SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Noninvasive Bone Growth Stimulator
Device Trade Name:	Xstim Spine Fusion Stimulator
Device Procode:	LOF
Applicant's Name and Address:	Xstim, Inc. 1320 Greenway Drive, Suite 200-F Irving, Texas 75038

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P230025

Date of FDA Notice of Approval: February 09, 2024

II. INDICATIONS FOR USE

The Xstim Spine Fusion Stimulator is a non-invasive bone growth stimulator indicated as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels. The device is for prescription use only and is intended for single patient use in adult patients only.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Xstim Spine Fusion Stimulator labeling.

V. DEVICE DESCRIPTION

Xstim Spine Fusion Stimulator is a small, portable, wearable, noninvasive capacitively coupled (CC) bone growth stimulator (BGS) that is indicated as an adjunct electrical

treatment to primary lumbar spinal fusion surgery for one or two levels. Xstim Spine Fusion Stimulator delivers a 60 kHz symmetric sine wave signal to the patient electrodes which are placed 2-3 inches on either side of the surgery site.

The Xstim Spine Fusion Stimulator consists of the signal generating control unit (controller) and belt clip, a rechargeable lithium-ion battery pack and charging unit, lead wires (controller cables) and cutaneous hydrogel electrodes, optional electrode covers (e.g., shower covers for use with electrodes only when showering), and a carry case.

The Xstim Spine Fusion Stimulator promotes bone healing by passing a specific current between the patient electrodes, which generates a low-energy electrical field at the fusion site.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

For patients undergoing lumbar spinal fusion, there are several other alternatives to the Xstim Spine Fusion Stimulator for providing adjunct treatment to primary lumbar spinal fusion surgery. These include:

- Invasive bone growth stimulators
- Physical therapy
- External Bracing
- Pulsed Electromagnetic Field Therapy

Additionally, other capacitive coupling devices have been approved and are available on the market. 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 Xstim Spine Fusion Stimulator has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The adverse events that may occur with treatment with Xstim Spine Fusion Stimulator are among those that may occur in association with lumbar spinal fusion and adjunctive treatment with non-invasive bone growth stimulators, and include failure or delay of osteogenesis, burns, electric shock, electromagnetic interference, adverse tissue reaction such as skin irritation, pain at the fusion site, or pain at the treatment site.

For the specific adverse events that occurred in the clinical studies of a non-invasive bone growth stimulator with similar design characteristics (Biomet SpinalPak®, approved under P850022/S009), please see Section X below. Based on the clinical study, the most common, and only device-related, adverse event was skin irritation, occurring in 9 patients (2.6% of the patient population) – four (4) patients treated with the active device and five (5) patients treated with the placebo device.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

A summary of laboratory studies is presented in the following table (Table 1):

Table 1: Nonclinical Study Summary

Test	Purpose	Acceptance Criteria	Results
Electrical Safety Testing	To demonstrate that the hazards related to electrical safety are mitigated.	Compliance with: • American National Standards Institute (ANSI)/ Association for the Advancement of Medical Instrumentation (AAMI) ES 60601- 1:2005/(R)2012 and A1:2012, C1:2009/(R)2012 and A2:2010/(R)2012 Medical Electrical equipment – Part 1: General requirements for basic safety and essential performance • International Electrotechnical Commission (IEC) 60601-1-11 Edition 2.0 (2015) Medical electrical equipment - Part 1-11 General requirements for basic safety and essential performance – Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment • IEC 60529 Edition 2.2 b:2013 Degrees of Protection Electrical Enclosures Package	Passed

Test	Purpose	Acceptance Criteria	Results
Electromagnetic Compatibility Testing	To demonstrate that the device is protected from electrical interference (immunity) and meets appropriate standards for electrical emissions.	Compliance with: • IEC 60601-1-2, Edition 4.0 (2014) Medical electrical equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests • International Special Committee on Radio Interference (CISPR)) 11:2009 Industrial, scientific and medical equipment - Radio-frequency disturbance characteristics – Limits and methods of measurement	Passed
Other Electrical Testing	To assess if the device met supplemental requirements of additional applicable electrical standards.	Compliance with: • IEC 60601-1-6 Edition 3.1 2010 & A1:2013 Medical electrical equipment – Part 1-6: General requirements for basic safety and essential performance – Collateral standard: Usability • ANSI AAMI IEC 60601 18:2006 & A1:2012 Medical electrical equipment Part 1-8: General requirements for basic safety and essential performance – Collateral standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems • IEC 60601-2-10 Edition 2.1 2012 & A1:2016 Medical electrical equipment – Part 2-10: Particular requirements for the basic safety and essential performance of nerve and muscle stimulators	Passed .
Software	To demonstrate that the software meets the design specifications, and that risks related to the software have been mitigated.	Software documentation was provided in accordance with the FDA Guidance Document "Content of Premarket Submissions for Device Software Functions," and "Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions" ; and in consideration of IEC 62304:2006/Amendment (AMD) 1:2015 "Medical device software- Software life-cycle processes." for a minor level of concern.	Passed

Test	Purpose	Acceptance Criteria	Results
Controller Verification	To verify the implementation of the signal generator system requirements.	Testing included evaluation of: • Physical characteristics verification – manufactured device meets all design specifications • User interface verification – device visually or audibly display all required information to the user • Electrical verification – electrical system design specifications are met • Controller Reliability - Components survive 270 days of simulated use.	Passed
Electrode and Electrode Lead Verification	To show there is no functional or performance difference between the electrodes used in the Xstim Spine Fusion Stimulator and those used for the SpinalPak®. Xstim Spine Fusion Stimulator will be provided with two types of electrodes to allow for choice based on patient preference.	The electrodes were evaluated to assess the following: • Insertion and removal force is less than 35 N • Demonstration the electrode leads can survive 60 insertion/removal cycles without damage	Passed
Shelf Life	To show the Xstim Spine Fusion Stimulator system and electrodes maintain their performance characteristics for the labeled shelf life (1-year).	Accelerated aging of the system components was performed, followed by revalidation of electrode verification testing. Electrodes must meet all specifications following aging.	Passed
Cleanability	To assess if the control unit could withstand repeated cleaning as expected for the use-life of the device.	Repeated cleaning simulating the expected use-life of the device was performed on the control unit, followed by revalidation of system performance. Device must meet all system requirements following repeated cleaning.	Passed
Battery Safety and Functional Verification	To demonstrate the suitability of the battery's performance for use with the Xstim Spine Fusion Stimulator.	Xstim Spine Fusion Stimulator relies on a Lithium-ion battery. A series of functional verification tests were performed to evaluate Lithium- ion battery's performance and conformity to IEC 62133-2:2017/AMD1:2021, United Nations (UN)/ Department of Transportation (DOT) 38.3, Edition 7, and Underwriters Laboratories (UL) 1642:2020	Passed

Test	Purpose	Acceptance Criteria	Results
Shipping and Transportation	To ensure the packaging was appropriately designed to allow for shipment of the device.	The Xstim Spine Fusion Stimulator packaging configuration was tested according to the applicable requirements of International Safe Transit Association (ISTA) 3A:2018.	Passed
Additional System Requirements Verification	Additional verification testing was performed to demonstrate that the Xstim Spine Fusion Stimulator device in its final finished form fulfills all the defined system requirements.	Testing included verification of the belt clip, button durability on the generator, verification of labeling, operating environment parameters, and confirmation of compliance to applicable consensus standards.	Passed
User Needs Validation Study	Product requirements related to use of Xstim Spine Fusion Stimulator were considered and addressed throughout the development of the product, including analysis of the intended use, user interface specification development, analysis of use related hazards and tasks, formative and formal evaluations.	A simulated-use validation study was conducted with fourteen representative users to demonstrate that the Xstim Spine Fusion Stimulator fulfills the defined designed specifications to suit the intended user. The study considered FDA guidance "Applying Human Factors and Usability Engineering to Medical Devices" and IEC 62366-1 (2019)	Passed

B. Animal Studies

No Animal Studies were provided in the submission.

C. Additional Studies

Biocompatibility

Biocompatibility of the patient contacting surfaces was evaluated according to International Organization for Standardization (ISO) 10993-1:2018 and FDA Guidance Document "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process'." The electrodes, electrode cover, controller shell, and lead wires may have long-term exposure on intact skin and were evaluated in biocompatibility tests. The biocompatibility tests conducted included Cytotoxicity (ISO 10993-5), Irritation (ISO 10993-10), and Sensitization (ISO 10993-10). Results of testing in combination with a biologic risk evaluation and labeling demonstrated biocompatibility in line with the requirements of ISO 10993-1.

Technology Comparison

In lieu of providing a clinical dataset for Xstim Spine Fusion Stimulator, the applicant provided a series of nonclinical comparison studies of Xstim Spine Fusion Stimulator and SpinalPak®, another BGS previously approved under P850022/S009 with the same indications for use as Xstim Spine Fusion Stimulator. The purpose of these nonclinical signal characterization tests was to establish sufficient similarity of the two BGS devices such that FDA could apply Section 216 of the Food and Drug Modernization Act (FDAMA), i.e., the "six-year rule," to assess the safety and effectiveness profiles of the Xstim Spine Fusion Stimulator.

As a first step, a comparison of the characteristics of the two products has been made. This is shown in the following table.

Table 2: Technological Comparison

Device Component	Function	Xstim Spine Fusion Stimulator	SpinalPak® (P850022/S009)
Stimulator/ Generator	Promotes healing by inducing low electrical current between electrodes at the fusion site.	Promotes healing by inducing low electrical current between electrodes at the fusion site.	Promotes healing by inducing low electrical current between electrodes at the fusion site.

Battery Pack and Battery Charger	Rechargeable battery (3.7V) allowing for ambulatory use.	2 battery packs provided	2 battery packs provided
Electrodes	Hydrogel electrodes transmit current to patient	1 option measuring 35mm (+/-2mm) in diameter	3 options with range of stickiness: all measuring 35mm (+/2mm) in diameter
Electrode Covers	Water resistant covers to enhance electrode security to the skin, may be used in the shower	Pack of 20 provided	Pack of 20 provided
Device Holster/ Belt Clip	Securely holds simulator in place allowing wear on a waistband or belt.	Belt clip provided	Holster with belt clip provided
Lead Wires/ Cables	2 different lengths	49" and 20" lengths	48" and 20" lengths

While there are, as shown in Table 2, modest differences in the components (i.e., hydrogel electrodes) and user interface, none of these differences would lead to appreciable differences in the safety or effectiveness profiles of the two devices. For example, while the Xstim Spine Fusion Stimulator only has one electrode option (with regard to stickiness), the hydrogel electrodes have been tested for electrode adhesion and have the same function which is to transmit current to the patient. This is supported by the results of the testing described below (Table 4), as well as the comparative signal and system characterization.

Subsequently, comparative bench testing was performed to establish adequate evidence that the Xstim Spinal Fusion Stimulator device and Biomet SpinalPak® device have sufficient operational similarity of key signal and system characteristics in support of leveraging the clinical dataset for the Biomet SpinalPak® device (P850022/S009).

To establish sufficient operational similarity of the devices, the following parameters that are key to the therapeutic treatment signal were considered:

1. **Therapeutic waveform**: The main properties of the therapeutic signal are voltage amplitude and frequency, with current proportional to voltage and load impedance per Ohms Law. Duty Cycle, Jitter, and Harmonic Content are measures of deviation from an ideal sinusoidal waveform shape that indicate sources of error from the intended output signal with potential clinical relevance.

2. **Waveform generation**: The time taken to detect and adjust to changing

impedance and the impedance range over which the therapeutic signal will be applied are important with regard to preventing suboptimal therapy and alerting the patient to improper operation such as loosely attached or touching electrodes.

3. **Current delivery/Dispersivity**: Electrode impedance determines waveform attenuation and effective operating impedance range. Dispersivity is a measure of localized current across the surface of the electrodes.

4. **Electrode Adhesion**: The adhesion of the electrodes must be balanced to ensure both secure placement during therapy and ease of removal when therapy is complete.

Both the Xstim Spine Fusion Stimulator and the SpinalPak® operate by capacitively coupling a sinusoidal electrical signal through two non-polarized electrodes to provide therapy to the patient. The electrical and mechanical parameters in Table 3 were selected for comparison because they fully characterize the delivered therapeutic treatment signal and coupling mechanism:

Table 3: Summary of parameters tested and their results

Test	Pass/Fail
Signal Frequency – High/Med/Low Resistance	PASS
Signal Frequency Jitter – High/Med/Low Resistance	PASS
Duty Cycle	PASS
Signal Voltage – Full Impedance Range	PASS
Signal Current – Full Impedance Range	PASS
Electrode Impedance	PASS
Electrode Dispersivity	PASS
Impedance Discovery Time	PASS
Impedance Operating Limit	PASS
Harmonic Content	PASS

The detailed testing results are then summarized in Table 4**.**

Table 4: Detailed summary of comparative testing results

Parameter	Xstim Spine Fusion Stimulator		SpinalPak®	
	Min	Max	Min	Max
Frequency (kHz)	60.35	61.01	59.61	61.46
Treatment Current (Arms, mA) @ 100 - 700 Ohms	3.331	9.557	3 3.244	9.576
Impedance Operating Limit (Ohms)	100	734	100	815.5
Treatment V_{rms} (mV) @ 100 - 700 Ohms	0.9157	2.431	0.9120	2.610
Impedance Discovery Time (s)	-	5.72	-	5.82
Duty Cycle	49.782	50.218	49.496	50.504
Jitter (ns)	-	101.6	-	323.5
Harmonic Content (%)	-	3.40	-	4.27
Electrode Impedance (Ohms)	73.4	81.5	40.4	100.518
Electrode Dispersivity mA/cm^2) @100 Ohms	0.98		1.01	
Electrode Dispersivity mA/cm^2) @700 Ohms	0.35		0.36	
Electrode Adhesion (g/cm^2)	114.8	332.2	82.105	332.4

As shown in Table 4 above, testing of the Xstim Spine Fusion Stimulator signal and system characteristics described above demonstrated similarity between the Xstim Spine Fusion Stimulator and SpinalPak®. Where a specification was defined by a range or operating windows, the Xstim Spine Fusion Stimulator results were shown to be within the window/range (control frequency is set to 60kHz +/-10%), often showing a tighter distribution than what was observed for the SpinalPak® device (defined as the mean ± 3x standard deviation; Min Frequency = 54kHz, Max Frequency = 66kHz). Where a specification was solely defined by a maximum or minimum value, the Xstim device did not exceed those values. For electrode adhesion, six electrodes were tested for each system, with the results showing the mean and standard deviation of the low and high adhesion electrodes. Based on the comparative testing results, the Xstim is sufficiently similar to SpinalPak®, such that the "six-year rule" can be applied to assess the safety and effectiveness profiles of the Xstim device.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

Since the Xstim Spine Fusion Stimulator and the SpinalPak® Fusion Stimulator were determined to have sufficient operational similarity of key signal and system characteristics, the clinical outcomes for SpinalPak® in the controlled clinical study can be leveraged to support the safety and effectiveness of the Xstim Spine Fusion Stimulator. In this section, an overview of the relevant outcomes, both safety and effectiveness, from the clinical investigation are presented.

A. Study Design

The clinical data to support the safety and effectiveness of the SpinalPak® Fusion Stimulator were collected through a rigorous multi-center trial. The Study design that was followed was a randomized, double-blinded, prospective study which was conducted at multiple sites. The objective of this study was to determine whether the SpinalPak® Fusion Stimulator increased the frequency of overall success (defined as the combination of both clinical and radiographic success) when compared to placebo (inactive) units, after primary (first-time) one-level or two-level fusions within L3 to S1.

Subjects were eligible if they had degenerative disc disease and had undergone one-level or two-level fusions of the lumbar spine between L3 and S1. The surgical procedures qualifying for inclusion were:

- an interbody fusion, including either a posterior lumbar interbody fusion

(PLIF) or anterior lumbar interbody fusion (AUF), or
- a bilateral posterolateral fusion
- a combination of both procedures

Subjects could also receive either autograft or allograft graft material, while internal fixation was allowed as well. Subjects were randomized to receive either active or placebo device within three weeks of surgery.

Xstim Inc. referenced the P850022/S009 (SpinalPak®) clinical study to establish a reasonable assurance of safety and effectiveness for its noninvasive bone growth stimulator indicated as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels. A logistic regression analysis, performed as part of the SpinalPak® study, determined that age and sex were not significantly associated with overall clinical and radiographic success after controlling for other variables. The effects of race and ethnicity were not evaluated.

1. Clinical Inclusion and Exclusion Criteria

In order to have a well-controlled study, specific inclusion and exclusion criteria were strictly adopted. These included the following:

To be included, subjects were to meet the following criteria:

- degenerative disc disease
- spine segments: L3/L4, L4/L5, LS/S1, L3/L5, L4/S1
- interbody fusion, either posterior lumbar interbody fusion (PLIF) or anterior lumbar/interbody fusion (ALIF), or bilateral posterolateral fusion (with or without fixation hardware)
- primary fusion, within three weeks of enrollment
- one-level or two-level fusion
- autograft or allograft graft material
- closed epiphyses

Subjects who exhibited any of the following conditions were not eligible:

- pathologic process at spine level - spondylosis, infection, Paget's disease
- systemic disease that may affect fusion - cancer, diabetes mellitus, renal disease
- osseous trauma of the lumbar spine
- pregnancy
- cardiac pacemaker
- inability of patient to understand or comply with study instructions

- osteoporosis

2. Follow-up Schedule

During this trial, assessments of radiographic (x-ray) and clinical status (pain and function) were made. The subjects were instructed to use the device continuously, except for periods of personal hygiene, until a physician had assessed overall success or for a period of nine months (the period of time allocated for this study). Preoperatively, the Patient Self-Assessment Form (PSAF) was collected. Postoperatively, the objective parameters measured during the study included both assessments of radiographic (x-ray) and clinical status (pain and function).

Radiographic Assessment: Radiographic assessments were gathered in 2 formats:

a. Interim Assessments (Follow-Up Case Report Form at 6 weeks and, at three, six, nine and 12 months after the initial use of the device)

Radiographic assessments on the Follow-Up Case Report Forms consisted of checking the appropriate description of the patients' radiographic condition from the following list: Complete; Incomplete - progressing; Incomplete - not progressing; and No Fusion Evident. No additional definitions were provided of these descriptive terms. Interim assessments were not used as a determinant of overall success within the approved Investigational Protocol.

b. Final Evaluation (Final Success Evaluation Form at the final office visit)

Radiographic assessments on the Final Success Evaluation Case Report Form were made in the following fashion: The following definitions (Table 5) were used in evaluating the interbody fusion (ALIF and PLIF) and the bilateral posterolateral fusion.

Table 5: Radiographic Evaluation – Final Success Evaluation

ALIF/PLIF	
a. > 75% assimilation of graft and vertebrae	SUCCESS
b. 50-75% assimilation of graft and vertebrae	SUCCESS
c. 25-50% assimilation of graft and vertebrae	FAILURE
d. <25% assimilation of graft and vertebrae	FAILURE
Bilateral Posterolateral Fusion	
a. Fusion	SUCCESS
b. Incomplete fusion	FAILURE
c. Absence of fusion mass	FAILURE

When a subject completed the study and received a radiographic assessment of "success" from the investigator, a series of the subject's radiographs were forwarded to a blinded, independent radiologist for a second opinion. If the independent radiologist agreed with the investigator's evaluation of "success", the investigator's assessment remained as the radiographic outcome. If the independent radiologist disagreed with the investigator, the radiographs were to be sent to a second blinded, independent reviewer. The opinion of this reviewer served as the radiographic outcome. Any subject receiving a negative radiographic assessment from the investigator at the completion of the study was automatically classified as a study failure.

Clinical assessments were gathered in 3 formats:

a. Interim Assessments: (Follow-Up Case Report Forms completed by the attending physician (at 6 weeks and, at three, six, nine and 12 months after the initial use of the device)

Clinical assessments on the Follow-Up Case Report Forms consisted of checking the appropriate description of the patient's clinical condition from the following list: Excellent, Good, Fair, and Poor. No additional definitions were provided for these descriptive terms. Interim assessments were not used as a determinant of overall success within the approved Investigational Protocol.

b. Final Evaluation: (Final Success Evaluation Form completed by the attending physician at the final office visit) Clinical assessments on the Final Success Evaluation Case Report Form were made in the following fashion:

Excellent:	Resumption of normal activities; no pain.	SUCCESS
Good:	Resumption of normal or modified activities;	SUCCESS
	Occasional episodes of back or leg pain;	
	Occasional pain medication.	
Fair:	Resumption of activities on a limited basis	FAILURE
	Daily back and/or leg pain;	
	Requires frequent pain medication.	

Poor: Unable to resume normal or modified activities FAILURE

Severe back and/or leg pain;

Requires daily pain medication.

c. Patient Self-Assessment Form (PSAF): Completed by the patient at baseline, 6 weeks, and, at three, six, nine and 12 months after the initial use of the device. The patient self-assessment questionnaire consists of 14-questions which describe a patient's perception of their pain and their ability to function. The patient answered each question, by providing the degree of their symptom. To analyze the results of the questionnaire, each answer was given a numeric score and the sum of the results was used as an indicator of outcome. The highest score, i.e., the worst possible pain and function score, would be 57 while the best score would be 0. The PSAF was not used as a determinant of success within the approved Investigational Protocol.

3. Clinical Endpoints

With regards to safety, every patient entered into the study was evaluated for adverse events.

With regards to effectiveness, a patient was considered to be a success in this study if he/she was considered both clinically and radiographically successful at the time of the final evaluation. Patient progress at the interim (follow-up) visits was not taken into consideration in making the final evaluation. A radiographic success at the final evaluation was either:

For ALIF/PLIF

- 75% assimilation of graft and vertebrae
- 50-75% assimilation of graft and vertebrae

For Bilateral Posterolateral:

- "Fusion”

A clinical success at the final evaluation was a determination by the physician of either:

- Excellent: Resumption of normal activities; no pain;
  or
- Good: Resumption of normal or modified activities; occasional episodes of back or leg pain; occasional pain medication.

Study Success

Study success was determined by making a comparison between the percentage of active patients in the core group considered to be overall successes (as defined above) as compared to the percentage of placebo patients in the core group considered to be overall successes (as defined above). If the comparison between the active and placebo core patients considered to be successful overall yields a statistically significant result (p-value less than or equal to 0.05), the study is considered to be successful.

B. Accountability of PMA Cohort

Study Subject Enrollment and Discontinuation:

Table 6: Summary of Subject Accountability All Subjects Enrolled as of 12/31/97

	All Subjects	Active	Placebo
Enrolled (does not include 4 who received ID No., but not entered)	349	177	172
Not Reached Twelve Months Post Surgery, or Fused	-6	-3	-3
Twelve Months Post Surgery, Potentially Eligible for Evaluation	343	174	169
Withdrawals	-83	-43	-40
--Reasons Unknown	(59)	(32)	(27)
--Adverse Reactions	(12)	(5)	(7)
--Compelled (jail, secondary surgery)	(7)	(4)	(3)
--Requested (violated entry criteria)	(5)	(2)	(3)
Twelve Months Post Surgery, Eligible for Evaluation (Intent to Treat Population)	260	131	129
Protocol Deviations (Censored Population)	-45	-21	-24

	All Subjects	Active	Placebo
Twelve Months Post Surgery, Meet Protocol (Core Population)	215	110	105

As Table 6 shows, 349 subjects were initially enrolled in the study and randomized to receive either an active or inactive (placebo) unit. Eighty-three subjects (24%) withdrew from the study and six had not yet completed the study as of the data cut-off date, leaving 260 subjects who completed the study and were available for analysis.

Of the 260 subjects who completed the study (Intent-To-Treat Population), 45 did not meet the entry criteria, had an intervening surgical/medical event that precluded an unbiased evaluation of overall success, or did not have an independent assessment of their radiographs (Censored Population). This left a total of 215 subjects who met all the protocol criteria and completed the study (Core Population).

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a randomized controlled pivotal study performed in the US of a non-invasive bone growth stimulator for use as an adjunct treatment to spinal fusion surgery.

Clinical Characteristics of Core Subjects (n=215)

The demographic and clinical characteristics of the active and placebo subjects in the core group were comparable. The mean age for the active and placebo groups was 46.54 years and 44.75 years, respectively. The active and placebo groups included an approximately equal number of men and women (active female = 46.4%, active male = 53.6%, placebo female= 51.4%, placebo male= 48.6%). Of the active subjects, 24.5% smoked; 21.0% of the placebo subjects smoked.

A number of subjects had prior (pre-operative) surgeries; 29.1% of the actives, and 36.2% of the placebos. 67% of the actives and 59.1% of the controls had a posterolateral fusion. The remaining subjects had some type of interbody fusion, including a posterior interbody fusion, an anterior interbody fusion, or a combination of an interbody and posterolateral fusion. Approximately, one half of the subjects in both groups had a one-level fusion.
Subjects could receive either autograft or allograft graft material; and 26.4% of the actives and 20.0% of the placebos had fusions with internal fixation (hardware).
The 99 active core subjects had a baseline summed mean pain and dysfunction score of 31.44 from their 14-question self-assessment form; the 99 placebo subjects had a summed mean of 33.35 at baseline.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on both the active and placebo 215 evaluable patients of the core group (n=215) at the 12-month time point.

Every subject entered into the study was analyzed for adverse events. Of the 349 subjects enrolled in the clinical study and who used the device at least once, nine experienced skin irritations and cited this as a reason to withdraw from the study (2.6%). Of the nine subjects, four were in the active group and five were in the placebo group.

Three other subjects withdrew from the study because of adverse events: one placebo had a wound infection (non-device related); one placebo had back spasms; and one active was "not progressing." (While lack of progression is normally not considered an adverse event, the investigator reported it that way.)

Eight subjects who completed the study experienced adverse events: (1) leg pain (placebo); (2) recurrent pain due to over-activity (placebo); (3) post-surgical wound seroma (active); (4) superficial wound disruption from a staple reaction (placebo); (5) pedicle fracture - screw removed (placebo); (6) a pedicle screw placement (active); (7) an aneurysm clipping (placebo); and (8) a cluneal nerve neuroma at the graft site (active). These eight subjects continued in the study and were included in the effectiveness analyses.

2. Effectiveness Results

Table 7 compares success in the active and placebo subjects of the core group (n=215). An overall success required an independent confirmation of radiographic successful outcome on the Final Assessment Case Report Form and also a successful clinical outcome on the Final Assessment Case Report. For each group the number of successes is shown. The p-value presented for "Overall Success" indicates statistical significance (a p-value of less than or equal to 0.05 denotes significance). The data were analyzed using a two-tail Fisher exact test.

Table7: Frequency of Success of the Core Group, by Treatment (n = 215)

	Overall Success (Clinical AND Radiographic Success)	Clinical Success	Radiographic Success	Average PSAG Score Baseline/12 months
Active (N = 110)	87 (79%)	95 (85%)	94 (85%)	31.44/23.03

	Overall Success (Clinical AND Radiographic Success)	Clinical Success	Radiographic Success	Average PSAG Score Baseline/12 months
Placebo (N = 105)	64 (61%)	79 (75%)	82 (78%)	33.35/23.44
P-value	0.0018			

Note: A patient was considered to be a success in this study if he/she was considered both clinically and radiographically successful at the time of the final evaluation. Patient progress at the interim (follow-up) visits was not taken into consideration in making the final evaluation.

In the 215-core group, 87 active subjects (79%) achieved an overall success (defined as a combination of both physicians described clinical success and also a radiographic success at the time of final evaluation) whereas 64 placebo subjects (61 %) achieved overall success at the time of final evaluation. This difference in the rates of overall success (18.1 %) was statistically significant (p=0.0018).

This trial was not designed to look at either clinical success or radiographic success independently. However, in the 215 core group, 94 of 110 active subjects (85%) were reported by the treating physician as being radiographically successful at the time of final evaluation; whereas 82 of 105 placebo subjects (78%) were reported by the treating physician as being radiographically successful at the time of final evaluation This difference in the rates of success (7%) was not statistically significant (p=0.0535). In the 215 core group, 95 active subjects (85%) achieved clinical success at the time of final evaluation; whereas 79 placebo subjects (75%) achieved a clinical success at the time of final evaluation. This difference in the rates of success (10%) was statistically significant (p=0.0163). However, these values were not adjusted for multiplicity and were also not adjusted for additional confounding factors (e.g., prior surgery, posterolateral fusion, or smoking).

As presented previously, the PSAF was also used to compare treatment groups. At baseline, the active and placebo core treatment groups were similar, with the active core subjects having a summed mean score of 31.44 and the placebos having a mean summed score of 33.35. The 1.91-point difference between core active and placebo mean patient self-assessment scores is not statistically significant (Z= - 1.62426). At the time of final evaluation, active core subjects have a mean summed scores of 23.03 and placebo core subjects have a mean summed score of 25.44. The 2.41 point difference between core active and placebo mean patient self-assessment scores is not statistically significant (Z = -0.2675).

Logistic Regression Analysis

A number of subject characteristics and demographics may affect the frequency of overall success. A logistic regression analysis was conducted to determine if any variable(s) may have affected overall success. A logistic regression analysis tests whether any variable is statistically associated with success after controlling for the other variables and provides an odds ratio to indicate the nature and strength of the relationship. A logistic regression was conducted using the following 13 variables that may have had an effect on the likelihood of an overall successful:

(1) the active device;
(2) history of prior surgery (treatment);
(3) gender;
(4) age;
(5) overweight;
(6) smoking;
(7) use of pre-operative medications, including steroidal and non-steroidal anti-inflammatory medications;
(8) a secondary diagnosis of herniated disc pulposus;
(9) a secondary diagnosis of spondylolisthesis;
(10) occupational type, such as sedentary employment or moderate/heavy labor;
(11) type of fusion, such as posterolateral or interbody;
(12) level of fusion (single or multiple); and
(13) the use of fixation hardware.

A logistic regression analysis determines whether any of the variables is statistically associated with success after controlling for the other variables and provides an odds ratio to indicate the nature and strength of the relationship. This analysis was performed to determine if this variable was responsible for the outcome rather than the device being studied.

The following four variables were associated with frequency of overall success and were statistically significant: the active device, a history of prior surgery, fusion type, and smoking. The other variables, including the use of fixation hardware, were not significantly associated with overall success after controlling for the other variables. The analysis was then conducted with only the four identified variables and is shown below in Table 8.

Table 8: Logistic Regression Analysis For the Core Group (n=215)

Variable	Odds Ratio	95% Confidence Interval	p-value

Prior Surgery	0.48	0.25-0.92	0.0276
Posterolateral Fusion	2.40	1.26-4.55	0.0073
Smoker	0.33	0.16-0.68	0.0024
Active Device	2.33	1.21-4.48	0.0110

This analysis showed that subjects with a history of prior surgery were less likely to achieve success, regardless of other factors (odds ratio = 0.48; p=0.0276). Subjects who had a posterolateral fusion were more likely to be overall successes, regardless of the other variables (odds ratio = 2.40, p=0.0073). Subjects who smoked were also less likely to achieve overall success (odds ratio= 0.33, p=0.0024). The subjects in the active group were more likely (odds ratio= 2.33) to achieve overall success regardless of their type of fusion, their prior history of surgery, or smoking. This odds ratio was statistically significant (p=0.0110).

The clinical results establish the spine fusion stimulator delivering the same output parameters as Xstim Spine Fusion Stimulator may be used as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels.

3. Subgroup Analyses

In order to assure patient withdrawals and losses do not affect study outcome or introduce bias, statistical analyses were performed to determine if patients in the sub-populations (core, censored, and withdrawn) were comparable. First, all active and placebo subjects were compared with respect to 63 preoperative demographic and clinical characteristics to determine if there were any significant differences between these treatment groups overall. There were none. This same analysis was performed for the active and placebo subjects in the Censored Population and in the Core Population. Only two statistically significant differences between the active and placebo subjects in the Censored Population were found "race" (p=0.0365) and the recorded use of "preoperative NSAIDs" (p=0.0247)). Then, using the same 63 factors, the withdrawn subjects were compared to the 260 Intent-To-Treat Population. Then the population that withdrew, combined with the Censored Population, was compared to the Core Population. All these analyses established that the comparability of the Core Population treatment groups was not adversely affected by the absence of the withdrawn and censored subjects, and that the active and placebo subjects in the Core Population had similar demographic and clinical characteristics.

To further establish the comparability of the active and placebo groups in the Core

Population summed pain and dysfunction scores from a 14-question PSAF (gathered either pre-operatively or post-operatively) were statistically compared and no significant differences were found at baseline.

4. Pediatric Extrapolation

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

E. Financial Disclosure

This section is not applicable.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

This section is not applicable.

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 Orthopedic and Rehabilitation 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 this PMA the sponsor provided adequate evidence of the sufficient similarity of Xstim Spine Fusion Stimulator and SpinalPak® Bone Growth Stimulator with regard to the delivered therapeutic signal power and waveform characteristics. Because of this, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for SpinalPak® in support of the reasonable assurance of its effectiveness is directly applicable towards establishing reasonable assurance of the effectiveness of Xstim Spine Fusion Stimulator.

As detailed in the SSED for SpinalPak® (P850022/S009), a comparative clinical trial of SpinalPak® to a placebo control successfully demonstrated and improved clinical and radiographic success of fusion following 12 months of treatment. The treatment group had an overall (clinical and radiographic) success of 79%, compared to the control arm which had a 61% success rate ($p = 0.0018$), demonstrating a statistically significant

effect of the treatment.

B. Safety Conclusions

Non-clinical bench testing of the device was provided to demonstrate a similarity in design of the Xstim Spine Fusion Stimulator and the SpinalPak® Bone Growth Stimulator, including assessment of the generated signal, electrical safety, electromagnetic compatibility, and biocompatibility. This testing was used to provide evidence of the reasonable assurance of the safety of the SpinalPak® under P850022/S009 apply equally to the Xstim Spine Fusion Stimulator.

As detailed in the SSED for the SpinalPak® Bone Growth Stimulator, a clinical study was provided which included 349 subjects. Of the 349 enrolled in the clinical study who used the device at least once, nine experienced skin irritation and cited this as a reason to withdraw from the study. Of the nine subjects, four were in the active group and five were in the control group. Three other subjects withdrew from the study because of adverse events; one placebo had a non-device related wound infection, one placebo had back spasms, and one active was "not progressing."

Eight subjects who completed the study experienced adverse events: (1) leg pain (placebo); (2) recurrent pain due to over-activity (placebo); (3) post-surgical wound seroma (active); (4) superficial wound disruption from a staple reaction (placebo); (5) pedicle fracture - screw removed (placebo); (6) a pedicle screw placement (active); (7) an aneurysm clipping (placebo); and (8) a cluneal nerve neuroma at the graft site (active). These eight subjects continued in the study and were included in the effectiveness analyses.

C. Benefit-Risk Determination

The benefit risk profile for the Xstim Spine Fusion Stimulator is based on both the preclinical data collected for the device itself as well as the data collected in a clinical study conducted to support PMA approval of the SpinalPak® device.

Through the preclinical testing, a biocompatibility and usability profile has been established. Additionally, through bench testing, the device was demonstrated to have the same therapeutic treatment signal as SpinalPak®. This confirms that the therapeutic signal produced by Xstim Spinal Fusion Stimulator is well within the parameters required for the clinical indication, as has been established by SpinalPak®.

Results of comparative non-clinical testing provided evidence of the sufficient

similarity of the SpinalPak® and Xstim Spine Fusion Stimulator devices, such that FDA could then apply Section 216 of the FDAMA and cite evidence of clinical effectiveness presented in the SSED for the SpinalPak® device in support of a determination of reasonable assurance of the effectiveness of the Xstim Spine Fusion Stimulator device.

A comparative clinical trial of the SpinalPak® device to a placebo control successfully demonstrated improved clinical and radiographic success of fusion following 12 months of treatment. The treatment group had an overall (clinical and radiographic) success of 79%, compared to the control arm which had a 61% success rate ($p = 0.0018$), demonstrating a statistically significant effect of the treatment with the SpinalPak® device compared to a placebo control.

As documented in the SSED for the SpinalPak®, the probable risks consisted of various transitory, non-serious adverse events that were observed in the clinical trial. The only device-related event was skin irritation at the treatment site. With a clinical benefit in the context of a very limited, and controlled risk profile, it can be clearly stated that the Benefit Risk Profile for Xstim Spine Fusion Stimulator is positive and the use of Xstim Spine Fusion Stimulator on the market, similar to that for SpinalPak® Bone Growth Stimulator, is well supported.

In conclusion, given the available information above, the data support that for an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels the probable benefits outweigh the probable risks.

Patient Perspectives Conclusions

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

D. Overall Conclusions

The data in this application supports the reasonable assurance of safety and effectiveness of the Xstim Spine Fusion Stimulator when used in accordance with the indications for use.

With regard to reasonable assurance of the safety and effectiveness of the Xstim Spine Fusion Stimulator the sponsor provided adequate evidence of the sufficient similarity of the Xstim Spine Fusion Stimulator and the SpinalPak® Bone Growth Stimulator. This similarity was established through nonclinical side-by-side characterization and testing of the two devices to demonstrate that a closely similar

therapeutic signal is generated and delivered to the subject.

Furthermore, the Xstim Spine Fusion Stimulator was evaluated to ensure that it complies with all of the appropriate safety standards including biocompatibility, electrical safety, and electromagnetic compatibility. Due to the inherent similarity between the devices, FDA was able to apply Section 216 of the FDAMA and confirm that the clinical evidence for the SpinalPak® Bone Growth Stimulator presented in the SSED for P850022/S009 in support of the reasonable assurance of the safety and effectiveness of the SpinalPak® device is directly applicable towards establishing a reasonable assurance of the safety and effectiveness of the Xstim Spine Fusion Stimulator.

XIV. CDRH DECISION

CDRH issued an approval order on February 09, 2024.

The applicant's manufacturing facilities have been determined, through prior on-site inspection of similar devices, a review of relevant manufacturing site documentation and compliance history, 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.

XVI. REFERENCES

None