose any significant risk of adverse subchronic toxicological effects
Subchronic toxicity: Intramuscular implantation (4-week Rabbit)	Evaluate the potential subchronic toxicity of a test article and provide general information on the health hazards likely to arise from continuous exposure to the device under investigation for local tissue response to implantation sites per ISO 10993-6.	Non-toxic, non-irritant
Subchronic toxicity - Safety assessment of the SQUID LEA in Chronic Swine Rete Mirabile Model	Evaluate the potential subchronic toxicity of a test article and provide general information on the health hazards likely to arise from continuous exposure to the device under investigation for local tissue response to implantation sites per ISO 10993-6.	Non-toxic, non-irritant
Genotoxicity	Evaluate the genotoxicity potential of substances that may leach or be extracted from the test article by CC and TRA.	Compounds detected and identified in extracts of the test articles were present at levels that would not be expected to pose any significant risk of adverse genotoxic effects
Implantation: Intramuscular Implantation with Histopathology (4-week Rabbit)	Evaluate the potential for intramuscular response at implantation sites and provide general information on the health hazards likely to arise from continuous exposure to the device over 4 weeks with histopathological assessment per ISO 10993-6.	Non-toxic, non-irritant
Implantation: Intramuscular Implantation with Histopathology (4-week Swine Rete)	Evaluate the potential for intramuscular response at implantation sites and provide general information on the health hazards likely to arise from continuous exposure to the device over 4 weeks with histopathological assessment per ISO 10993-6.	Non-toxic, non-irritant
Hemocompatibility - Hemolysis (Extract Method)	Evaluate the potential for the test article to cause hemolysis and demonstrate compatibility with indirect contact with circulating blood per ISO	Non-hemolytic

Test	Test Description	Results
	10993-4.	
Hemocompatibility - Hemolysis (Direct Contact Method)	Evaluate the potential for the test article to cause hemolysis and demonstrate compatibility with direct contact with circulating blood per ISO 10993-4.	Non-hemolytic
Hemocompatibility - Partial Thromboplastin Time Test (PTT)	Evaluate the potential for the test article to affect clotting time and demonstrate no statistically significant difference compared to control device per ISO 10993-4.	Results of test article comparable to control article
Hemocompatibility - Complement Activation (SC5b-9)	Evaluate the potential for the test article to cause activation of the complement system per ISO 10993-4.	No risk to activate complement
Chronic toxicity	Evaluate the potential for chronic toxicity from long-term exposure to substances that may leach or be extracted from the test article by CC and TRA.	Compounds detected and identified in extracts of the test articles were present at levels that would not be expected to pose any significant risk of adverse chronic toxicological effects
Carcinogenicity	Evaluate the carcinogenic potential of substances that may leach or be extracted from the test article by CC and TRA.	Compounds detected and identified in extracts of the test articles were present at levels that would not be expected to pose any significant risk of adverse carcinogenic effects

Table 3: Summary of Biocompatibility Testing of SQUID Accessories (Syringe and Adapter)

Test	Test Description	Results
Cytotoxicity	Evaluate the potential for substances that may leach or be extracted from the test article to cause cytotoxicity per ISO 10993-5.	Non-cytotoxic
Sensitization	Evaluate the potential for substances that may leach or be extracted from the test article to cause skin sensitization per ISO 10993-10.	Non-sensitizing
Irritation or Intracutaneous reactivity	Evaluate the potential for substances that may leach or be extracted from the test article to cause local irritation in the dermal tissues of rabbits per ISO 10993-10.	Non-irritating
Acute systemic toxicity	Evaluate the potential acute systemic toxicity per ISO 10993-11.	Non-toxic
Material-mediated pyrogenicity	Evaluate the potential for saline extracts of the test article to cause a febrile response in rabbits per ISO 10993-11.	Non-pyrogenic
Hemocompatibility (Extract and Direct Contact Methods)	Evaluate the potential for the test article to cause hemolysis and demonstrate that the accessory components do not induce hemolysis and is compatible for direct & indirect contact with circulating blood per ISO 10993-4.	Non-hemolytic

Sterilization

The SQUID and DMSO vials are sterilized using dry heat according to ISO-20857, "Sterilization of health care products - Dry heat - Requirements for the development, validation and routine control of a sterilization process for medical devices." The dry heat sterilization process was validated to achieve a sterility assurance level (SAL) of 10^{-6} for the SQUID and DMSO vials.

The syringes and adapters are sterilized using ethylene oxide (EO) according to ISO 11135, "Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices." The EO sterilization process was validated to achieve an SAL of 10^{-6} for the syringes and adapters. Sterilant residual levels met requirements in ISO 10993-7, "Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals."

Routine Limulus Amebocyte Lysate (LAL) batch release testing is performed on all sterile components according to ANSI/AAMI ST72, "Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing."

Packaging and Shelf Life

Testing was performed to validate the sterile barrier packaging as well as the device functionality over the shelf life of the SQUID LEA, to comply with ISO 11607-1, "Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems," and ISO 11607-2, "Packaging for terminally sterilized medical devices -- Part 2: Validation requirements for forming, sealing and assembly processes."

Results from testing the sterile barrier packaging and the device after sterilization and accelerated aging support a 3-year shelf life of the SQUID LEA.

B. Animal Studies

The sponsor conducted a Good Laboratory Practices (GLP) animal study to evaluate the safety and performance of the SQUID LEA in comparison to an approved control LEA in a swine rete mirabile embolization model. Animals were evaluated via clinical and neurologic examinations, and bloodwork at various intervals until termination timepoints at 30 or 90 days after embolization. Postmortem, animals were evaluated via gross necropsy; major organs, downstream tissues, and embolization sites were assessed through histopathology. The embolized rete mirabile were also assessed using micro computed tomography (micro-CT), and radiography.

No clinical or hematological differences were noted between animals embolized with test or control LEA during the study. At necropsy, none of the organs collected showed abnormalities that were attributed to either LEA. Micro CT images of the implanted regions ruled out the presence of tantalum nanoparticulates in the perivascular tissues. Radiographs of the embolized rete mirabile showed similar levels of diffusion of the embolic material throughout the length of the vascular bundle.

Histopathology of the implanted vessels showed similar levels of diffusion of the embolic material throughout the length of the vascular bundle and a minimal chronic vascular inflammatory response in both groups and timepoints. No evidence of either LEA was found in non-target organs (liver, spleen, lymph nodes, and brain).

The results of the animal study show that SQUID met safety and performance expectations at acute and chronic timepoints compared to the control and met biocompatibility endpoints for local implantation and systemic toxicity.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of MMAE with the SQUID LEA (hereby referred to as SQUID) as an adjunct to standard of care (SOC) treatment in patients with symptomatic chronic SDH measuring 10 mm or greater in thickness. The study was conducted in the United States (US) and the European Union (EU) under IDE # G190038. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between November 25, 2020, and May 20, 2023. The database for this PMA reflected data collected through August 27, 2024, and included 319 patients. There were 25 investigational sites in the US and 7 sites in the EU.

The study was a multi-center, prospective, randomized, controlled (1:1) clinical study titled, "The SQUID Trial for The Embolization of The Middle Meningeal Artery (STEM) For Treatment of Chronic Subdural Hematoma." After obtaining informed consent, eligible study subjects were divided into two cohorts (surgical management and non-surgical medical management (NSMM)) based on the clinical judgement of the treating team. The study stratified enrollment of eligible subject by those that were treated with SOC surgery, with and without adjunctive embolization (surgical cohort), and those that were treated with SOC NSMM, with and without adjunctive embolization (non-surgical cohort). Subjects requiring emergency surgery were excluded from the study.

Once assigned to a cohort, each subject was randomized 1:1 to the test or control arm. The control group received SOC treatment consisting of either surgical management alone (burr hole evacuation or Subdural Evacuating Port System (SEPS)) for the surgical cohort, or NSMM alone (medication management, observation, lifestyle modifications) for the non-surgical cohort. The test arm received SOC treatment (surgery or NSMM) in addition to MMAE with SQUID. Subjects who were placed in the surgical cohort received SOC surgery within 48 hours of randomization. Subjects who were randomized into the treatment arm were assigned to receive MMAE within 24 hours of randomization (followed by SOC surgery within 48 hours of randomization, if applicable). Crossover was not permitted between the randomized arms.

The STEM study used an independent Data Safety and Monitoring Board (DSMB) and a Clinical Events Committee (CEC) to minimize bias, to assess the primary effectiveness and safety endpoints, as well as to oversee the safety of the study. A central independent radiological Core Lab was also engaged in the study for uniform and independent evaluation of the imaging data from baseline (i.e., prior to randomization), 180-day follow-up, and all unscheduled visits.

1. Clinical Inclusion and Exclusion Criteria
   Enrollment in the STEM study was limited to patients who met the following inclusion criteria.

   1) Male or female subject whose age is ≥ 30 at the time of consent.
   2) Pre-morbid modified Rankin Score (mRS) 0-1 within the previous 12 months.
   3) Chronic SDH (cSDH) measures ≥ 10 mm in greatest thickness.
   4) cSDH exerts mass effect upon the subjacent brain as indicated by local cortical flattening or midline shift.
   5) Imaging characteristics indicative of chronicity (≥ 50% of the volume of the collection should be isodense or hypodense to normal cortical gray matter on Computed Tomography (CT)).
   6) Subject presents with one or more of the following neurological symptoms:
      - Headache,
      - Cognitive decline,
      - Speech difficulty or aphasia,
      - Gait impairment or imbalance,
      - Focal neurological deficit (weakness, paresthesia or sensory deficit involving of one or more extremities or facial droop), and/or seizure.
   7) Subject, or his/her legally authorized representative, understands the nature of the procedure, consents to participation in the study and provides a signed Informed Consent Form.
   8) Female subjects of child-bearing potential must be able to provide a current negative urine pregnancy test and agree to an appropriate method of contraception throughout the trial.
   9) Subject is able and willing to return to the investigational site for all follow-up visits (e.g., 30-day, 90-day, 180-day and 1-year), as required per protocol.

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

   1) Subject with prior ipsilateral craniotomy or burr hole evacuation of cSDH.
   2) Subject with prior embolization of either MMA.
   3) Subject requires (in the opinion of the treating surgeon) a full or mini craniotomy.
   4) Subject with urgent or emergent (within 1 hour of assessment) subdural hematoma evacuation needed.
   5) Subject with a cSDH with a focal location (confined to the frontal or temporal base or the interhemispheric space without cerebral convexity involvement).
   6) cSDH developed due to underlying condition such as a vascular lesion, brain tumor, arachnoid cyst, spontaneous intracranial hypotension or secondary to a previous craniotomy.
   7) Life expectancy of <1 year.
   8) Subject who presents with an intracranial mass other than subdural hematoma.

9) Subject who presents with a meningioma with mass effect and/or ≥ 1 cm or currently undergoing radiation therapy for carcinoma or sarcoma of the head or neck region.
10) Subject with serum creatinine level > 3.0 mg/dL at time of enrollment (this will restrict the use of contrast) and not on dialysis.
11) Subject with significant liver function impairment at time of enrollment.
12) Subject with a life-threatening allergy to radiographic contrast (unless treatment for allergy is tolerated or can be managed medically).
13) Subject who is currently enrolled in another investigational study protocol that could potentially confound the current study endpoints.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days, 90 days, 180 days, and 1 year post-intervention. Additional assessments were performed at baseline (e.g., screening), randomization, at the time of the intervention or immediately before, within 24 hours post-intervention, and at discharge (or 7 days post-intervention, whichever is first). Pre-intervention and post-intervention follow-up evaluations include physical and functional assessments, laboratory measurements, imaging tests, surveys of concomitant medications, and quality of life (QoL) questionnaires. Adverse events (AEs) and complications were recorded at all visits.

3. Clinical Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint was treatment failure, defined by any of the following:

- Residual or re-accumulation of the SDH ≥ 10mm on 180-day scan from intervention; or
- Re-operation (after index procedure) or surgical rescue within 180-days of intervention (Reoperation or surgical rescue includes cSDH drainage via any surgical procedure or embolization of the MMA with any commercially available product); or
- Any new, major disabling stroke, myocardial infarction (MI) or death from any neurological cause within 180-days of intervention.

In this endpoint, re-operation or surgical rescue includes cSDH evacuation via any surgical procedure OR MMAE with any commercially available product on the index side (left, right, or bilateral) as designated at the time of screening. Success on both sides was required for bilateral cSDH. Major disabling stroke was defined as an increase in the National Institutes of Health Stroke Scale (NIHSS) of 4 points or more from baseline that persists for 24 or more hours from the time of the event (major stroke), AND results in the modified Rankin Scale a (mRS) of 3 or greater at 90 days from the event (disabling stroke).

The primary effectiveness endpoint was evaluated as a superiority analysis comparing the test arm (SOC + MMAE) to the control arm (SOC alone) using a Cochran-Mantel-Haenszel (CMH) test, where NSMM vs SM serves as the stratification factor. Formal hypotheses for a test of superiority are as follows:

$$H_0: R = 1$$
$$H_A: R \neq 1$$

where R is the odds ratio of experiencing treatment failure at 180 days in the treatment (SOC + MMAE) and control (SOC alone) arms, respectively.

With regard to success/failure criteria, rejection of the null hypothesis at the 5% level, with a lower observed incidence for SQUID embolization than control (< 1), constituted a finding of superiority of treatment (SOC + MMAE) to control (SOC alone).

Primary Safety Endpoint

The primary safety endpoint was major disabling stroke or any death within 30-days from intervention. Major disabling stroke was defined as an increase in the National Institutes of Health Stroke Scale (NIHSS) of four points or more from baseline that persists for 24 or more hours from the time of the event (major stroke) AND results in an mRS of three or greater at 90 days from the event (disabling stroke). The primary safety endpoint was evaluated descriptively.

Hypothesis Driven Secondary Effectiveness Endpoint

The clinical secondary effectiveness endpoint evaluated the mRS (analyzed as shift) at 180-days from intervention. The 'shift' analysis evaluated the entire range of the mRS at a visit (all 7 levels: 0 = no symptoms at all, 1 = no significant disability, 2 = slight disability, 3 = moderate disability, 4 = moderately severe disability, 5 = severe disability, and 6 = death) unlike the binary mRS analysis which classifies the 7 levels into two groups (<2 and 2). Treatments were compared using a van Elteren test. Formal hypotheses for a test of superiority are as follows:

$$H_0: F_{T,i} = F_{C,i} \text{ for i =1 and 2}$$
$$H_A: F_{T,i} \neq F_{C,i} \text{ for i =1 or 2}$$

where $F_{T,i}$ and $F_{C,i}$ are the cumulative distribution functions of the mRS scores for the treatment and control arms, respectively, and i indexes the two cohorts (surgery and NSMM).

B. Accountability of PMA Cohort

At the time of database lock, of 319 patients enrolled in the STEM study, including 149 test patients, 161 control patients, and 9 screen failures. The following analysis populations were defined and used in the protocol:

Intention-to-Treat (ITT) Population: This set includes all subjects who sign informed consent and were randomized. Subjects included in the ITT population were analyzed per their assigned treatment.

Safety Population: This set includes all subjects who sign informed consent and were randomized. Subjects included in the safety population were analyzed according to the treatment actually received regardless of randomization assignment. This population was used for safety analyses.

Modified Intention-to-Treat (mITT) Population: This set includes all subjects who signed informed consent, were randomized, and the assigned intervention was initiated. This population was used for the primary effectiveness analysis.

Per Protocol (PP) Population: This set includes all subjects who complete the study without major protocol deviations. Major protocol deviations are deviations that affect the scientific integrity of the study and were identified prior to database lock for final analysis.

Subject accountability throughout the study is shown in **Figure 2** and **Table 4**.

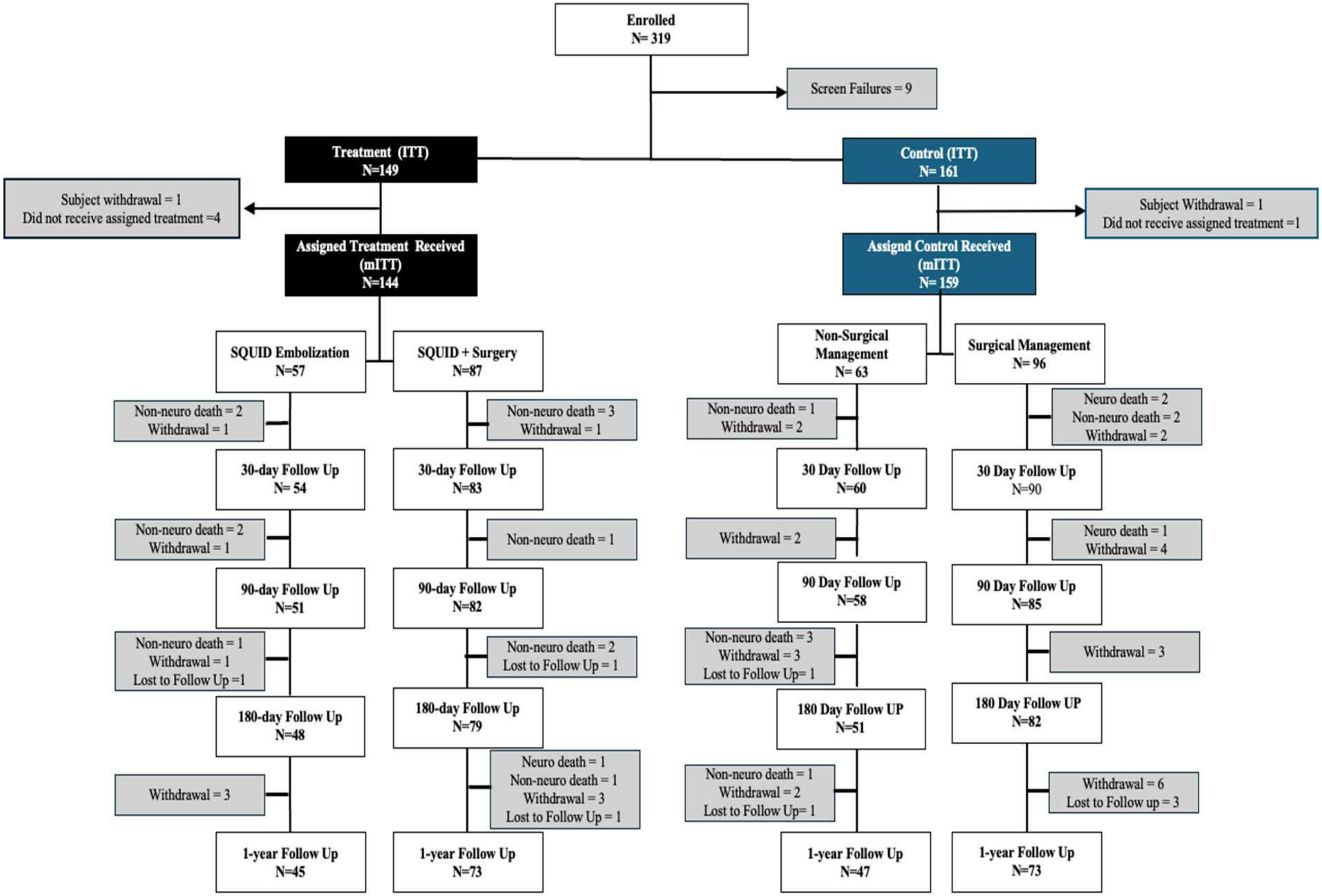

Figure 2: Subject Accountability

Table 4: Study Compliance at the 180-Day Primary Endpoint Visit (mITT Population)

	Treatment		Control	
	SQUID + NSMM	**SQUID + Surgery**	**NSMM alone**	**Surgery alone**
Total ITT Subjects	**149**		**161**	
Total mITT Subjects[1]	**57**	**87**	**63**	**96**
Non-Eligible or Non-Evaluable for 180-Day Follow-up	12	16	17	26
Death prior to 180-Day Follow-up	5	6	4	5
Lost to Follow-up	1	1	1	0
Withdrawal prior to 180-Day Follow-up	3	1	7	9
Eligible but not Evaluable Reason for non-evaluable: Missed Visit Reason for non-evaluable: No Imaging	3 2 1	8 5 3	5 3 2	12 10 2
Eligible for 180-Day Follow-up	48	79	51	82
180-day Follow-up Visit Completed	46	74	47	69
Missed Visit	2	5	4	13
Eligible with Evaluable observed data at 180-day Visit*	45[2]	71	46	70
Had event prior to visit (Evaluable)*	1[2]	0	4[3]	3[4]
Subjects evaluable for primary endpoint*	**46**	**71**	**50**	**73**
Subjects imputed for the primary endpoint	11	16	13	23
Total subjects used in primary endpoint analysis (including imputed data)	**57**	**87**	**63**	**96**

[1]Total mITT patients excludes 1 test subject and 1 control subject who withdrew from the study prior to intervention starting, and 4 test subjects and 1 control subject who did not receive the assigned treatment based on clinical judgment of patient conditions at the time of index procedure as depicted in **Figure 2**.
[2]One test subject in the NSMM cohort exited early due to a misunderstanding of the required timeframe for follow up after meeting a primary endpoint criterion. This patient is considered evaluable since they had a primary endpoint failure despite not completing the 180-day visit.
[3]Two control (NSMM cohort) subjects died and two subjects were withdrawn after meeting primary endpoint criterion, all prior to the visit window. These patients are considered evaluable since they had a primary endpoint failure despite not completing the 180-day visit.
[4]Three control (surgery cohort) subjects died, one of which occurred after meeting primary endpoint criterion 2, all prior to the visit window. These patients are considered evaluable since they had a primary endpoint failure despite not completing the 180-day visit.
*Total evaluable for the primary endpoint is the sum of the "Eligible with Evaluable observed data at 180-day Visit" and "Had event prior to visit (Evaluable)" rows.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a study evaluating treatment of cSDH performed in the US. A listing of patient demographics and baseline characteristics are shown in **Table 5**. A listing of baseline cSDH clinical characteristics are shown in **Table 6**. A listing of treatment and procedural details are shown in **Table 7**.

Table 5: Patient Demographics and Baseline Characteristics (ITT Population)

Parameter	Treatment (N=149)	Control (N=161)
Country		
United States	128 (85.9%)	133 (82.6%)
France	12 (8.1%)	17 (10.6%)
Germany	7 (4.7%)	8 (5.0%)
Spain	2 (1.3%)	3 (1.9%)
Age (years)	72.8 ± 10.35 (149) 74.0 (41.0, 96.0)	73.4 ± 11.31 (161) 73.0 (39.0, 97.0)
Gender		
Male	97 (65.1%)	119 (73.9%)
Female	52 (34.9%)	42 (26.1%)
Race[1]		
Native American or Alaskan Native	0 (0.0%)	0 (0.0%)
Asian	9 (6.0%)	7 (4.3%)
Black or African American	8 (5.4%)	15 (9.3%)
Native Hawaiian or Other Pacific Islander	0 (0.0%)	0 (0.0%)
White	105 (70.5%)	108 (67.1%)
Unknown	5 (3.4%)	3 (1.9%)
N/A, EU Subject[2]	21 (14.1%)	28 (17.4%)
Other	2 (1.3%)	1 (0.6%)
Ethnicity		
Hispanic or Latino	11 (7.4%)	8 (5.0%)
Not Hispanic or Latino	114 (76.5%)	124 (77.0%)
N/A, EU Subject	21 (14.1%)	28 (17.4%)
Unknown	3 (2.0%)	1 (0.6%)
Smoking History		
Current Smoker	15 (10.1%)	14 (8.7%)
Previous Smoker	56 (37.6%)	46 (28.6%)
Never Smoked	78 (52.3%)	101 (62.7%)
Addiction - Alcohol	17 (11.4%)	15 (9.3%)
Ongoing use	8 (5.4%)	9 (5.6%)
Addiction - Drugs/Other Substance Abuse (includes use of marijuana)	10 (6.7%)	6 (3.7%)
Ongoing use	8 (5.4%)	4 (2.5%)
Prior Stroke	2 (1.3%)	2 (1.2%)
Anti-coagulant, Anti-platelet, and Steroid Use		
Aspirin	29 (19.5%)	28 (17.4%)
Heparin	2 (1.3%)	8 (5.0%)
Thienopyridines	7 (4.7%)	8 (5.0%)
Warfarin/Other Vitamin K Antagonist	10 (6.7%)	11 (6.8%)
Other – ASA-dipyridamole	2 (1.3%)	0 (0.0%)
Other – NOAC/DOAC	6 (4.0%)	12 (7.5%)
Total (on one or AC/AP[3] medications)	56 (37.6%)	67 (41.6%)
Total (on one or more) steroid medications	13 (8.7%)	18 (11.2%)

Note: continuous data displayed as mean ± SD (n); median (minimum, maximum); categorical data displayed as n/N (%), the number and percentage of participants with that particular response.
Note: For additional details of baseline characteristics stratified by cohort, see device labeling.
[1]Subjects may indicate more than one race.
[2] Race and ethnicity data was captured only for the US population as privacy laws do not allow collection of this information in the EU population.
[3]AC/AP is anticoagulant or antiplatelet medications, ASA-dipyridamole is aspirin and dipyridamole

Table 6: Baseline cSDH Clinical Characteristics (ITT Population)

	Treatment (N=149)	Control (N=161)
Anatomic Side of cSDH		
Bilateral	26/149 (17.4%)	37/161 (23.0%)
Unilateral - Left Side	57/149 (38.3%)	52/161 (32.3%)
Unilateral - Right Side	66/149 (44.3%)	72/161 (44.7%)
Unilateral - Total	123/149 (82.6%)	124/161 (77.0%)
cSDH Thickness (mm)[1]		
Mean ± SD (n)	18.9 ± 6.11 (148)	19.1 ± 6.33 (161)
Median (minimum, maximum)	18.0 (10.0, 40.0)	19.0 (10.0, 36.2)
Symptoms[*]		
Headache	98/149 (65.8%)	95/161 (59.0%)
Cognitive decline	43/149 (28.9%)	48/161 (29.8%)
Speech difficulty or Aphasia	26/149 (17.4%)	41/161 (25.5%)
Gait impairment or imbalance	72/149 (48.3%)	77/161 (47.8%)
Focal neurological deficit (weakness, paresthesia, sensory deficit involving of one or more extremities or facial droop)	60/149 (40.3%)	63/161 (39.1%)
Seizure	7/149 (4.7%)	9/161 (5.6%)
Other	43/149 (28.9%)	42/161 (26.1%)
Assessment		
Baseline NIHSS	1.49 ± 2.619	1.68 ± 2.340
Baseline mRS	1.57 ± 1.284	1.58 ± 1.297

Note: categorical data displayed as n/N (%), the number and percentage of participants with that particular characteristic.
[*]Subjects may have more than one symptom.
[1]cSDH thickness measurements stratified by brain side can be found in the device label

Table 7: Treatment and Procedure Characteristics – Treatment Subjects (Safety Population)

	Treatment	
Characteristic	**SQUID + NSMM (N=57)**	**SQUID + Surgery (N=87)**
Anatomic Side (target)		
Bilateral	10/57 (17.5%)	16/87 (18.4%)
Unilateral	47/57 (82.5%)	71/87 (81.6%)
Anatomic Side (target with embolization)		
Bilateral	25/57 (43.9%)	21/86 (24.4%)
Unilateral	32/57 (56.1%)	65/86 (75.6%)
Surgical Procedure Type		
Burr-hole Evacuation		76/87 (87.4%)
SEPS		10/87 (11.5%)
Other		1/87 (1.1%)
Total Embolization time[1] (minutes)	82.3 ± 40.21 (57)	79.3 ± 43.32 (87)
Total Surgical time (minutes)		51.8 ± 35.58 (86)
Anesthesia (Embolization)		
Conscious Sedation/Local Anesthesia	2/57 (3.5%)	7/87 (8.0%)
General Anesthesia	55/57 (96.5%)	80/87 (92.0%)

Characteristic	Treatment	
	SQUID + NSMM (N=57)	**SQUID + Surgery (N=87)**
Anesthesia (Surgery)		
Conscious Sedation/Local Anesthesia		3/87 (3.4%)
General Anesthesia		84/87 (96.6%)
Target Vessel Location[2]		
Posterior Middle Meningeal Artery Branch 1	37/57 (64.9%)	50/87 (57.5%)
Posterior Middle Meningeal Artery Branch 2	13/57 (22.8%)	15/87 (17.2%)
Anterior Middle Meningeal Artery Branch 1	47/57 (82.5%)	60/87 (69.0%)
Anterior Middle Meningeal Artery Branch 2	20/57 (35.1%)	12/87 (13.8%)
Duration of SQUID Injection[3]		
<1 minute	41/123 (33.3%)	46/162 (28.4%)
1-5 minutes	68/123 (55.3%)	80/162 (49.4%)
>5 minutes	14/123 (11.4%)	36/162 (22.2%)
SQUID Product Formulation[2]		
SQUID 12	35/57 (61.4%)	56/87 (64.4%)
SQUID 12LD	0/57 (0.0%)	2/87 (2.3%)
SQUID 18	36/57 (63.2%)	39/87 (44.8%)
SQUID 18LD	0/57 (0.0%)	1/87 (1.1%)
SQUID 34	0/57 (0.0%)	0/87 (0.0%)
SQUID 34LD	1/57 (1.8%)	0/87 (0.0%)
cSDH evacuation adequate (yes)		84/86 (97.7%)
Access Site[2]		
Radial Artery	21/57 (36.8%)	35/87 (40.2%)
Femoral Artery	37/57 (64.9%)	53/87 (60.9%)

Note: continuous data displayed as mean ± SD (n); categorical data displayed as n/N (%), the number and percentage of participants with that particular response.
[1] Some subjects had nontarget side treated with SQUID and that is included in the total embolization time.
[2] Subjects could be counted in more than one category.
[3] Based on total number of injections.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the safety population cohort of 310 patients available for the evaluation at 30-day post-intervention. The key safety outcomes for this study are presented below in **Table 8** through **Table 12**.

Primary Safety Endpoint

The primary safety endpoint was major disabling stroke or any death within 30 days from intervention. Major disabling stroke was defined as an increase in the National Institutes of Health Stroke Scale (NIHSS) of four points or more from baseline that persists for 24 or more hours from the time of the event (major stroke) AND results in an mRS of three or greater at 90 days from the event (disabling stroke). Results from the primary safety endpoint were evaluated descriptively and are presented for the combined cohorts for test and control in **Table 8** and stratified by cohort in **Table 9**. The primary safety event rates were generally comparable across groups.

The sponsor conducted a post-hoc analysis for the primary safety endpoint through 180 days post-intervention, and the results are presented by treatment and control arm and by strata in **Table 10**. Twelve (12) additional deaths occurred in the safety population between 30 days through the 180-day window, equating to 21 deaths in total. None of the additional deaths were adjudicated as neurological by the CEC.

Table 8: Primary Safety Endpoint Events (CEC Adjudicated) [Safety Population]

	Treatment (SQUID + SOC) (N=144)	**Control (SOC) (N=166)**
	n/N (%) [95% CI]	**n/N (%) [95% CI]**
Major disabling stroke or any death within 30-days, from intervention	4/144 (2.8%) [0.8, 7.0]	5/166 (3.0%) [1.0, 6.9]
Major disabling stroke within 30-days	0/144 (0.0%) [0.0, 2.5]	1/166 (0.6%) [0.0, 3.3]
Any death within 30-days	4/144 (2.8%) [0.8, 7.0]	5/166 (3.0%) [1.0, 6.9]
Event rates based on a per patient analysis; more than one event may have occurred in a patient Note: Data displayed as n (%), the number and percentage of subjects with a primary safety event.		

Table 9: Primary Safety Endpoint Events by Treatment Arm and Strata (CEC Adjudicated) [Safety Population]

	Treatment (N=144)		**Control (N=166)**	
	SQUID + NSMM (N=57)	**SQUID + Surgery (N=87)**	**NSMM alone (N=66)**	**Surgery alone (N=100)**
	n/N (%) [95% CI]	**n/N (%) [95% CI]**	**n/N (%) [95% CI]**	**n/N (%) [95% CI]**
Major disabling stroke or any death within 30-days, from intervention	2/57 (3.5%) [0.4, 12.1]	2/87 (2.3%) [0.3, 8.1]	1/66 (1.5%) [0, 8.2]	4/100 (4.0%) [1.1, 9.9]
Major disabling stroke within 30-days	0/57 (0.0%) [0.0, 6.3]	0/87 (0.0%) [0, 4.2]	0/66 (0.0%) [0, 5.4]	1/100 (1.0%) [0, 5.5]
Any death within 30-days	2/57 (3.5%) [0.4, 12.1]	2/87 (2.3%) [0.3, 8.1]	1/66 (1.5%) [0, 8.2]	4/100 (4.0%) [1.1, 9.9]
Event rates are based on a per patient analysis and more than one event may have occurred in a given patient Note: Data displayed as n (%), the number and percentage of participants with a primary safety event.				

Table 10: Primary Safety Endpoint Events through 180-Day Follow-up* by Treatment arm and Strata (CEC adjudicated) [Safety Population]

	Treatment (N=144)		Control (N=166)	
	SQUID + NSMM (N=57)	**SQUID + Surgery (N=87)**	**NSMM alone (N=66)**	**Surgery alone (N=100)**
	n/N (%) [95% CI]	**n/N (%) [95% CI]**	**n/N (%) [95% CI]**	**n/N (%) [95% CI]**
Major disabling stroke or any death within 180-days, from intervention	5/57 (8.8%) [2.9, 19.3]	8/87 (9.2%) [4.1, 17.3]	5/66 (7.6%) [2.5, 16.8]	5/100 (5.0%) [1.6, 11.3]
Major disabling stroke within 180-days	0/57 (0.0%) [0.0, 6.3]	2/87 (2.3%) [0.3, 8.1]	1/66 (1.5%) [0.0, 8.2]	1/100 (1.0%) [0.0, 5.5]
Any death within 180-days	5/57 (8.8%) [2.9, 19.3]	7/87 (8.0%) [3.3, 15.9]	4/66 (6.1%) [1.7, 14.8]	5/100 (5.0%) [1.6, 11.3]

*All events through the close of the 180-day visit window are included, i.e., 222 days.
Event rates are based on a per patient analysis and more than one event may have occurred in a given patient
Note: Data displayed as n (%), the number and percentage of participants with a primary safety event.

Site Reported Adverse Events:

Device- and embolization procedure-related AEs and serious AEs (SAEs) through 180 days are shown in **Table 11.** Neurologic deaths and neurologic events of interest through 180 days are shown in **Table 12**. A listing of all adverse events observed in the study can be found in the labeling.

The 180-day rate of SAEs related to the embolization procedure alone was 5.6% (8/144), and the 180-day rate of SAEs related to SQUID was 1.4% (2/144). The overall rates of AEs and SAEs through 180 days in the treatment arm (SQUID + SOC) were 75% (108/144) and 63.2% (91/144), respectively. Worsening of subdural hematoma was the most reported AE in the treatment arm and occurred in 18/144 (12.5%) subjects.

The overall rates of AEs and SAEs through 180 days for the control arm (SOC alone) were 66.9% (111/166) and 44.0% (73/166), respectively. The most frequently reported SAE in the control arm was worsening subdural hematoma occurring in 40/166 (24.1%) subjects.

Neurologic death occurred in 0.7% (1/144) of treatment arm subjects and 1.8% (3/166) of control arm subjects.

Table 11: Overall Incidence of AEs by Seriousness and Relation Through 180 Days (Safety Population)

Relatedness*	Treatment Arm n/N (%)	Control Arm n/N (%)
All AEs (including SAEs, non-SAEs) through 180 days	108/144 (75.0%)	111/166 (66.9%)
Non-SAEs	54/144 (37.5%)	65/166 (39.2%)
SAEs	91/144 (63.2%)	73/166 (44.0%)
SAEs Related to Embolization Procedures through 180 days	8/144 (5.6%)	Not Applicable
SAEs Related to SQUID through 180 days	2/144 (1.4%)	Not Applicable
Non-SAEs Related to SQUID through 180 days	4/144 (2.8%)	Not Applicable
Unintended Vessel Occlusion	0/144 (0.0%)	Not Applicable
Catheter Entrapment	1/144 (0.7%)	Not Applicable
Access Site Complications	2/144 (1.4%)	Not Applicable
Unintended SQUID Migration	0/144 (0.0%)	Not Applicable
Worsening SDH	18/144 (12.5%)	40/166 (24.1%)

Note: Data presented as the number and percentage of subjects in which the event occurred. More than one event may have occurred in a given subject

*Device and procedure relatedness was adjudicated by CEC if available, otherwise by investigational sites.

An event was considered related to the device or procedure if it was adjudicated as "possibly," "probably," or "causally" related.

Table 12. Neurologic Death and Neurologic Events of Interest through 180 Days (Safety Population)

	Treatment Arm	Control Arm
	SQUID + SOC	SOC Alone
Death Classification and Relatedness[1]	n/N (%)*	n/N (%)*
All Neurologic Deaths[1]	1/144 (0.7%)	3/166 (1.8%)
Related to Study Device[1]	0/144 (0.0%)	0/166 (0.0%)
Related to Embolization Procedure[1]	0/144 (0.0%)	N/A
Related to Surgery Procedure[1,2]	0/144 (0.0%)	N/A
Other[3]	1/144 (0.7%)	3/166 (1.8%)
Neurologic Events of Interest[1]	n/N (%) [# events]*	n/N (%) [# events]*
Stroke[1]	9/144 (6.3%) [9]	7/166 (4.2%) [7]
Cerebral Infarction	0/144 (0.0%) [0]	1/166 (0.6%) [1]
Serious Intracranial Hemorrhage	1/144 (0.7%) [1]	1/166 (0.6%) [1]
New onset of seizures	13/144 (9.0%) [13]	6/166 (3.6%) [6]
TIA	2/144 (1.4%) [3]	1/166 (0.6%) [1]

*Data presented as the number and percentage of subjects in which the event occurred [with total number of events for neurologic events of interest].

[1] Neurological deaths and relatedness, and stroke and relatedness, were adjudicated by the Clinical Events Committee (CEC), and all other events were site reported.

[2]Denominator is based on the number of patients receiving surgery.

[3]Other relatedness is defined as relatedness not pertaining to study device, embolization procedure, or surgery procedure.

2. Effectiveness Results

The primary effectiveness analysis was based on the mITT population at the 180-day time point. Key effectiveness outcomes are presented in **Table 13** through **Table 15**.

Primary Effectiveness Results

The primary effectiveness endpoint was treatment failure, defined by any of the following:

- Residual or re-accumulation of the SDH greater ≥ 10mm on 180-day scan from intervention; or
- Re-operation (after index procedure) or surgical rescue within 180-days of intervention (Reoperation or surgical rescue includes cSDH drainage via any surgical procedure or embolization of the MMA with any commercially available product); or
- Any new, major disabling stroke, myocardial infarction (MI) or death from any neurological cause within 180-days of intervention.

As shown in **Table 13**, 144 subjects in the treatment arm (57 SQUID + NSMM and 87 SQUID + surgery) and 159 subjects in the control arm (63 NSMM alone and 96 surgery alone) contributed to the 180-day primary endpoint. Multiple imputation was used to impute missing data for subjects with missing primary endpoint data at 6 months (e.g., due to early withdrawal from the study, loss to follow up, death, unevaluable data, or missed visit as shown in **Table 4**). In the mITT population, the observed failure rate in the treatment arm was 16.2% (19 failures in 117 evaluable patients) and the observed failure rate in the control arm was 38.2% (47 failures in 123 evaluable patients). The odds ratio (OR) was 0.36 (p = 0.0010) favoring a lower failure rate for the treatment arm. The primary effectiveness endpoint was met.

The sponsor conducted a sensitivity analysis on the primary effectiveness endpoint which showed consistent results across all study populations (OR [95% confidence intervals] of ITT population: OR 0.36 [0.20, 0.63], safety population: OR 0.31 [0.17, 0.57], and PP population: 0.30 [0.16, 0.56]) in support of the robustness of the study outcome.

A pre-specified exploratory analysis of the composite primary endpoint within each cohort (Surgery and NSMM), was performed. As noted in **Table 13**, the failure rate in subjects receiving SQUID + NSMM was 19.6% (9 failures in 46 evaluable patients) and the failure rate in subjects receiving NSMM alone was 58.0% (29 failures in 50 evaluable subjects). The failure rate in subjects receiving SQUID + Surgery was 14.1% (10 failures in 71 evaluable subjects) and the failure rate in subjects receiving surgery alone was 24.7% (18 failures in 73 evaluable subjects). This exploratory analysis resulted in an odds ratio of 0.21 (95% CI: 0.09, 0.50) for the NSMM cohort and an odds ratio of 0.56 (95% CI: 0.25, 1.28) for the surgical cohort, where the NSMM cohort demonstrated a more favorable trend compared to the control than that of the surgical cohort when considering the primary effectiveness endpoint.

Table 14 shows the reasons for primary effectiveness outcome events stratified by cohort. Reoperation or surgical rescue was the most common primary endpoint event for each cohort. When comparing test and control stratified by cohort, the test arm trended favorably in comparison to the control (SQUID + NSMM: 15.2% vs. NSMM alone: 54.0%, and SQUID + surgery: 7.0% vs. surgery alone: 16.4%). Although residual or re-accumulation of the cSDH was observed more frequently in subjects receiving SQUID + NSMM compared to NSMM alone, the sample sizes were low and should be taken with caution.

Table 13: Primary Effectiveness Endpoint Failures (mITT Population)

	Observed Data[1]		**Treatment Effect**	
	Treatment (N=144)	**Control (N=159)**	**Odds Ratio[2] [95% CI]**	**P-value**
Primary effectiveness outcome	19/117 (16.2%)	47/123 (38.2%)	0.36 [0.20, 0.65]	0.0010
Non-surgical Management Strata	9/46 (19.6%)	29/50 (58.0%)	0.21 [0.09, 0.50]	
Surgical Management Strata	10/71 (14.1%)	18/73 (24.7%)	0.56 [0.25, 1.28]	

CI=Confidence interval.
[1]The observed data includes 117 Treatment and 123 Control subjects with evaluable data
[2]The odds ratio calculation was based on multiple imputation methods by imputing data for subjects with missing data or unevaluable data.

Table 14: Components of Primary Effectiveness Endpoint (mITT Population)

	Treatment		**Control**	
	SQUID + NSMM (N=57)	**SQUID + Surgery (N=87)**	**NSMM alone (N=63)**	**Surgery alone (N=96)**
Primary Effectiveness endpoint at 180-day visit	9/46 (19.6%)	10/71 (14.1%)	29/50 (58.0%)	18/73 (24.7%)
Missing data, n	11	16	13	23
Primary Endpoint Component				
Residual or re-accumulation of the SDH (≥10 mm) on scan at the 180-day visit	2/46 (4.3%)	2/71 (2.8%)	1/50 (2.0%)	3/73 (4.1%)
Re-operation (after index procedure) or surgical rescue within 180-days of intervention*	7/46 (15.2%)	5/71 (7.0%)	27/50 (54.0%)	12/73 (16.4%)
Any new major disabling stroke, myocardial infarction (MI) or death from any neurological cause within 180 days of intervention*	0/46 (0.0%)	3/71 (4.2%)	1/50 (2.0%)	3/73 (4.1%)

	Treatment		Control	
	SQUID + NSMM (N=57)	SQUID + Surgery (N=87)	NSMM alone (N=63)	Surgery alone (N=96)
Event rates are based on a per patient analysis and more than one event may have occurred in a given patient **Note:** Rate for individual components only includes subjects whose first failure was for that component (i.e. if they failed multiple components, they are only included as a failure in the first component they failed). * Based on treatments or events through the 180-day visit window close (222 days).				

Hypothesis Driven Secondary Effectiveness Analysis

The sponsor evaluated a mRS shift analysis at 180 days as a powered secondary endpoint. When compared across the entire spectrum of mRS scores, there was no evidence of a difference in the distribution of mRS scores between treatment arms (p=0.6524).

Table 15: Secondary Effectiveness Endpoint mRS Shift Analysis at 180-day Visit (mITT Population)

mRS Value	Treatment (N=144)	Control (N=159)	Total (N=303)
0	57/117 (48.7%)	53/116 (45.7%)	110/233 (47.2%)
1	31/117 (26.5%)	39/116 (33.6%)	70/233 (30.0%)
2	10/117 (8.5%)	4/116 (3.4%)	14/233 (6.0%)
3	5/117 (4.3%)	9/116 (7.8%)	14/233 (6.0%)
4	2/117 (1.7%)	2/116 (1.7%)	4/233 (1.7%)
6	12/117 (10.3%)	9/116 (7.8%)	21/233 (9.0%)
Van-Elteren Test P-value (stratified)=0.6524			
Wilcoxon rank-sum P-value (non-stratified) =0.6583			
P-values based on multiple imputation methods. n/N (X.x%): denominator is subjects in that arm with an available mRS at 180 days. If subject died prior to the visit and mRS missing then set as a 6 in this analysis.			

Additional Analyses

The sponsor conducted a Kaplan-Meier analysis of time to re-operation (after index procedure) or surgical rescue within 180-days of intervention for the test and control groups stratified by cohort as shown in **Figure 3**. In all groups, the majority of re-interventions occurred within 30 days. One test arm subject underwent re-intervention after 90 days due to ongoing balance issues and one additional reintervention occurred in a test subject as a result of imaging at 180 days.

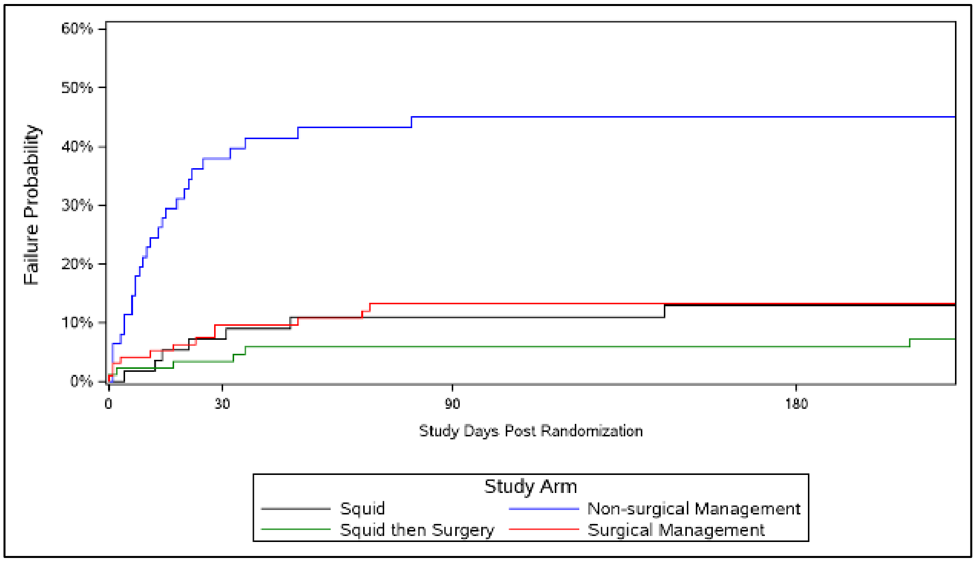

Figure 3: Kaplan-Meier Analysis of Time to Re-Intervention Post-Randomization by Randomized Treatment and Surgical Strata

3. Subgroup Analyses

The consistency of treatment effects and safety was evaluated through subgroup analyses across various baseline characteristics. Statistical testing for heterogeneity showed no significant differences in treatment effects and safety between subgroups, indicating consistent benefit across the studied patient populations. Detailed subgroup analysis results for the primary effectiveness endpoint are provided in **Table 16.** Caution should be taken when interpreting these results due to small sample sizes.

Table 1617: Primary Effectiveness Endpoint Subgroup Analyses (mITT Population)

	Treatment (N=144)	Control (N=159)	Odds Ratio [95% CI]
Strata			
Non-surgical Management	9/46 (19.6%)	29/50 (58.0%)	0.18 [0.07, 0.44]
Surgical Management	10/71 (14.1%)	18/73 (24.7%)	0.50 [0.21, 1.18]
cSDH type (corelab)			
Bilateral	6/22 (27.3%)	13/29 (44.8%)	0.38 [0.11, 1.34]
Unilateral	13/95 (13.7%)	34/94 (36.2%)	0.28 [0.14, 0.58]
cSDH size (corelab)			
<20 mm	13/69 (18.8%)	25/66 (37.9%)	0.35 [0.16, 0.79]
≥20 mm	5/42 (11.9%)	17/45 (37.8%)	0.25 [0.08, 0.76]
Both*	1/6 (16.7%)	5/12 (41.7%)	0.38 [0.04, 3.43]
Subdural Evacuating Port System (SEPS) device use			
Yes	1/8 (12.5%)	1/3 (33.3%)	0.29 [0.01, 6.91]
No	18/109 (16.5%)	46/120 (38.3%)	0.31 [0.16, 0.58]

	Treatment (N=144)	Control (N=159)	Odds Ratio [95% CI]
Antiplatelet/anticoagulant medication usage			
Yes	4/38 (10.5%)	17/42 (40.5%)	0.17 [0.05, 0.56]
No	15/79 (19.0%)	30/81 (37.0%)	0.40 [0.19, 0.82]
Age (years)			
≤85	19/107 (17.8%)	39/109 (35.8%)	0.39 [0.20, 0.74]
>85	0/10 (0.0%)	8/14 (57.1%)	0.00 [--]
Age (years)			
≤65	4/34 (11.8%)	10/29 (34.5%)	0.29 [0.08, 1.07]
>65	15/83 (18.1%)	37/94 (39.4%)	0.32 [0.16, 0.65]
Sex			
Female	5/43 (11.6%)	11/28 (39.3%)	0.22 [0.07, 0.72]
Male	14/74 (18.9%)	36/95 (37.9%)	0.37 [0.18, 0.76]
Race			
White	13/83 (15.7%)	36/81 (44.4%)	0.24 [0.11, 0.49]
Black	2/7 (28.6%)	5/12 (41.7%)	0.35 [0.03, 3.74]
EU/Other/Unknown	4/27 (14.8%)	6/30 (20.0%)	0.77 [0.18, 3.31]
Baseline mRS			
0-1	14/73 (19.2%)	25/74 (33.8%)	0.50 [0.22, 1.11]
2+	4/43 (9.3%)	22/49 (44.9%)	0.15 [0.05, 0.45]
BMI			
≤26	11/66 (16.7%)	22/55 (40.0%)	0.27 [0.11, 0.65]
>26	8/51 (15.7%)	25/68 (36.8%)	0.34 [0.14, 0.82]
Number of burr holes			
None	10/51 (19.6%)	29/53 (54.7%)	0.20 [0.08, 0.49]
1 or more	9/62 (14.5%)	15/66 (22.7%)	0.58 [0.23, 1.44]
Region			
US	17/104 (16.3%)	44/100 (44.0%)	0.25 [0.13, 0.48]
OUS	2/13 (15.4%)	3/23 (13.0%)	1.26 [0.15, 10.80]
*Both pertains to bilateral cases.			

4. Pediatric Extrapolation

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

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 166 investigators of which none were full-time or part-time employees of the sponsor and 7 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 7
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were assessed by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Neurological Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

In the STEM clinical study, treatment arm patients receiving MMAE with SQUID LEA as an adjunct to SOC surgery or NSMM demonstrated clinically meaningful benefit as compared to the patients in the control arm when considering the primary composite endpoint of incidence of residual or re-accumulation of the SDH, re-operation or surgical rescue, or any new, major disabling stroke, MI or death (16.2% vs. 38.2%, respectively, p=0.001). The effectiveness outcome was primarily driven by a reduction in reoperation or surgical rescue. The sponsor conducted a sensitivity analysis on the primary effectiveness endpoint which showed consistent results across all study populations (ITT, mITT, safety, and PP) in support of the robustness of the study outcome. Together these findings demonstrate the benefit of MMAE with SQUID LEA as an adjunct to standard treatment (surgical and NSMM) in patients with symptomatic cSDH to reduce the incidence of residual or re-accumulation of the SDH, re-operation or surgical rescue, or any new, major disabling stroke, MI or death.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and/or animal studies as well as data collected in the STEM clinical study conducted to support PMA approval as described above. A total of 4/144 (2.8%) patients in the treatment group and 5/166 (3.0%) patients in the control group failed the primary safety endpoint as described by suffering a major disabling stroke or any death within 30 days post-intervention. The sponsor conducted a post-hoc analysis of the primary safety endpoint through 180-days post-intervention which identified one additional stroke in the control arm and 12 additional deaths, all non-neurologic, that occurred at similar rates between test and control arms. Of the 144 subjects in the test arm that received SQUID, 4/144 (2.8 %) experienced non-serious AEs related to the device and 2/144 (1.4%) experienced SAEs related to the device through 180 days. In addition, 8/144 (5.6%) subjects experienced SAEs related to the embolization procedure through 180 days. Worsening of subdural hematoma was the most reported AE in the treatment and control arms and occurred in 18/144 (12.5%) subjects in the treatment arm and 24.1% of subjects in the control arm. Based on the totality of the safety data, the STEM clinical study demonstrated that MMAE with SQUID LEA is safe as an adjunct to standard treatment (surgical and NSMM) in patients with symptomatic cSDH measuring 10 mm or greater in thickness in whom an intervention is deemed necessary as determined by a neurosurgeon.

C. Benefit-Risk Determination

The probable benefits of the SQUID LEA include reduced incidence of re-operation (after the index procedure) or surgical rescue within 180 days of the intervention while avoiding major disabling stroke, MI or death.

The probable risks of the SQUID LEA include seizure, stroke, arterial rupture, vascular access site complications, and other adverse events common to neurointerventional procedures.

Additional factors to be considered in determining probable risks and benefits for the SQUID LEA include: As noted above and in **Table 13**, the pre-specified exploratory analysis of the primary endpoint within each cohort (Surgery and NSMM) resulted in an odds ratio of 0.21 (95% CI: 0.09, 0.50) for the NSMM cohort, and an odds ratio of 0.56 (95% CI: 0.25, 1.28) for the surgical cohort. While both cohorts demonstrated favorable trends for the device when used adjunctively with SOC therapy, the device treatment effect was more prominent in the NSMM cohort compared to the surgical cohort. The study was not powered for analysis of individual cohorts.

Additionally, the rate of missing data (approximately 23%) was higher than the anticipated attrition rate for the study. However, the sponsor addressed this concern by performing a sensitivity analysis demonstrating the robustness of the study outcomes across analysis populations.

Finally, uncertainty exists when evaluating treatment effect of surgical and NSMM cohorts given that stratification of patients into groups receiving surgery or NSMM was not objectively defined, nor implemented uniformly across study sites. For this reason, a clear distinction between these groups cannot be defined. However, the sensitivity analysis described above demonstrates the robustness of the primary endpoint outcome in support of benefit.

1. Patient Perspective

   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that the probable benefits of MMAE with SQUID LEA as an adjunct to usual care treatment in patients with symptomatic cSDH(s) measuring 10 mm or greater in thickness in whom an intervention is deemed necessary as determined by a neurosurgeon outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the SQUID LEA when used in accordance with the indications for use. The STEM trial demonstrated that MMAE with the SQUID LEA as an adjunct to surgical and NSMM for symptomatic cSDH reduced re-operation or surgical rescue compared to standard treatment alone, without an increased incidence of disabling stroke or death within 180 days.

These results demonstrate that MMAE embolization with SQUID LEA as an adjunct to standard surgical and NSMM is safe and effective for the treatment of symptomatic cSDH, and that the benefits are significant and outweigh the risks associated with the procedure.

XIV. CDRH DECISION

CDRH issued an approval order on January 30, 2026. The final clinical conditions of approval cited in the approval order are described below.

The purpose of the Post-Approval Study (PAS) is to characterize the safety and effectiveness of the SQUID Liquid Embolic Agent (LEA) during real-world use for middle meningeal artery (MMA) embolization in patients with symptomatic chronic subdural hematoma (SDH). This study will include prospective all-comers enrollment to include all subjects in whom the SQUID LEA is used for MMA embolization in a single-arm trial with a minimum total enrollment of 500 subjects – 250 subjects in the surgical management (SM) cohort and 250 subjects in the non-surgical medical management (NSMM) cohort. The primary outcome will be the rate of hematoma recurrence/progression requiring surgical drainage within 180 days stratified by cohort. Additional outcome measures will include neurologic death, change in modified Rankin Scale (mRS), change in hematoma thickness, and change in midline shift with respect to baseline (pre-embolization) and the primary endpoint for the pooled cohort. All relevant adverse events (AEs) will be recorded and reported throughout the study. The primary outcome will be compared to historical outcomes of standard of care (SOC) management of SDH derived from literature and the subjects in the control arm of the STEM clinical trial. Procedural information including timing of embolization with respect to surgery, device model (SQUID 12 vs SQUID 18 vs SQUID 34), access challenges, delivery catheter entrapment, and device embolization into unintended vessels will be assessed descriptively. The all-comers study should also record all devices used to deliver the study device during the procedure, such as the access and delivery catheters, delivery syringe size, and any adjunctive device use with SQUID LEA. Follow up will occur at baseline (pre-embolization procedure), 24-48 hours post-procedure (surgery + MMA embolization) or prior to hospital discharge, 30 days, 90 days, and 180 days. Radiographic imaging assessments will be performed at baseline (prior to any intervention with surgery or MMA embolization), within 24-48 hours post-procedure (MMA embolization) or prior to hospital discharge (whichever comes first), 90 days if performed by the site as usual clinical care, and 180 days to assess hematoma size, neurologic assessments, and a survey of adverse events.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.