SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

DEVICE GENERIC NAME:	Orthopedic Extracorporeal Shock Wave Therapy Device
DEVICE TRADE NAME:	Orthospec™ Orthopedic ESWT
APPLICANT'S NAME AND ADDRESS:	Medispec Ltd. 12850 Middlebrook Road, Suite 1 Germantown, MD 20874 Phone: 301-944-1575 Fax: 301-972-6098
PREMARKET APPROVAL APPLICATION (PMA) NUMBER:	P040026
DATE OF PANEL RECOMMENDATION:	None
DATE OF NOTICE OF APPROVAL TO THE APPLICANT:	April 1, 2005

II. INDICATIONS FOR USE

Orthospec™ Extracorporeal Shock Wave Therapy (ESWT) is indicated for the treatment of Proximal Plantar Fasciitis with or without heel spur in patients 18 years of age or older. Orthospec™ ESWT is a non-invasive alternative method for patients with symptoms of Proximal Plantar Fasciitis for 6 months or more and a history of unsuccessful conservative therapies to relieve heel pain.

Proximal Plantar Fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the plantar calcaneal tuberosity.

III. CONTRAINDICATIONS

Use of the Orthospec™ is contraindicated in the following situations:

1. Over or near bone growth centers until bone growth is complete.
2. When a malignancy is known to be present in or near the treatment area.
3. Over ischemic tissues in individuals with vascular disease where the blood supply would be unable to follow the increase in metabolic demand and tissue necrosis may result.
4. Patient has coagulation disorder or is taking anticoagulant medications, either for acute or chronic anticoagulant therapy.
5. Patient has infection at the area to be treated with Orthospec™. This is due to the risk of spreading infection.
6. This product contains natural rubber latex which may cause allergic reactions.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the physicians labeling.

V. DEVICE DESCRIPTION

The Orthospec™ Extracorporeal Shock Wave Therapy device provides a non-invasive method of therapy for the treatment of Proximal Plantar Fasciitis with or without heel spur. The Orthospec™ employs an electro-hydraulic, or "spark gap" method of creating the shock wave. With this technique, an electrode (spark plug) ignites an electrical charge within a water-containing stainless steel semi-ellipsoid chamber and contact membrane, evaporating a small portion of the water and creating a shock wave reflecting outward off the ellipsoid. The shock wave is generated within the reflector chamber and transmitted through the skin surface of the patient to the treatment site. The reflector chamber is an apparatus used to apply the shock wave to the treatment zone. Water enters the chamber through an intake valve that is controlled from the control panel. The water cushion can be inflated or deflated from the control panel to assure contact with the skin. This chamber must remain filled during the treatment procedure.

The energy of the shock wave can be adjusted between levels 1 and 7. The frequencies of shock waves are 96, 120 and 160 shocks per minute. Coupling solution is used on both the contact membrane and the patient's skin to enhance conductivity. The device has a linear motor for height adjustment and casters for lateral positioning of the reflector towards the treatment area. Imaging or sedation is not required with use of the Orthospec™.

The Orthospec™ is a portable, self-contained unit and does not require special installation. The operational platform consists of a cast iron base with a high voltage generator, contained in a locked cabinet, operating from a standard 115 or 230 voltage electrical wall socket. The major components consist of the Main Frame, Shock Wave Head and Control Panel.

Main Frame

The main frame is a single, mobile unit that cases the high voltage generator. It includes the shock wave unit and control panel.

Shock Wave Head

The Shock Wave Head is integrated within the main frame. It consists of a stainless steel semi-ellipsoid reflector, a dry natural rubber membrane filled with water, an underwater electrode, and a high voltage power supply. These components together form a water chamber in which the shock wave is generated. The shock wave is generated from the electrode by an electric spark and transmitted to the treatment site via the contact membrane.

Control Panel

The control panel allows for the operation of the device. It is a touch panel built with an array of switches with transparent regions through which the system indication lights and displays can be seen. The main power key switch, energy and frequency levels, water inflate and deflate operation, height control and shock wave counter are all functions of the control panel.

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VI. ALTERNATIVE PRACTICES AND PROCEDURES

Conservative therapies to treat Plantar Fasciitis consist of physical therapy, anti-inflammatory pharmaceuticals, steroid injections, deep heat treatments, and orthotics. Surgical options include endoscopic plantar fasciotomy or open plantar fascia release.

VII. MARKETING HISTORY

The Orthospec™ device has been commercially marketed and sold in over 25 countries outside the United States since 1998. Currently there are 65 devices placed in 25 countries around the world including, Europe, Asia, and South America. The Orthospec™ system been recalled for safety and/or effectiveness reasons.

VIII. ADVERSE EVENTS OF THE DEVICE ON HEALTH

ADVERSE EVENTS

During the Orthospec™ clinical study, there were 3 reported cases of adverse events out of 172 treated patients. They included two cases of bruising and one case of mild local swelling observed by the patient but not by the physician. None of the adverse events was severe, and none required medical intervention or subsequent medical care.

Summary of All Adverse Events			
	Orthospec™ (N = 115) n (%)	Placebo (N = 57) n (%)	P-Value
Any Adverse Event	3 (2.6%)	0 (0%)	0.55
Bruising	2 (1.7%)	0 (0%)	1.0
Mild local swelling	1 (0.9%)	0 (0%)	1.0

POTENTIAL ADVERSE EVENTS

Potential adverse events when using the Orthospec™ device include:

- Pain during ESW treatment
- Petechia
- Superficial hematoma
- Neurosensory conditions (Hypesthesia or Paresthesia)
- Rare allergic or sensitivity reaction to the Latex membrane or to the coupling solution applied to the skin during treatment
- Tendon rupture

IX. SUMMARY OF PRECLINICAL STUDIES

Shock Wave Characterization (Pressure Measurements)

Shock Wave Characterization Produced by the Orthospec™ Shock wave pressure measurements were performed in accordance with IEC 61846, "Ultrasonics - Pressure pulse lithotripters - Characteristics of fields" (1998). The Orthospec™ was typically configured with a fluid-filled membrane and a 25 um spot-poled membrane-type Polyvinylidene Difluoride PVDF hydrophone with a 0.5 mm geometrical diameter.

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Measurements of the shock wave field were based on an average of over thirty measurements at the focal location. The mean peak positive pressure and mean peak negative pressure were 340±127 bar and 49±15 bar, respectively, at 24kV. From the integration of the pressure-time waveform, and the scans through the focal region, the integrated energy per pulse was 0.11 J at 24kV.

Calculations of the focal energy per pulse were based upon equation 3 in Clause 7.3.3 of IEC 61846. The measurement was conducted by integrating over the focal plane in an approach similar to that used to measure diagnostic ultrasound equipment. The measured pressure-time waveforms were squared to get pressure-squared vs. time, and then integrated.

In order to measure the rise time and pulse duration of the shock waveform, the measurement was repeated with the oscilloscope sampling rate increased to 100 Msmp/s. From a series of measurements, the average rise time was 400±100 ns; the average pulse width was 1200±45 ns.

These results indicate that the device was designed to produce output characteristics that fall within the range of those used in extracorporeal shock wave lithotripsy. Preclinical data was extracted from the animal study using the Medispec Econolith™ Shockwave Lithotripsy System (P950043). The intended use for the Econolith™ Shockwave Lithotripsy System is for internal tissues, to fragment upper urinary tract calculi, which provides much more energy and pressure than the Orthospec™, intended for orthopedic applications. The Orthospec™ ESWT device is a low energy shock wave modification of the Econolith™ Shockwave Lithotripsy System by Medispec, Ltd. Medispec, Ltd. includes this study as part of the Orthospec™ PMA based on its FDA approval as a validated demonstration of safety and effectiveness. The animal study was conducted under more severe energy and intensity parameters than the Orthospec™. Both devices work on the same range of voltage, however for orthopedic applications, the shock wave pressure is greatly reduced from that utilized in kidney stone treatments (ESWL). Soft tissue effects of the lower energy shockwaves were quantified in animal studies. Based on these soft tissue animal study results, Medispec, Ltd. developed their performance parameters for the Orthospec™ device.

Standards Testing

Testing was conducted on the Orthospec™ ESWT to demonstrate compliance with IEC 60601-1[1], IEC 60601-2-36[2], IEC 60601-1-2[3], ISO 14971[4] and IEC 61846[5].

In Vitro and Animal Studies

Animal study data and acoustic characteristic data were extracted from the FDA approved PMA P950043 of the Econoltih Lithotripter Shock Wave Lithotripsy System to show both safety and effectiveness. Both devices are technically equivalent in terms of the primary component, the Shock Wave Generator, and functionality. The Econolith's applied use is for internal tissues to fragment upper urinary tract calculi, thus the Orthospec™ uses less energy and less pressure on less sensitive body tissue during treatment than the Econolith™ Lithotripter, which uses more energy and operates on more sensitive tissue of the body.

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[1] IEC 60601-1: Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use, Part 1: General Requirements

[2] IEC 601-2-36: Medical Electrical Equipment Part 2: Particular Requirements for the Safety of Equipment for Extracorporally Induced Lithotripsy

[3] IEC60601-1-2: Medical Electrical Equipment Part 1- 2: General Requirements for Safety-Collateral Standard: Electromagnetic Electric Systems Compatibility

[4] ISO 14971: Medical Devices – Application of Risk Management to Medical Devices

[5] IEC 61846: Ultrasonics – Pressure Pulse Lithotripters – Characteristics of Field (1998).

X. SUMMARY OF CLINICAL STUDIES

Clinical Investigation

Study Design

A multicenter, double-blind, randomized, placebo-controlled clinical investigation of 172 patients was conducted to determine the safety and effectiveness of the Orthospec™ ESW treatment in patients with chronic Proximal Plantar Fasciitis with or without heel spur who had not responded to conservative therapy.

Proximal Plantar Fasciitis is defined as heel pain in the area of the insertion of the plantar fascia on the plantar calcaneal tuberosity.

Patients were randomized 2:1 to either the active Orthospec™ treatment or placebo. Patients were followed out 1, 2, 3 months post-treatment for efficacy and safety evaluations, and then 6 and 12 months post-treatment for further safety assessment. Three clinical sites participated including up to two blinded investigators and one unblinded investigator at each site. The blinded investigators conducted pre- and post-evaluations and the unblinded investigator performed all treatments.

Treatment Procedure

Up to two blinded investigators and one unblinded investigator participated at each of the three clinical sites. Blinded investigators conducted all pre- and post-treatment evaluations and the unblinded investigators performed the ESW treatments. Patients were randomized to either the active treatment group or placebo control group. Both treatments were performed in parallel with each patient receiving 3,800 shocks. For patients who received the placebo treatment the contact membrane of the device was lined with an internal foam insert to absorb the shock waves. No anesthetic was given during or after treatment.

Inclusion/Exclusion Criteria

Patients with the following criteria were eligible for enrollment:

- Male or female eighteen years of age or older. If female is of childbearing potential, she must not be pregnant at the time of enrollment and she must be using an accepted form of birth control during the study.
- Diagnosed with proximal plantar fasciitis on the basis of history and physical examination with symptoms present for more than 6 months and has been treated by a licensed healthcare professional for at least 4 months
- Pain intensity score of $\geq$ 5 cm on the VAS scale in the investigator's heel pain assessment and the subject's self-assessment of pain upon the first few minutes of walking in the morning
- Failed two pharmacological and two nonpharmacological treatment modalities for relief of pain and will not undergo such treatments within the following time windows prior to treatment:
    - Local steroid injections – 6 weeks
    - NSAIDS – 1 week
    - Physical therapy – 2 weeks
- Single site of tenderness with local pressure over the plantar calcaneal tuberosity on passive dorsiflexion of the foot
- Chronic conditions such as osteoarthritis, diabetes, peripheral vascular diseases that do not affect foot pain

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Patients with the following criteria were excluded:

- Recent history of significant cardiac, neurological, hepatic, renal, metabolic, or hematological disease or impairment. Significance determined by pre-admission testing, medical history (recent and previous), and specialist evaluations
- Previous surgery for plantar fasciitis
- Chooses to continue physical therapy or other conservative treatments during the time he/she is enrolled in the study
- Corticosteroid injection within 6 weeks of treatment
- Neuropathic, malignant, or infectious causes of pain
- Coagulation disorders or is taking anticoagulant medications, either for acute or chronic anti-coagulant therapy
- Tears of the fascia
- Bilateral plantar fasciitis
- Condition in which the exposure to radiation is not advisable (i.e. pregnancy)
- Infection or malignancy at the area to be treated with Orthospec™
- Simultaneously participating in another device or drug study, or who has participated in any clinical trial involving an experimental device or drug within 30 days of entry into this study. Patients may be enrolled only one time in this study.
- Significant medical illness that may cause the patient to be non-compliant with the protocol or confound the data interpretation
- Require narcotics for plantar pain relief or other medical conditions prior to treatment

Evaluation Methods

Only blinded investigators performed pre- and post-treatment evaluations. Evaluations consisted of:

- Investigator's heel pain assessment
- Subject's self-assessment of heel pain
- Subject's self-assessment of activity and function
- The use of heel pain medications

During the investigator's evaluation of heel pain, a pressure sensor (PressureSpec®) was used to apply and record the amount of pressure that elicited a pain response at baseline, and then used the pressure sensor to apply the same amount of pressure at each subsequent follow-up visit for consistency in the evaluation.

Primary Objective

- The primary objective was to demonstrate a statistically significant difference between the Orthospec™ treatment and placebo treatment with respect to the change in pain intensity from baseline to 3 months post-treatment as measured on the Visual Analog Pain Score (VAS scale 0-10 cm) in the investigator's heel pain assessment. The investigator's heel pain assessment for a successful response required a minimum improvement from baseline of at least 50% with a VAS score of ≤ 4.0 cm.

Secondary Objectives

The secondary objectives of the study were to demonstrate statistically significant differences between the Orthospec™ treatment and placebo treatment with respect to:

- The change in pain intensity from baseline to 3 months post-treatment as measured on the Visual Analog Pain Score (VAS scale 0-10 cm) in the subjects self-assessment of pain (upon

the first few minutes of walking in the morning). The subject's heel pain assessment for a successful response required a minimum improvement from baseline of at least 50% with a VAS score of ≤ 4.0 cm.

- Subject's self-assessment of activity and function measured by the distance the subject is able to walk without heel pain
- The use of pain medications

Study Enrollment

As shown in Table 1, a total of 196 subjects were screened. 172 patients were enrolled and randomized (2:1) to either the active Orthospec™ treatment group or the placebo treatment group. One patient randomized to the Orthospec™ treatment group received placebo treatment by mistake. This patient was kept in the Orthospec™ treatment group for all analyses except where indicated otherwise. The subjects had a mean age of 51 years, and the mean duration of foot pain was 30 months. Thirty-three percent (33%) were male, 87% were white, and the mean weight was 184 pounds. Of the 172 enrolled patients, a total of 152 patients (88.4%) completed the study out to 3 months post-treatment and 20 patients terminated prematurely. The protocol specified that all patients who return for at least one post-treatment visit would be included in the primary efficacy analysis; a total of 168 patients were thus included.

Table 1 - Patient Accountability

	Orthospec™ n (%)	Placebo n (%)	Total N (%)
Screened		196	
Randomized	115	57	172
Completed 3 Months	101 (87.8%)	51 (89.5%)	152 (88.4%)
Terminated Prematurely	14 (12.2%)	6 (10.5%)	20 (11.6%)
Condition Worsened	5 (4.3%)	0 (0%)	5 (2.9%)
Healed	1 (0.9%)	0 (0%)	1 (0.6%)
Other	0 (0%)	1 (1.8%)	1 (0.6%)
Lost to Follow-up	8 (7.0%)	5 (8.8%)	13 (7.6%)
Included in primary analysis of effectiveness[1]	112 (97.4%)	56 (98.2%)	168 (97.7%)
Completed Month 1 Visit	111 (96.5%)	54 (94.7%)	165 (95.9%)
Completed Month 2 Visit	97 (84.3%)	48 (84.2%)	145 (84.3%)
Completed Month 3 Visit	101 (87.8%)	51 (89.5%)	152 (88.4%)

[1] Had at least one investigator assessment of heal pain post treatment.

Effectiveness Analysis

Primary Effectiveness Results

The primary endpoint, mean change from baseline in the investigator's Assessment of heel pain at three months achieved statistical significance (p=0.045). Table 2 summarizes the mean changes from baseline in investigator's assessment of heel pain at each monthly follow-up visit.

Table 2 – Mean Change from Baseline in Investigator's Assessment of Heel Pain Last Observation Carried Forward			
	Orthospec™	Placebo	P-Value
Month 1			
N	111	54	
Mean[1]	-1.61	-1.27	0.34
Difference (95% CI)	-0.34 (-1.06, 0.37)		
Month 2			
N	111	54	
Mean[1]	-2.30	-1.31	0.026
Difference (95% CI)	-0.99 (-1.86, -0.12)		
Month 3			
N	112	56	
Mean[1]	-2.51	-1.57	0.045
Difference (95% CI)	-0.94(-1.87, -0.02)		

[1] Estimated from an analysis of variance and adjusted for baseline assessment and clinical site.

Table 3 summarizes the mean change from baseline in investigator's assessment of heel pain as a function of the maximum tolerated energy applied. The patient mistakenly treated with placebo is included in the placebo group for this analysis. These results show that patients who received a maximum energy level of 4.5 or less is not therapeutic.

Table 3 – Mean Change from Baseline to Month 3 in Investigator's Assessment of Heel Pain by Maximum Shock Wave Energy Applied Last Observation Carried Forward		
	N	Mean[1]
Placebo	57	-1.53
Level 2 – 4.5	14	-1.09
Level 4.6 – 5.9	12	-1.71
Level 6 – 6.9	53	-2.87
Level 7	32	-2.93

[1] Adjusted for clinical site and baseline assessment

Secondary Effectiveness Results

Table 4 summarizes the results for each of the secondary effectiveness endpoints at three months. As seen in this table, the patient self-assessment of heel pain and the change in use of pain medication achieved statistical significance, supporting the findings of the primary effectiveness endpoint. Patients in the Orthospec™ treatment group had a higher point estimate of the response rate with regard to activity and function than patients in the placebo group, although this endpoint was not statistically significant.

Table 4 – Summary of Secondary Effectiveness Results at Three Months[1]			
Measure	Orthospec™ N=115	Placebo N =57	P-Value
Patient's Assessment of Heel Pain			
Mean change from baseline	-3.39	-1.78	<0.001
Response rate	52.7%	28.6%	0.003
Patient's Assessment of Activity and Function Response Rate	64.3%	57.1%	0.33
Change in the use of Pain Medication			
Increased	1.0%	11.8%	<0.001
No change	65.0%	74.5%	
Decreased	34.0%	13.7%	

[1] The last value was carried forward for all patients missing an assessment at month 3 and all analyses (except change in pain medication, which was adjusted for clinical site) were adjusted for clinical site and the corresponding baseline assessment.

As noted in Table 3 above, patients treated with an energy level of ≤ 4.5 did not, as a group, obtain a therapeutic benefit. To demonstrate the effectiveness among patients treated with an energy level > 4.5, the primary analysis and each of the secondary analyses are repeated in Table 5 excluding Orthospec™ patients who received an energy level of ≤ 4.5.

As these tables demonstrate, there is a higher rate of pain relief and improvement in activity and function when patients were treated at energy level higher than 4.5.

Table 5 – Summary of Effectiveness Results at Three Months[1] Orthospec Patients With Energy Level > 4.5			
Measure	Orthospec™ N = 97	Placebo N = 57	P-Value
Investigator's Assessment of Heel Pain			
Mean change from baseline	-2.75	-1.52	0.011
Response rate	46.4%	19.3%	<0.001
Patient's Assessment of Heel Pain			
Mean change from baseline	-3.69	-1.72	<0.001
Response rate	57.7%	28.1%	<0.001
Patient's Assessment of Activity and Function Response Rate	67.0%	56.1%	0.16
Change in the use of Pain Medication			
Increased	1.1%	11.5%	<0.001
No change	61.4%	75.0%	
Decreased	37.5%	13.5%	

[1] The last value was carried forward for all patients missing an assessment at month 3 and all analyses (except change in pain medication, which was adjusted for clinical site) were adjusted for clinical site and the corresponding baseline assessment.

Gender Analysis/Bias

The statistical analysis showed no significant correlation between age, gender, weight, and treatment effectiveness.

Complications and Adverse Events

The adverse events are presented in Section VIII above.

Device Failures and Replacements

There were six treatment interruptions and one aborted treatment. Five interrupted treatments were due to minor device malfunctions, i.e., shock wave counter and spark plug adjustment (user error). One interrupted treatment was due to pain. All treatments that were interrupted satisfied the required number of shocks or the required duration of treatment, and therefore the patients were able to complete the full treatment session. During the aborted treatment, a minor malfunction caused the treatment session to abort after the patient received 3,011 shocks. The Orthospec™ device was replaced at two sites due to service logistics.

Additional Clinical Experience

Medispec Ltd. previously conducted clinical studies of the Orthospec™ Extracorporeal Shock Wave Therapy (ESWT) for various orthopedic therapeutic indications including the treatment of pain of Plantar Fasciitis. A total of 1,117 Orthospec™ EWST treatments were performed at 17 medical centers and clinics in 12 countries.

No significant adverse events were reported by any of the investigation sites. Minor adverse events included mild bruising, weakness, diaphoresis, and vomiting which all resolved without medical intervention.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

All assessments of the reduction of heel pain were found to be statistically significant when compared to placebo. During the clinical investigation, there were three reported cases of adverse events, all reported from the active treatment group. They included two mild cases of bruising and one case of mild local swelling noted only by the patient. These reported cases required no medical intervention or subsequent medical care.

The investigation demonstrates that the Orthospec™ device provides a reasonable assurance of safety and effectiveness for patients with symptoms of Proximal Plantar Fasciitis for 6 months or more and a history of unsuccessful conservative therapies to relieve heel pain.

XII. PANEL RECOMMENDATIONS

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA application was not referred to the General Surgical 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. CDRH DECISION

FDA issued an approval order on April 1, 2005.

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

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See the Device Labeling.

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

Post Approval Requirements and Restrictions: See Approval Order.