

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Orthopedic Shock Wave Unit

Device Trade Name: Storz Medical Duolith SDI Shock Wave Therapy Device

Device Procode: NBN

Applicant's Name and Address: Storz Medical AG
Lohstampfstrasse 8
CH-8274 Tagerwilen
Switzerland

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P080028

Date of FDA Notice of Approval: January 8, 2016

II. INDICATIONS FOR USE

The Duolith SDI is indicated for extracorporeal shock wave treatment of heel pain due to chronic proximal plantar fasciitis for patients of age greater than 18 years with a history of failed alternative conservative therapies for at least 6 months. Chronic proximal plantar fasciitis is defined as traction degeneration of the plantar fascial band at the origin on the medial calcaneal tuberosity that has persisted for six months or more.

III. CONTRAINDICATIONS

- Over or near bone growth center until bone growth is complete
- When a malignant disease is known to be present in or near the treatment area
- Infection in the area to be treated
- Patient has a coagulation disorder or taking anti-coagulant medications
- Patient has a prosthetic device in the area to be treated

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Duolith SDI device labeling.

V. DEVICE DESCRIPTION

The Duolith SDI is an extracorporeal shock wave (ESWT) treatment device. Key components of the Duolith SDI are the control unit, hand piece (with two (2) stand-offs), and optional foot pedal. The depth of penetration is determined by the standoff that is attached to

the distal end of the hand piece.

The principle of operation of the Duolith SD1 is functionally similar to that of Storz Medical Lithotripters. It uses an electromagnetically generated shock wave produced within a hand-held applicator (F-SW Hand piece). The shock wave is generated by discharging a high voltage capacitor located in the Control Unit into a cylindrically shaped coil system in the Hand piece which is surrounded by a cylindrical metallic membrane. The transient magnetic field produced by the coil induces eddy currents in the metal membrane, causing it to repel from the coil, producing a pressure wave. The membrane is immersed in water and the pressure wave produced by the membrane propagates through the water to a concentric parabolic reflector, where it is reflected to a focal point outside of the Hand piece in front of the reflector.

The Duolith SD1 incorporates micro-processor control of the operating parameters. The software was determined to be a minor level of concern (as described in FDA Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (May 11, 2005) and based on a software hazard analysis conducted by Storz Medical AG).

The Duolith SD1 F-SW Hand piece and Stand-Offs are provided non-sterile to the user. Instructions for cleaning and low level disinfection are provided in the Operating Instructions. The hand piece and applicator can be cleaned using a soft cloth and a general purpose surface disinfectant. Because the device is for use in intact skin only, neither high level disinfection nor sterilization are necessary.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of heel pain due to chronic proximal plantar fasciitis, including non-surgical alternatives. 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. Most patients with chronic proximal plantar fasciitis do not require surgery to relieve the symptoms. The use of shoe inserts (cups and pads), orthotics, oral non-steroidal anti-inflammatory agents, and local steroid injections provide pain relief in most patients. However, symptoms may persist in some patients over an extended period of time despite all forms of conservative management. These patients can be offered a variety of surgical procedures. However, even surgical intervention does not always result in success and could be associated with surgical complications.

VII. MARKETING HISTORY

The Duolith SD1 is marketed worldwide except for in the United States and is authorized to bear the CE Mark. The Duolith SD1 has not been withdrawn from marketing for any reason related to its safety and 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: petechiae, hematoma, tendon rupture, bruising, rupture of plantar fascia (a very rare side effect), temporary or permanent damage of nerve and blood vessels.

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Shock Wave Characterization

Measurements to characterize the Duolith SD1 shock waves are listed in Table 1 below and are in accordance with the performance criteria, stated in the guidance document outline in FDA's "Guidance for the Content of Premarket Notifications [510(k)s] for Extracorporeal Shock Wave Lithotripters Indicated for the Fragmentation of Kidney and Ureteral Calculi," issued in August 2000, with the exception that the parameter "Distance between the focus and target location" is not applicable to the Duolith SD1 since there is no localization system or target marker. The testing showed that typical value for the different parameters met the acceptance/performance criteria.

Testing was conducted for energy flux density settings of 0.10, 0.35, and 0.55mJ/mm², which is the operational range of the Duolith SD1. In addition, peak positive and negative acoustic pressures were also determined for the minimum flux density setting of 0.01mJ/mm². Test results are summarized in Table 1 below.

Table 1: Summary of Shock Wave Characterization Tests

Energy Flux Density Setting: mJ/mm²	0.01	0.10	0.35	0.55
Peak-positive acoustic pressure (MPa)	3	14	36	62
Peak-negative acoustic pressure (MPa)	3	9	13	15
Rise Time (ns, 10% to 90%)	--	330	190	100
Compressional pulse duration (ns, FWHM)	--	620	350	200
Fx- Maximum focal width (mm, -6 dB)	--	5.4	3.8	2.8
Fy-Orthogonal focal width (mm, -6 dB)	--	5.4	3.8	2.8
Fz-Focal extent (mm, -6 dB)	--	57	49	34
Focal volume (cm ³)	--	0.87	0.37	0.14
Distance between focus and target location	N/A	N/A	N/A	N/A
Derived focal acoustic pulse energy (mJ)	--	2.0	3.8	3.5
Derived acoustic pulse energy for 5 mm diameter focal area (mJ)	--	1.7	5.5	8.5
Derived acoustic pulse energy for 8 mm diameter focal area (mJ)	--	3.3	12	18

B. Hand piece Longevity

Duolith F-SW hand piece longevity was demonstrated to exceed 1,000,000 shocks and ranged from 1,154,201 to 3,184,414 shocks (mean: 2,105,739.143; SD: 735,653.976).

The guaranteed service life of the F-SW hand piece is 1,000,000 SW. When it reaches the limit of 1,000,000 SW the F-SW hand piece should be replaced as soon as possible.

C. Electrical Testing

The Duolith SD1 was tested for electrical safety and found in conformance with all applicable requirements of IEC60601-1 (1988), Amendment 1 (1991), and Amendment 2 (1995). EMC testing has been repeated for both the investigational T-Top and the PMA Tower versions.

The Duolith SD1 was tested for EMC safety and for safety of the extracorporeally induced lithotripsy and was found to be in conformance with all applicable requirements of EN 60601-1-2:2001 (Medical electrical equipment, General requirements for safety, EMC) and EN 60601-1-2-36:1997 (Particular requirements for safety of equipment for extracorporeally induced lithotripsy). The Duolith SD1 complied with the emissions requirements for Class B equipment and the minimum immunity requirements of these standards. Test results are summarized in Table 2 below.

The Duolith SD1 complies with UL60601.1 and CAN/CSA C22.2 No.601- M90 by CSA International.

Table 2: Summary of Duolith SD1 Emissions and Immunity Testing

Description	Criteria*	Results	
		T-Top Report Numbers: 2005-1294-2347 2006-1435-2347	Tower Report Number: 2005-1294-2138
<i>Emissions Tests</i>			
Radiated Emissions (30 to 1000 MHz)	Class B	Pass	Pass
Conducted Emissions at AC mains terminals (0.15 to 30 MHz)	Class B	Pass	Pass
Harmonic current emissions	Class A	Pass	Pass
Voltage fluctuations and flicker	IEC 61000-3-3	Pass	Pass
<i>Immunity Tests</i>			
Electrostatic Discharge Immunity	8 kV air 6 kV contact	Pass	Pass
Radiated RF Electromagnetic Field Immunity	3 V/m, 80% 1kHzAM	Pass (80-2500 MHz)	Pass (80-1000 MHz)
Electric Fast Transient (Burst)	2 kV-AC mains 1kV-Other	Pass	Pass

Surge Immunity (AC mains)	1kV/2kV	Pass	Pass
Radio Frequency, conducted	0.15-80 MHz 3 V, 80% 1 kHz AM	Pass	Pass
Magnetic fields	50/60 Hz, 3 Nm	Pass	Pass
Voltage Dip and Interrupt Immunity	30%- 100% main voltage, 0.01-5 sec. duration	Pass	Pass

- * Class A equipment is equipment suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
- * Class B equipment is equipment suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.

D. Software Verification and Validation Testing

System level software verification and validation testing was conducted and the Duolith SD I was found to meet all test requirements according to the FDA Guidance “Guidance for the Content of Pre-Market Submissions for Software Contained in Medical Devices,” issued on May 11, 2005, with no known unresolved anomalies remaining.

E. Biocompatibility Testing

The only portions of the Duolith SD1 intended to come in contact with the patient are the polyurethane coupling membrane and the stand-offs (made of the same polyurethane membrane). These components are classified as having short duration contact on intact skin according to FDA's guidance "Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices," issue on May 1, 1995, which was subsequently superseded by "AAMI/ANSI/ISO 10993-1:2003." Biocompatibility testing included cytotoxicity testing, irritation, and sensitization testing performed in compliance with FDA's biocompatibility guidance and demonstrated that the materials in direct contact with the patient are non-toxic and biocompatible. The ultrasound coupling gel recommended for use with the Duolith SD1 is legally marketed in the United States.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of ESWT procedure with Duolith SD1 device for the treatment of heel pain due to plantar fasciitis in the US under IDE G050236. 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 June 12, 2006 and June 9, 2007. The database for this PMA reflected data collected through September 5, 2007 and included 233 patients. The study was conducted at six (6) clinical sites, all in the United States, with two (2) of the six (6) geographic sites for a single investigator. Therefore, results are based on a five (5) clinical sites.

The study was a multicenter, randomized, placebo-controlled, prospective, double-blind clinical study enrolling 250 subjects (in 1:1 allocation to active treatment with the Duolith SD1 or the placebo-control which received a sham treatment with a device identical to the active device but in which the transmission of the shockwaves to the patient was blocked). The study was conducted to assess the safety and effectiveness of the Duolith SD1 when used to treat unsuccessful conservatively treated subjects suffering from painful heel syndrome. For the purpose of this study, painful heel syndrome was defined as chronic proximal plantar fasciitis that had persisted for at least 6 months before study enrollment. The patient and the clinician performing the efficacy assessments were blinded; the clinician administering the treatment (active and placebo) was not blinded. All study procedures for both groups were identical except that of the stand-off used. Active or sham procedures were administered at three (3) treatment visits approximately 1 week apart, with subsequent follow-up visits at 6 weeks, 3 months, 6 months, and 12 months after the last treatment session. The primary endpoint of comparison between the Duolith Group and Placebo Group is 3 months after the last treatment session (approximately 14 weeks after randomization). Subjects considered to be "responders" at the three (3) month follow up, continued to be followed at 6 and 12 months after the last treatment session. A responder is a subject whose heel pain percentage decrease is > 60% from baseline at Visit 6 (3 months) for at least two (2) of the three (3) heel pain Visual Analog Scale (VAS) measurements: Heel pain when taking the first steps of the day, Heel pain while doing daily activities, and Heel pain after application of a standardized pressure device (F-meter). The VAS has an 11 point scale of 0 to 10 with 0 being no pain and 10 being the highest pain.

1. Clinical Inclusion and Exclusion Criteria

After a screening visit to determine eligibility (Visit 1), the study started at Visit 2 with the first treatment (after randomization). However, Visit 1 and 2 procedures could be performed at a single visit.

- a. Enrollment in the clinical study (G050236) was limited to patients who met the following inclusion criteria:
 - i. Age greater than 18 years
 - ii. Ability of subject or legal respondent to give written informed consent after being told of the potential benefits and risks of participating in the study

- iii. Singed informed consent
- iv. Diagnosis of painful heel syndrome (i.e., chronic proximal plantar fasciitis) proven by clinical examination. Chronic proximal plantar fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the medial calcaneal tuberosity
- v. Six (6) months of unsuccessful conservative treatment (i.e., must have undergone at least 2 unsuccessful non-pharmacological treatments and at least 2 unsuccessful pharmacological treatments within the past year). The following conservative treatments could have been completed as single, combined, or consecutive treatments:
 - Non-pharmacological treatments
 - Physical therapy (e.g., ice, heat or ultrasound)
 - Physiotherapy (e.g., massage and stretching)
 - Over The Counter (OTC) devices like orthosis, taping, and heel pads
 - Prescribed orthosis
 - Shoe modification like higher heels
 - Cast/immobilization
 - Night splints
 - Pharmacological treatments
 - External (topical) application of analgesic and/or anti-inflammatory gels
 - Therapy with prescription analgesics and/or Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
 - Local anesthetic injections
 - Local corticosteroid injections
- vi. Time gap of at least:
 - Six (6) weeks since the last corticosteroid injection
 - Four (4) weeks since the last anesthetic injection; iontophoresis, ultrasound, and electro-myostimulation
 - One (1) week since the last NSAIDs
 - Two (2) days since the last prescription or non-prescription analgesics, heat, ice, massage, stretching, night splinting, and orthosis
- vii. Scores of ≥ 5 on the three (3) VAS pain scales
- viii. Score of 3 (fair) or 4 (poor) on the Roles and Maudsley Scale
- ix. Willingness to refrain from the following painful heel related, concomitant therapy: iontophoresis; electro-myostimulation; ultrasound; NSAIDs; steroid injections or surgery - Until Visit 6 (3 months) of this study (shoe modifications and rescue pain medication are allowed during the entire

study)

- x. Willingness to keep a Subject Heel Pain Medication and Other Heel Pain Therapy Diary until 12 months after the last treatment
 - xi. Females of childbearing potential may be entered if they provide a negative urine pregnancy test immediately before the first ESWT treatment
 - xii. Willingness of females of childbearing potential to use contraceptive measures for 2 months after enrollment into the study
- b. Patients were not permitted to enroll in the clinical study if they met any of the any of the following exclusion criteria:
- i. Inflammation of the lower and upper ankle
 - ii. History of rheumatic diseases, and/or collagenosis and/or metabolic disorders
 - iii. Patients with a history of hyperthyroidism
 - iv. Active malignant disease with or without metastases
 - v. Patients suffering from Paget disease or calcaneal fat pad atrophy
 - vi. Patients suffering from Osteomyelitis (acute, sub-acute, chronic)
 - vii. Patients suffering from fracture of the Calcaneus
 - viii. Patients with an immunosuppressive therapy
 - ix. Patients with a long-term (≥ 6 months duration) treatment with any corticosteroid
 - x. Patients suffering from insulin-dependent diabetes mellitus, severe cardiac, or respiratory disease
 - xi. Patients suffering from coagulation disturbance and/or therapy with Phenprocoumon, Acetylsalicylic acid, or Warfarin
 - xii. Bilateral painful heel, if both feet need medical treatment
 - xiii. Patients who, at entry, are known to have treatment planned within the next 8 weeks, which may abruptly alter the degree or nature of pain experienced such that the extracorporeal shock wave therapy will no

longer be necessary (e.g., surgery)

- xiv. Time gap of less than:
 - 6 weeks since the last corticosteroid injection
 - 4 weeks since the last anesthetic injection; iontophoresis, ultrasound, and electro-myostimulation
 - 1 week since the last NSAIDs
 - 2 days since the last prescription or non-prescription analgesics, heat, ice, massage, stretching, night splinting, and orthosis
- xv. Previous surgery of the painful heel syndrome
- xvi. Previous unsuccessful treatment of the painful heel with a similar shock wave device
- xvii. History of allergy or hypersensitivity to bupivacaine or local anesthetic sprays
- xviii. Patients with significant abnormalities in hepatic function
- xix. Patients in a poor physical condition
- xx. Pregnant female
- xxi. Active infection or history of chronic infection in the treatment area
- xxii. History or documented evidence of peripheral neuropathy such as nerve entrapment, tarsal tunnel syndrome, etc.
- xxiii. History or documented evidence of systemic inflammatory disease such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, aseptic bone necrosis, Reiter's syndrome, etc.
- xxiv. History or documented evidence of worker's compensation or litigation
- xxv. Participation in an investigational device study within 30 days prior to selection, or current inclusion in any other clinical study or research project
- xxvi. Patients who, in the opinion of the investigator, will be inappropriate for inclusion into this clinical study or will not comply with the requirements of the study
- xxvii. Patients with implanted pacemakers, insulin pumps, defibrillators, and/or neuro-stimulators

- xxviii. Patients with prosthetic devices implanted in the area of treatment
- xxix. Patients with open wounds or skin rashes
- xxx. Patients suffering from tendon rupture, neurological, or vascular insufficiencies of the painful heel, as assessed using the Semmes-Weinstein Monofilament test and the Ankle Brachial Index

2. Follow-up Schedule

All patients were scheduled to return to follow up examination at Visits 5 (6 week) and 6 (3 month) after the last treatment session (Visit 4 ; 2 week after the last ESWT treatment session).

a. Patient Eligibility for Long Term Follow Up (FII):

Patients defined as "responders" according to the definitions provided below were also being followed at Visits 7 (6 month) and 8 (12 month).

A responder was defined as follows:

- A patient whose percentage decrease of heel pain was greater than 60 percent from baseline to Visit 6 (3 months) for at least two (2) of the three heel pain (VAS) measurements, or
- A patient that fulfilled three (3) conditions at the 3 month follow up visit (Visit 6): (1) Able to return to work, (2) satisfied with the treatment outcome, and (3) required no concomitant therapy to control heel pain

In addition, all patients with at least one FII visit were included in the long term follow up analysis. There were no exclusion criteria.

b. Study Procedures

The primary follow-up visit for comparison of the Duolith SD1 and the placebo-controlled sham groups is 3 months after the last treatment (Visit 6, 3 months after randomization). At this visit, the decision was made whether a patient had a sufficient response to the extracorporeal shock wave treatment to continue in the study. Sufficient response was considered as a reduction in pain larger than 60% on at least two (2) of the three (3) VAS measurements or, if the reduction in pain was < 60%, then the patient must be able to work and complete activities of daily living, must be satisfied with the outcome of the treatment, and must not require any other treatment to control heel pain. Patients who showed sufficient response to the treatment during the follow-up I period (visit 6) continued in the follow-up II period (visit 8). Otherwise, the patient was discontinued from the study and may receive further treatment for painful heel as necessary.

Patients who consented to enrollment were randomized but were blinded to treatment assignment. The treatment was repeated three (3) times approximately one week (± 4 days) apart (at Visits 1 or 2, 3, and 4). The study procedures, except for the treatment devices, were the same for all patients. The protocol specified up to 2000 impulses at each of the three (3) treatment visits. Follow up for all patients consisted of Visits 5 and 6. Subjects defined as responders are also being followed at Visits 7 (6 month) and 8 (12 Month). A responder is a patient who fulfills the conditions as stated above. Safety and effectiveness data were analyzed through the Visit 6 (3 months) follow up performed for all subjects and the 12 month follow up of responders.

In general, therapy was performed without local anesthesia. Due to a possible pain sensation caused by the shock wave treatment, the applied energy was increased smoothly from lowest energy level of 0.01 mJ/mm^2 up to a level of 0.25 mJ/mm^2 within the first 500 impulses. After these 500 introductory impulses, 2000 treatment impulses were performed with the regular working application level of 0.25 mJ/mm^2 . Only one subject in the Duolith Group required local anesthesia at Visit 2 (baseline visit with first ESWT application).

Post-operative parameters measured during the study included the following:

At Visit 5: Follow-Up I (6 weeks ± 1 week after the last ESWT treatment)

- Investigation of the primary criteria (VAS, Roles and Maudsley-Score)
- Investigation of the secondary criteria (analgesic medication consumption)
- Safety Criteria: Adverse reactions related to previous ESWT and local anesthesia
- Assessment of local tissue effects
- Documentation of concomitant therapy and medication
- Review entries in the Subject Heel Pain Medication and Other Painful Heel Therapy Diary and reissuing

Visit 6: Primary Endpoint: Follow-Up I (3 month ± 7 days after the last ESWT treatment)

- Physical examination
- Vital signs
- Investigation of the primary criteria (VAS, Roles and Maudsley-Score)

- Investigation of the secondary criteria (analgesic medication consumption, Physician's Judgment; Subject's Satisfaction, and Subject's Treatment Recommendation)
- Safety Criteria: Investigator's global assessment of tolerability
- Response to ESWT treatment
- Assessment of local tissue effects
- Subject's satisfaction and treatment recommendation, Physician's judgment
- Record Adverse Events (AE)/Serious Adverse Events (SAE)
- Documentation of concomitant therapy and medication
- Review entries in the Subject Heel Pain Medication and Other Painful Heel Therapy Diary

Visit 7: Follow-Up II (6 month \pm 1 month after the last ESWT treatment)

- Investigation of the primary criteria (VAS, Roles and Maudsley-Score)
- Investigation of the secondary criteria (analgesic medication consumption)
- Assessment of local tissue effects
- Record AE/SAE
- Documentation of concomitant therapy and medication
- Review entries in the Subject Heel Pain Medication and Other Painful Heel Therapy Diary

Visit 8: Secondary Endpoint: Follow-Up II (12 months \pm 1 month after the last ESWT treatment)

- Investigation of the primary criteria (VAS, Roles and Maudsley-Score)
- Investigation of the secondary criteria (analgesic medication consumption,

- Physician's Judgment; Subject's Satisfaction and Subject's Treatment Recommendation)
- Safety Criteria: Investigator's global assessment of tolerability
- Response to ESWT treatment
- Assessment of local tissue effects
- Record AE/SAE
- Documentation of concomitant therapy and medication

Adverse events and complications were recorded at all visits. The key time points are shown below in the tables for safety and effectiveness (Tables 7-12).

3. Clinical Endpoints

a. Safety:

Safety endpoints were adverse events (type, intensity, severity, relationship to treatment, etc.) and the investigator's rating of treatment tolerability. The safety population consisted of all subjects receiving at least one (1) treatment.

b. Effectiveness:

The determination of effectiveness was based on two (2) criteria: a composite score for pain (using a 10 cm or 100 mm visual analog scale) and Roles and Maudsley scores when measured at the 3-month follow up visit (Visit 6). The composite score is the sum of three (3) pain measurements for the following:

- i. Heel pain when taking the first steps of the day
- ii. Heel pain while doing daily activities
- iii. Heel pain after application of a standardized pressure device (F-meter)

Heel pain after application of a standardized pressure device (F-Meter) was based on the subject-specific force level at Visit 2 (baseline visit with first ESWT application). Using this same pressure at subsequent visits, the pain level was assessed using the same anchored VAS.

The second primary criterion for effectiveness was the four (4) point Roles and Maudsley score (JBJS(A) 1972; Aug 54 3; 499-508) as follows:

- i. Excellent (No pain, full movement, full activity)
- ii. Good (Occasional discomfort, full movement, and full activity)
- iii. Fair (Some discomfort after prolonged activity)

- iv. Poor (Pain limiting activities)

There were eight (8) secondary criteria for effectiveness criteria as follows:

- i. Physician's Global Judgment of Effectiveness at Visits 6 (3 month) and 8 (12 month) rated as very good (0), good (1), moderate (2), unsatisfactory (3), or poor (4)
- ii. Satisfaction with the Outcome of the Treatment as rated by subjects on a 7-Point Numeric Rating Scale (at Visit 6 and 8 only) rated as very dissatisfied (-3), moderately dissatisfied (-2), slightly dissatisfied (-1), neutral (0), slightly satisfied (1), moderately satisfied (2), or very satisfied (3)
- iii. Willingness to recommend treatment as judged by patient (at visit 6 and 8 only): Yes/No
- iv. Patient's analgesic medication consumption for painful heel (Acetaminophen (Tylenol[®]), Non-prescription analgesics, Prescription analgesics, or others as specified in concomitant therapy form in the Case Report Form (CRF) and patient's diary)
- v. Heel pain overall success defined as percentage decrease of heel pain (VAS) larger than 60% from baseline at the 3 month follow up visit (Visit 6) for at least two (2) of the three (3) heel pain measurements.
- vi. Heel pain single success when taking the first steps of the day defined as percentage decrease of heel pain (VAS) larger than 60 % from baseline at the 3 month follow up visit (Visit 6)
- vii. Heel pain single success while doing daily activities defined as percentage decrease of heel pain (VAS) larger than 60 % from baseline at 3 month follow up visit (Visit 6)
- viii. Heel pain single success after application of a standardized pressure device (F- meter) defined as percentage decrease of heel pain (VAS) larger than 60 % from baseline at 3 month follow up visit (Visit 6)

The intent-to-treat (ITT) population consisted of all subjects who received at least one treatment and who had at least one evaluation visit. Missing values were handled using the Last Observation Carried Forward (LOCF) technique.

B. Accountability of PMA Cohort

Patients were randomized immediately before treatment at Visit 1 (before first application of ESWT) or Visit 2 (baseline visit with first ESWT application) using a block randomization scheme with sealed randomization envelopes. At the time of database lock, there were 126 subjects assigned to the Duolith Group and 124 subjects assigned to the Placebo Group. Treatment allocation and the numbers of subjects in each of the data sets (safety population, intent-to-treat population (ITT), and per-protocol population (PP)) are summarized in Table 3 below. A total of 17 subjects discontinued the study prematurely before Visit 6 (3 month) (Duolith Group: 7 subjects, Placebo Group: 10 subjects). Reasons for premature discontinuation are summarized by

treatment group in Table 4 below.

Table 3: Distribution of Subjects by Treatment Group and Data Set

Data Set	Number of Subjects (Percent of Subjects)		
	Duolith Group	Placebo Group	Total Subjects
Safety Population	126	124	250 (100%)
ITT Population	125 (99.2%)	121 (97.6%)	246 (98.4%)
PP Population	122 (96.8%)	117 (94.4%)	239 (95.6%)

Missing values were handled using Last Observation Carried Forward (LOCF) technique.

Table 4: Reasons for Premature Discontinuation of Patients in the Safety Population (by Treatment Group)

Reason for Premature Discontinuation	Duolith Group (N=126)	Placebo Group (N=124)	Total (N=250)
Worsening of condition	2 (1.6%)	4 (3.2%)	6 (2.4%)
Adverse Event	2 (1.6%)	1 (0.8%)	3 (1.2%)
Worsening of condition and Adverse Event	1 (0.8%)	2 (1.6%)	3 (1.2%)
Administrative Reason	0	2 (1.6%)	2 (0.8%)
Lost to follow-up	2 (1.6%)	1 (0.8%)	3 (1.2%)
Total	7 (5.6%)	10 (8.1%)	17 (6.8%)

C. Study Population Demographics & Baseline Parameters

The demographics of the study population are typical for a primary study performed in the U.S. A tabular summary of subject demographics and baseline characteristics for the ITT population is provided by treatment group in Table 5 and a summary of the baseline characteristics for the efficacy criteria is provided in by treatment group Table 6. Differences between groups in demographic and baseline characteristics are minimal and the largest effect size (0.56 observed for age) is categorized as "small."

Table 5: Summary of Demographic and other Baseline Characteristics by Treatment Group- ITT Population

Baseline Characteristics		Duolith Group (N= 125)	Placebo Group (N= 121)	Effect Size Mann-Whitney*
Age (Years)	Mean(SD, Range)	50.0 (11.18, 27 - 79)	47.4 (10.63, 23 - 77)	0.5600
Gender: Number of subjects (% of subjects)	Male	40 (32.0 %)	33 (27.3 %)	0.4764
	Female	85 (68.0 %)	88 (72.7 %)	
Ethnic Origin:	White	111 (88.8 %)	104 (86.0 %)	Not

Number of subjects (% of subjects)	American Indian	4 (3.2 %)	1 (0.8 %)	Applicable
	Asian	4 (3.2 %)	4 (3.3 %)	
	African	5 (4.0 %)	6 (5.0 %)	
	Hispanic	1 (0.8 %)	5 (4.1 %)	
	Other	0 (0.0 %)	1 (0.8 %)	
Height (cm)	Mean (SD, Range)	169.5 (10.73, 145-193)	168.9 (9.65, 150-191)	0.5090
Weight (kg)	Mean(SD, Range)	82.1 (18.76, 48-148)	84.5 (23.89, 50-204)	0.4861
BMI (kg/m ²)	Mean(SD, Range)	28.6 (6.18, 18.0-56.0)	29.5 (7.19, 19.3-60.2)	0.4731
Systolic B/P (mmHg)	Mean(SD, Range)	124.1 (13.53, 90-172)	123.1 (12.76, 96-170)	0.5120
Diastolic B/P (mmHg)	Mean(SD, Range)	77.3 (8.77, 58- 108)	78.2 (8.27, 55- 104)	0.4690
Heart Rate (B/min)	Mean(SD, Range)	69.0 (10.45, 47-102)	70.1 (9.78, 52- 91)	0.4644
Activity: Number of subjects (% of subjects)	Sedentary	7 (5.6 %)	14 (11.6 %)	0.5120
	Active	101 (80.8 %)	87 (71.9 %)	
	Athletic	17 (13.6 %)	20 (16.5 %)	
Duration of Painful Heel: Number of subjects (% of subjects)	6 to 12 Months	40 (32.0 %)	37 (30.6 %)	0.4913
	> 12 Months	38 (30.4 %)	37 (30.6 %)	
	> 24 Months	47 (37.6 %)	47 (38.8 %)	
The Mann-Whitney estimator is the corresponding standardized effect size measure of the Wilcoxon-Mann-Whitney test, benchmarks: 0.5 equality, 0.44/0.56 small, 0.36/0.64 medium-sized, 0.29/0.71 large group difference.				

Table 6: Summary of Baseline Efficacy Characteristics by Treatment Group - ITT Population

Baseline Characteristics		Duolith Group (N = 125)	Placebo Group (N= 121)	Effect Size Mann-Whitney
Heel Pain (VAS) First Steps	Mean (SD; Range)	7.9 (1.55; 4.0- 10.0)	8.0 (1.61; 3.0 -10.0)	0.5066
Heel Pain (VAS) Daily Activities	Mean (SD; Range)	7.9 (1.55; 5.0- 10.0)	7.9 (1.51; 5.0- 10.0)	0.5087
Heel Pain (VAS) After F-Meter	Mean (SD; Range)	9.3 (1.25; 5.0- 10.0)	9.3 (1.28; 5.0- 10.0)	0.4907

Heel Pain (VAS) Composite Score	Mean (SD; Range)	8.38 (0.996; 5.30- 10.00)	8.38 (1.016; 5.30- 10.00)	0.5084
Roles and Maudsley	Mean (SD; Range)	3.6 (0.49; 3.0- 4.0)	3.7 (0.48; 3.0- 4.0)	0.5184
The Mann-Whitney estimator is the corresponding standardized effect size measure of the Wilcoxon-Mann-Whitney test, benchmarks: 0.5 equality, 0.44/0.56 small, 0.36/0.64 medium-sized, 0.29/0.71 large group difference.				

Treatment Characteristics: A majority of subjects in both groups completed the treatments without deviations (Duolith Group: 98.4%; Placebo Group: 98.4%). Five (5) subjects (Duolith Group: 2; Placebo Group: 3) were reported with treatment-related deviations at six (6) treatment sessions. Only one (1) subject in the Duolith Group required anesthesia for the second treatment visit.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the evaluable cohort of 250 patients available for 3 month evaluation. The key safety outcomes for this study are presented below in Tables 7 to 9.

Treatment Tolerability: The clinician's judgment of treatment tolerability (a safety endpoint) was rated as "very good" or "good" in 89.1% (106/119) of the patients in the Duolith Group and in 91.2% (104/114) patients in the Placebo Group at Visit 6 (3 months). This was based on the investigator's global rating of treatment tolerability. The difference between the two (2) treatment groups for tolerability was only 2.1 percentage points in favor of the Placebo Group (P = 0.1434, two-sided Wilcoxon-Mann-Whitney test, MW = 0.4522, LB-CI = 0.3888). However, 74.4% (n=93 patients) of the Duolith Group and 71.1% (n= 86 patients) in the Placebo Group required one or more concomitant analgesic medications during the study.

A total of 101 adverse events (77 events in the Duolith group and 24 in the placebo group) in 250 patients (126 in Duolith and 124 Placebo groups) were reported during the main study (enrollment through Visit 6 or 3 months). Adverse events reported for the Duolith SD 1 consist primarily of pain or discomfort during and after treatment. Events are summarized by treatment group and event category in the Table 7 below.

Table 7: Summary of Number and Percent of Adverse Events by Category and Treatment Group- Safety Population

Category	Duolith Group (n=126)		Placebo Group (n=124)		Total	
	Number of events	Percent of events	Number of events	Percent of events	Number of events	Percent of events

1	Pain and/or Discomfort During Treatment	39	50.7	3	12.5	42	41.6
6	Swelling	5	6.5	0	0.0	5	5.0
7	Pain After Treatment	21	27.3	8	33.3	29	28.7
8	Other	12	15.6	13	54.2	25	24.8
	Total	77		24		101	

In the Duolith Group, a total of 77 events were reported for 43/126 subjects (76.2 % of 101 adverse events; 34.1% of 126 subjects). In the Placebo Group, a total of 24 events were reported for 17/124 subjects (23.8% of 101 adverse events; 13.7% of 124 subjects). Pain and/or discomfort occurring during or after treatment represent 60 events in the Duolith Group (60 of 77 events; 77.9 %) and 11 events in the Placebo Group (11 of 24 events; 45.8 %). Swelling was observed only in the Duolith Group (5 of 77 events; 6.5 %). These differences are logical since subjects in the Duolith Group received active shock wave therapy.

Table 7 shows a total of 25 events among 250 patients were categorized as "other" (Duolith Group: 12 events, Placebo Group: 13 events). These events, their rated intensity, relationship, and seriousness are listed by treatment group in Table 8 below. Of these 25 events, none in the Duolith Group were rated as related to treatment. In the Placebo Group, however, two (2) events were rated as possibly related and for two (2) events the relationship was rated as doubtful.

Table8: Listing of "Other" Adverse Events by Treatment Group

Event Description	Intensity	Relation	Serious
Duolith Group			
bone fracture spontaneous	Severe	not related	No
false sensation	Moderate	not related	No
inflicted injury	Mild	not related	No
inflicted injury	Moderate	not related	No
inflicted injury	Moderate	not related	No
inflicted injury	Severe	not related	No
influenza-like symptoms	Mild	not related	No
Neuropathy peripheral	Mild	not related	No
Pneumonia	Severe	not related	Yes
Pyelonephritis	Severe	not related	Yes
Sinusitis	Mild	not related	No
Sinusitis	Mild	not related	No
Placebo Group			
bone fracture spontaneous	Moderate	not related	No
Bronchitis	Mild	not related	No
inflicted injury	Moderate	not related	No

inflicted injury	Severe	not related	No
joint pain	Severe	not related	No
painful heel	Moderate	possible	No
painful heel	Severe	not related	No
tendon disorder	Moderate	possible	No
tendon disorder	Moderate	doubtful	No
tendon disorder	Moderate	doubtful	No
tendon disorder	Moderate	not related	No
tooth ache	Moderate	not related	No
upper respiratory tract infection	Moderate	not related	No

For adverse events categorized as "other," there were 12 events in the Duolith Group (12 of 77; 15.6%) and 13 events in the Placebo Group (13 of 24 events; 54.2 %). Six (6) adverse events were reported for four (4) subjects during the long term follow up period of 12 months. No event was serious but one (1) subject discontinued during study participation during long term follow up due to ankle pain*. These events are summarized in Table 9 below:

Table9: Adverse Events During Long Term Follow Up (by Treatment Group)

Group	Reported Term	Intensity	Relation	Serious
Duolith	Sinus infection, took antibiotics	Moderate	Not Related	No
	Reaction to antibiotics - allergy	Moderate	Not Related	No
	Respiratory system involved with Asthma attack	Moderate	Not Related	No
Placebo	Fracture of 5 metatarsals while vacationing	Moderate	Not Related	No
	Patient believes he developed ankle pain*	Mild	Doubtful	No
	Feels ankle hurts from repositioning**	Moderate	Probable	No

*Either non-related or due to repositioning of ankle during sham treatment

**Repositioning of ankle during sham treatment

2. Effectiveness Results

The analysis of effectiveness was based on the 246 evaluable patients (ITT population) at the 3 month time point. Key effectiveness outcomes are presented in Tables 10 to 12. Results for the primary effectiveness criteria are statistically significant ($P < 0.025$ one-sided). All sensitivity analyses agreed with confirmatory results and showed statistically significant results. The same trend was demonstrated across study centers. A summary of changes in the median VAS composite score of heel pain and changes in the Roles and Maudsley Score is provided in Table 10 and 11 below.

Table10: Summary Comparison of Baseline and Visit 6 (3 months) Composite VAS Score for Pain with Score Correction* by Treatment Group- ITT Population (LOCF)

Composite VAS	Duolith Group (N=125)			Placebo Group (N=121)		
	Baseline	Visit 6	Change (%)	Baseline	Visit 6	Change (%)
Mean	8.38	3.80	-54.53	8.38	5.01	-40.31
Median	8.30	2.70	-69.20	8.30	5.30	-34.50
SD	0.996	3.247	38.495	1.016	3.400	39.968
Min	5.30	0.00	-100.00	5.30	0.00	-100.00
Max	10.00	10.00	43.80	10.00	10.00	37.50

*Score Correction for interfering analgesic therapy as defined in the statistical analysis plan

Using the Wilcoxon-Marm-Whitney, one-sided test for superiority, the results of the Duolith Group were determined to be superior to the Placebo Group (P = 0.0027 one-sided, MW = 0.6026, LB-CI = 0.5306). The mean Roles and Maudsley score was reduced from 3.6 to 2.5 in the Duolith Group and from 3.7 to 2.9 in the Placebo Group, with a final group difference for Roles and Maudsley scores of 0.4 in favor of the Duolith Group.

Table11: Comparison of Baseline and Visit 6 (3 months) Roles and Maudsley Scores with Score Correction* by Treatment Group- ITT Population (LOCF)

Composite VAS	Duolith Group (N=125)			Placebo Group (N=121)		
	Baseline	Visit 6	Change	Baseline	Visit 6	Change
Mean	3.6	2.5	-1.1	3.7	2.9	-0.8
Median	4.0	2.0	-1.0	4.0	3.0	-1.0
SD	0.49	0.94	1.02	0.48	0.97	0.92
Min	3.0	1.0	-3.0	3.0	1.0	-3.0
Max	4.0	4.0	1.0	4.0	4.0	1.0

*Score Correction for interfering analgesic therapy as defined in the statistical analysis plan

Using the Wilcoxon-Mann-Whitney, one-sided test for superiority, the results for the Duolith Group were determined to be superior to the Placebo Group (P = 0.0006 one-sided, MW = 0.6135, LB-CI = 0.5466).

Secondary Effectiveness. Results for secondary effectiveness criteria are summarized for the ITT population in Table 12 below.

Table12: Summary of Secondary Effectiveness Results by Treatment Group

Secondary Effectiveness Criterion	Rating/Result	Duolith Group Number of subjects (n=119) (Percent of subjects)	Placebo Group Number of subjects (n=114) (Percent of subjects)
Investigator's Global Judgment of Effectiveness at Visit 6 (3 months)	Very good	46 (38.66%)	41 (35.96%)
	Good	42 (35.29%)	21 (18.42%)
	Moderate	11 (9.24%)	11 (9.65%)
	Unsatisfactory	11 (9.24%)	16 (14.04%)
	Poor	9 (7.56%)	25 (21.93%)
Subject's global judgment of therapy Satisfaction	Very unsatisfied	9 (7.56%)	18 (15.79%)
	Moderately unsatisfied	13 (10.92%)	20 (17.54%)
	Less satisfied	6 (5.04%)	9 (7.89%)
	Neutral	15 (12.61%)	18 (15.79%)
	In general satisfied	19 (15.97%)	11 (9.65%)
	Satisfied	29 (24.37%)	17 (14.91%)
	Very satisfied	28 (23.53%)	21 (18.42%)
Subject's recommendation of therapy to a friend	Yes	95 (79.83%)	68 (59.65%)
	No	24(20.17%)	46 (40.35%)
Heel Pain Overall Success (larger than 60% from baseline at visit 6 (3 month) for at least two (2) of the three (3) heel pain (VAS) measurements	Success	68 (54.40%)	45 (37.19%)
	Failure	57 (45.60%)	76 (62.81%)
Heel pain single success when taking first steps of the day (percentage decrease of heel pain (VAS) measurements larger than 60% from baseline at visit 6 (3 month follow up))	Success	63 (50.40%)	44 (36.36%)
	Failure	62 (49.60%)	77 (63.64%)
Heel pain single success	Success	62 (49.60%)	47 (38.84%)

Secondary Effectiveness Criterion	Rating/Result	Duolith Group Number of subjects (n=119) (Percent of subjects)	Placebo Group Number of subjects (n=114) (Percent of subjects)
while doing daily activities (percentage decrease of heel pain (VAS) measurements larger than 60% from baseline at visit 6 (3 month follow up))	Failure	63 (50.40%)	74 (61.16%)
Heel pain single success after application of a standardized pressure device (F-meter) (percentage decrease of heel pain (VAS) measurements larger than 60% from baseline at visit 6 (3 month follow up))	Success	67 (53.60%)	51 (42.15%)
	Failure	58 (46.40%)	70 (57.85%)
Frequency count of subjects with at least one concomitant analgesic therapy during the study	No	32 (25.60%)	35 (28.93%)
	Yes	93 (74.40%)	86 (71.07%)

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

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

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The results of primary effectiveness criteria in composite VAS showed statistically significant pain reduction when the VAS pain scores were compared between treatment and placebo groups. The results of the Duolith group were found to be slightly superior to the placebo group ($p < 0.025$, one-sided) in terms of pain relief.

B. Safety Conclusions

A total of 77 adverse events in the Treatment Group and 24 adverse events in the

Placebo-Controlled Sham Group were reported through Visit 6 at 3 month. The adverse events primarily consist of pain or discomfort during and after treatment. Of the twenty five (25) events reported as "other" and listed in the Table 7 none were related to the treatment in the Duolith group, but two (2) events in the Placebo Group were rated as possibly related and two (2) events were rated as doubtful. It can be concluded therefore, the Duolith SD1 Shock Wave Therapy Device and the treatment for pain due to plantar fasciitis is safe.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The preclinical and clinical data presented in this PMA provide reasonable assurance that the Duolith SD1 is safe when used according to the device labeling.

The results of the multi-center, randomized, placebo controlled, double-blind clinical study demonstrate that treatment of heel pain due to chronic proximal plantar fasciitis with the Duolith SD1 may provide relief for up to 12 weeks duration in a significant proportion of the patient population who have previously failed conservative treatment for 6 months or more. The most likely side effect is pain during/after treatment which was reported by 50.7% of patients in the Duolith Group and 41.6% of patients on the Placebo-Controlled Sham Group. For this study 74.4% of the Duolith Group and 71.07% of the Placebo-Controlled Sham Group required one or more concomitant analgesic therapy during the study. The clinical data from the study demonstrate that the efficacy of the device outweighs the risk and the device is safe and effective for patients having symptoms of chronic proximal plantar fasciitis, for 6 months or more, and a history of unsuccessful conservative therapy.

XIII. CDRH DECISION

CDRH issued an approval order on January 8, 2016.

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

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See Approval Order