

**Premarket Approval (PMA) Package for
Dockets Management Branch**

**PMA Number P850022/S9
Docket # 00M-0901**

**Bioelectron, Inc.
SpinalPak Bone Growth Stimulator**

Includes:

**Approval Order
Summary of Safety and Effectiveness Data (SSED)
Labeling**

00M-0901

AAVI

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APPROVAL ORDER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

log

Mr. Donald W. Guthner
Bioelectron Incorporated
200 Holt Street
Hackensack, New Jersey 07601

SEP 24 1999

Re: P850022/S9
SpinalPak Bone Growth Stimulator
Filed: May 15, 1997
Amended: June 16, and October 17, 1997; January 6,
February 5, March 16, March 30, August 31, and October 13,
1998; February 16, March 24, May 21, June 3 11, June 15,
July 23, 1999, and September 14, 1999

Dear Mr. Guthner:

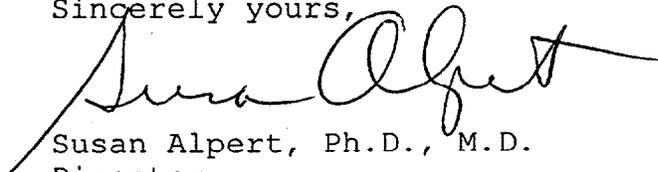
The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) supplement for the SpinalPak Bone Growth Stimulator. This device is indicated as a noninvasive bone growth stimulator for use as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels. The PMA supplement is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device as modified upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that, to ensure the safe and effective use of the device, the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Page 2 - Mr. Donald Guthner

If you have any questions concerning this approval order, please contact Ms. Jodi Anderson at 301-594-2036, extension 186.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Susan Alpert", written over the typed name.

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Issued: 3-4-98

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effectuated" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effectuated" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effectuated." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

- (1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
- (2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:
 - (a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and
 - (b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

- (1) A mix-up of the device or its labeling with another article.
- (2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and
 - (a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

- (1) May have caused or contributed to a death or serious injury; or
- (2) Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc.

Any written report is to be submitted to:

Food and Drug Administration
Center for Devices and Radiological Health
Medical Device Reporting
PO Box 3002
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336) and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers Assistance (DSMA) at 301-443-8818.

SUMMARY OF SAFETY AND
EFFECTIVENESS DATA (SSED)

**SUMMARY OF SAFETY
AND EFFECTIVENESS INFORMATION**

I. General Information

Device Generic Name:	Bone Growth Stimulator
Trade Name:	SpinalPak® Fusion Stimulator
Applicant's Name and Address:	Bioelectron, Inc. 25 Commerce Drive Allendale, NJ 07401
Premarket Approval (PMA) Application: Supplement Number:	P850022 S9
Date of Notice of Approval to Applicant:	September 24, 1999

II. Device Description

The SpinalPak® Fusion Stimulator is a bone growth stimulator utilizing capacitive coupling technology. It incorporates the same technological features of Bioelectron's OrthoPak® Bone Growth Stimulator System (P850022, approved February 18, 1996) which is indicated for the treatment of established non-unions acquired secondary to trauma, excluding vertebrae and all flat bones, where the width of the nonunion defect is less than half the width of the bone to be treated.

III. Indications

The SpinalPak® Fusion Stimulator is indicated as a noninvasive bone growth stimulator for use as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels.

IV. Warnings

- Cardiac pacemakers or cardioverters may be adversely affected by the SpinalPak® Fusion Stimulator. The concomitant use of the device and a pacemaker or cardioverter must be assessed on an individual basis, such as with an electrocardiogram, prior to use. The patient should be referred to a cardiologist for monitoring of pacemaker function while wearing the active SpinalPak® device. If there are any observable adverse changes in the pacemaker rhythm or output, the SpinalPak® device should not be used.
- The safety and effectiveness of the SpinalPak® Fusion Stimulator in pregnant women have not been studied, and the effects of the device on the mother or the developing fetus are unknown. A patient who is either pregnant or is intending to become pregnant should be referred to her doctor prior to treatment with the SpinalPak® device.

V. Precautions

- The safety and effectiveness of the SpinalPak® Fusion Stimulator in individuals with the following conditions have not been studied, and therefore the safety and effectiveness of the device in these individuals is therefore unknown:
 - spondylitis, infection, Paget's disease
 - cancer, diabetes mellitus, renal disease
 - trauma of the lumbar spine
 - osteoporosis
- The patient should be instructed to apply the electrode after the skin has been cleaned and dried. If erythema develops at the electrode sites, the electrodes should be relocated either immediately above or below the original sites. If the reaction does not resolve after 48 hours after relocating the electrodes, the patient should be instructed to consult with the physician.
- Do not submerge or expose the SpinalPak® Fusion Stimulator to water. The patient should be instructed to remove the stimulator during bathing, showering or swimming.
- Compliance with the treatment schedule, daily battery changes, proper maintenance of the device, and replacing the electrodes every five to seven days are essential for proper device function.
- The patient should be able to use the device in accordance with the instructions for use. If a patient cannot comply with these instructions for any reason, use of the device is not recommended.

VI. Adverse Events

During a multi-center clinical study of 349 patients treated with the SpinalPak Fusion Stimulator for the indication listed above, skin irritation was the most common adverse effect. It occurred in 9 patients (2.6% of the patient population) – 4 patients treated with the active device and 5 patients treated with the placebo device.

VII. Alternative Practices or Procedures

Alternatives to use of the SpinalPak Fusion Stimulator include physical therapy, medications, external bracing, chiropractic care, exercising, and spinal fusion therapy (with or without instrumentation) and with or without concomitant stimulation. Two other electrical stimulation devices are in commercial distribution and are indicated for "use as an adjunct electrical treatment to primary spine fusion surgery." These other devices utilize different methods to stimulate bone growth and consist of a noninvasive stimulator and an invasive stimulator.

VIII. Summary of the Pre-Clinical Studies

The SpinalPak® Fusion Stimulator device incorporates the same technological features of Bioelectron's OrthoPak® Bone Growth Stimulator System (P850022, approved February 18, 1996) and indicated for the treatment of established non-unions acquired secondary to trauma, excluding vertebrae and all flat bones, where the width of the nonunion defect is less than half the width of the bone to be treated. Pre-clinical studies were performed to support the relative safety of this product. Details of the pre-clinical studies gathered using the OrthoPak Bone Growth Stimulator System can be found in the Summary of Safety and Effectiveness for the OrthoPak® Bone Growth Stimulator System (P850022).

IX Summary of Clinical Trial

Clinical data to support the safety and effectiveness of the SpinalPak® Fusion Stimulator were collected as part of multi-center trial.

A. Study Design

The clinical study was a randomized, double-blinded, prospective study 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 (ALIF); a bilateral posterolateral fusion; or a combination of both procedures. Subjects could also receive either autograft or allograft graft material. Subjects could also receive internal fixation. Subjects were randomized to receive either an active or placebo device within three weeks of surgery.

Subjects were to be followed at six weeks, and at three, six, nine and 12 months after the initial use of the device. 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).

B. Inclusion/Exclusion Criteria

1. Inclusion Criteria

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

- degenerative disc disease
- spine segments: L3/L4, L4/L5, L5/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

2. Exclusion Criteria

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

- pathologic process at spine level - spondylitis, 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

C. Outcome Measure

During this trial, assessments of radiographic (x-ray) and clinical status (pain and function) were made.

1. 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 were used in evaluating the interbody fusion (ALIF and PLIF) and the bilateral posterolateral fusion.

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:

- | | | |
|---------------------------|----|---------|
| 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.

2. Clinical Rating

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; Occasional episodes of back or leg pain; Occasional pain medication.	-- SUCCESS
Fair:	Resumption of activities on a limited basis; Daily back and/or leg pain; Requires frequent pain medication.	-- FAILURE
Poor:	Unable to resume normal or modified activities; Severe back and/or leg pain; Requires daily pain medication.	-- FAILURE

- 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.

D. Patient Success

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:

ALIF/PLIF

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

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
- Good: Resumption of normal or modified activities; occasional episodes of back or leg pain; occasional pain medication.

E. 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.

F. Study Subject Enrollment and Discontinuation

Table 1 summarizes subject accountability, by "active" and "placebo" group as of a data-cut-off point of December 31, 1997.

**Table 1
Summary Of Subject Accountability
All Subjects Enrolled As Of 12/31/97**

	<u>All Subjects</u>	<u>Active</u>	<u>Placebo</u>
Enrolled (does not include 4 who received ID No., but not entered)	349	177	172
Not Reached Twelve Months Post Surgery, or Fused	<u>-6</u>	<u>-3</u>	<u>-3</u>
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)	<u>(5)</u>	<u>(2)</u>	<u>(3)</u>
Twelve Months Post Surgery, Eligible for Evaluation (Intent to Treat Population)	260	131	129
Protocol Deviations (Censored Population)	<u>-45</u>	<u>-21</u>	<u>-24</u>
Twelve Months Post Surgery, Meet Protocol (Core Population)	215	110	105

As Table 1 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 cutoff 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).

Different groups of subjects were analyzed to demonstrate the safety and effectiveness of the SpinalPak® Fusion Stimulator. The safety analyses included all subjects who used the device at least once and had the potential to experience an adverse event (n=349). The effectiveness analyses focused on the findings from the core group (n=215).

G. Safety Analyses (All Subjects n=349)

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.

H. Comparability of Core Groups / Effectiveness 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.

I. Clinical Characteristics of the Core Subjects (n=215)

As described above, the demographic and clinical characteristics of the active and placebo subjects in the core group are 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. Almost all subjects had a 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.

J. Success in the Core Group (n=215)

Table 2 compares success in the active and placebo subjects of the core group (n=215). An overall success requires 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.

**Table 2
Frequency Of Success The Core Group, By Treatment (n = 215)**

	Overall Success (Clinical AND Radiographic Success)	Clinical Success	Radiographic Success	Average PSAF Score Baseline/ 12 months
Active (N = 110)	87 (79%)	95 (85%)	94 (85%)	31.44/ 23.03
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 physician described clinical success and also a radiographic successes 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 ($Z = -0.2675$).

K. Logistic Regression Analysis

A number of subject characteristics and demographics may affect the probability of an overall successful outcome. 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 a an overall successful outcome:

- (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 steroids and NSAIDS
- (8) a secondary diagnosis of herniated disc pulposus;
- (9) a secondary diagnosis of spondylolsthesis;
- (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.

The following four variables were associated with 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. An analysis was then conducted with only the four identified variables, and is shown below in Table 3.

**Table 3
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).

X. Conclusions Drawn From Study

All of the data provided in the previous sections describing the pre-clinical, clinical studies provide reasonable assurance of the safety and effectiveness of the SpinalPak Fusion Stimulator when used by trained physicians as a non-invasive bone growth stimulator used as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels.

XI. Panel Recommendations

This is a PMA supplement which did not require panel review

XII. CDRH Decision

CDRH recommends approval for the SpinalPak Fusion Stimulator as a non-invasive bone growth stimulator used as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels.

XIII. Approval Specifications

A Post-market Study will not be required for this device. No significant clinical issues of safety and effectiveness remain to be collected which would yield clinically significant information which would necessitate modifications to device indications, adverse events, contra-indications, precautions or warnings.

LABELING

Draft Professional Labeling

SpinalPak® Fusion Stimulator

**Caution: Federal law restricts this device
to sale by or on the order of a physician.**

**This device has been APPROVED
by the U.S. Federal Food and Drug Administration
for the indications described below.**

INDICATIONS FOR USE

The SpinalPak® Fusion Stimulator is a noninvasive electric bone growth stimulator indicated as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels.

DEVICE DESCRIPTION

The SpinalPak® Fusion Stimulator is a bone growth stimulator utilizing capacitive coupling technology.

The SpinalPak® Fusion Stimulator system consists of two primary components: (1) the Patient Kit, which includes the SpinalPak® Fusion Stimulator, the hydrogel electrodes, the electrode lead wires, and a supply of 9-volt batteries; and, (2) the Physician Test Meter (which remains with the physician). The SpinalPak® Fusion Stimulator is a lightweight (less than four oz.), battery operated, portable signal generator. It produces a sinusoidal waveform of five Volts Peak-to-Peak amplitude, at a frequency of 60 Kilohertz, which is delivered to the patient by two hydrogel electrodes

The stimulator has a two-color light emitting diode (LED) and an audible alarm system to monitor device function. If the stimulator is functioning properly, the LED will emit an intermittent green light. If the stimulator is not functioning properly, the LED light will change to red and an audible alarm signal will be activated. A continuous red light and audible alarm indicate that the battery voltage is too low for effective treatment. An intermittent red light and audible alarm indicate there may be poor electrode contact with the skin or a poor connection of the wires. The "ALARM ON-OFF" switch located on the face of the stimulator may be used to temporarily turn off the audible alarm system.

The SpinalPak® Fusion Stimulator also has an internal elapsed time accumulator that stores the number of days the device was used. The device will automatically deactivate after 270 days of accumulated therapy. A health care professional may use the Physician Test Meter to determine the number of days of device use and to evaluate the stimulator's current treatment voltage and amperage levels. The Physician Test Meter provides a visual display of this information.

WARNINGS

- Cardiac pacemakers or cardioverters may be adversely affected by the SpinalPak® Fusion Stimulator. The concomitant use of the device and a pacemaker or cardioverter must be assessed on an individual basis, such as with an electrocardiogram, prior to use. The patient should be referred to a cardiologist for monitoring of pacemaker function while wearing the active SpinalPak® device. If there are any observable adverse changes in the pacemaker rhythm or output, the SpinalPak® device should not be used.
- The safety and effectiveness of the SpinalPak® Fusion Stimulator in pregnant women have not been studied, and the effects of the device on the mother or the developing fetus are unknown. A patient who is either pregnant or is intending to become pregnant should be referred to her doctor prior to treatment with the SpinalPak® device.

PRECAUTIONS

- The safety and effectiveness of the SpinalPak® Fusion Stimulator in individuals with the following conditions have not been studied, and therefore the safety and effectiveness of the device in these individuals is therefore unknown:
 - spondylitis, infection, Paget's disease
 - cancer, diabetes mellitus, renal disease
 - trauma of the lumbar spine
 - osteoporosis
- The patient should be instructed to apply the electrode after the skin has been cleaned and dried. If erythema develops at the electrode sites, the electrodes should be relocated either immediately above or below the original sites. If the reaction does not resolve after 48 hours after relocating the electrodes, the patient should be instructed to consult with the physician.
- Do not submerge or expose the SpinalPak® Fusion Stimulator to water. The patient should be instructed to remove the stimulator during bathing, showering or swimming.
- Compliance with the treatment schedule, daily battery changes, proper maintenance of the device, and replacing the electrodes every five to seven days are essential for proper device function.
- The patient should be able to use the device in accordance with the instructions for use. If a patient cannot comply with these instructions for any reason, use of the device is not recommended.
- This system should only be used with components and parts recommended by Bioelectron, Inc. Other components and parts may not be compatible, and may damage the device.
- If any component does not function properly, contact Bioelectron, Inc. at 1 (800) 524-0677. No attempt should be made to modify or repair the device.

ADVERSE EVENTS

During a multi-center clinical study of 349 patients treated with the SpinalPak® Fusion Stimulator for the indication listed above, skin irritation was the most common adverse effect associated with use of the SpinalPak® device. It occurred in 9 patients (2.6% of the trial population) – 4 patients treated with the active device and 5 patients treated with the placebo device.

CLINICAL STUDIES

A randomized, double-blinded clinical study was conducted to determine whether the SpinalPak® Fusion Stimulator increases the frequency of overall success (where overall success is defined as the combination of clinical and radiographic success) when compared to placebo (inactive) units, after primary (first-time) one or two level fusions within L3 to S1.

All subjects had degenerative disc disease. Investigators were instructed to apply the SpinalPak® within three weeks of surgery. Subjects may have undergone a posterior lumbar interbody fusion (PLIF), an anterior lumbar interbody fusion (ALIF), a bilateral posterolateral fusion, or a combination of these procedures with or without internal fixation. Subjects were to be excluded from the study if they:

- Had a pathologic process at spine level
- Had a systemic disease that may affect fusion
- Had osseous trauma of the lumbar spine
- Were pregnant
- Had a cardiac pacemaker
- Were unable to understand or comply with study instructions
- Had moderate to severe osteoporosis (osteoporosis was subjectively defined by individual physicians)

Subjects were randomly assigned an active or inactive (placebo) stimulator. The subjects were instructed to use the device continuously, except for periods of personal hygiene, until the physician had determined a patient was considered to be an overall success or for a period of nine months (the maximum treatment duration time).

Subjects were considered to be an overall success only if they were determined to be radiographically successful and clinically successful at the final evaluation timepoint. An independent blinded review process confirmed radiographic assessments.

Of all subjects entered into the study, 2.6% experienced skin irritation.

Two hundred and fifteen subjects met all the protocol requirements and formed the core group for the data analysis. The effectiveness results described below were analyzed using a two-tail Fisher exact test.

The active (n=110) and placebo (n=105) subjects were evaluated to determine if the treatment groups were comparable, and to assure that a 24% loss to withdrawal and a 14% loss to censure (subjects completed the study, but did not comply with all protocol requirements) did not bias study results. The groups were compared using 63 demographic and clinical characteristics, such as age, gender, body mass index, tobacco and alcohol use, type of occupation and preoperative primary and secondary diagnoses. There were no statistically significant differences between these treatment groups. The treatment groups were also compared preoperatively using data from a 14-question pain and dysfunction patient self-assessment questionnaire. The analysis of the summed pain and dysfunction scores showed no statistically significant differences in the preoperative status of the treatment groups.

Table 2 compares success in the active and placebo subjects of the core group (n=215). An overall success requires 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.

Table 2
Frequency Of Success The Core Group, By Treatment (n = 215)

	Overall Success (Clinical AND Radiographic Success)	Clinical Success	Radiographic Success	Average PSAF Score Baseline/ 12 months
Active (N = 110)	87 (79%)	95 (85%)	94 (85%)	31.44/ 23.03
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 physician described clinical success and also a radiographic successes

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 ($p=0.0018$).

A subjective patient self-assessment form (PSAF) was also used to collect information about subjects' perceptions of their ability to function. Scores from PSAF show that there is no statistically significant difference between active and placebo subjects at PSAF scores baseline and at the time of final evaluation.

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 a 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 spondylolysthesis;
- (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 3**.

Table 3
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 SpinalPak® Fusion Stimulator may be used as an adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels.

INSTRUCTIONS FOR USE

Patients should be instructed in the proper use and daily maintenance of the device. All instructions below are also presented in the Patient Manual, which is included with every SpinalPak® unit.

1. Electrodes and Placement

The low profile hydrogel electrodes are mounted on a release liner and may be used for five to seven days.

The two electrodes should be placed on each side of the patient's spinal column. The electrodes should be placed four to six inches apart at the mid-fusion level.

2. Electrode Application

Remove the two hydrogel electrodes from the packaging. Moisten the entire gel area of each electrode with tap water applied by fingertip. Gently press the electrodes on

the patient's skin in the proper position as described above. Connect the electrodes to the electrode lead wire.

With use, the electrode gel area may dry out and the electrode may lose its contact with the skin. (This may cause the LED display to blink red intermittently, and cause an audible intermittent warning sound) . If this occurs, the electrode may be reapplied. Again moisten the entire gel area of the electrode with tap water. Reapply the electrode to the patient's skin.

Adhesive covers (provided in the Patient Kit) may be used to protect the electrodes during bathing or showering. The protective covers are provided to prevent the necessity of completely removing the adhesive electrodes and then re-applying them following personal hygiene.

3. Commencement of Treatment

Insert the electrode lead plug carefully into the jack at the top of the stimulator, and rotate it clockwise, as shown in Figure 1.

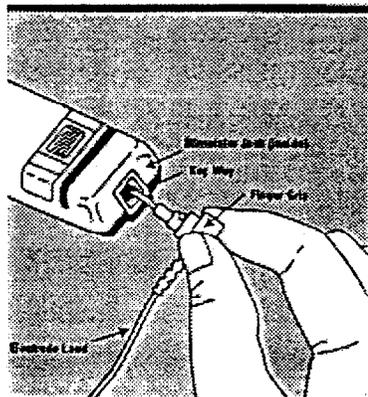


Figure 1

Open the battery compartment of the stimulator by sliding its cover down, as shown in Figure 2. Insert one of the supplied 9-volt alkaline batteries into the battery compartment. Replace the cover by pressing it down. The cover will snap into place.

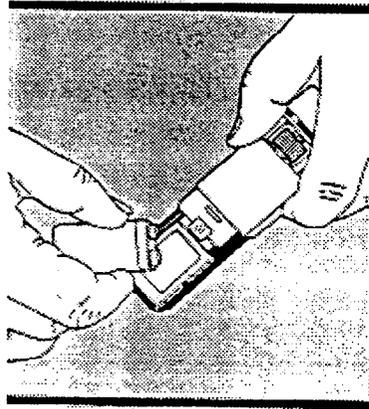


Figure 2

If the stimulator is functioning properly, there will be an intermittent green flashing light. This light means that the electrodes are properly applied, the battery is functioning, and the device is delivering a therapeutic current.

If the device is not functioning properly, an audible alarm and red light will appear. The type of alarm and red light will vary depending upon the cause of the problem.

If the audible alarm and red light are continuous, the battery voltage is too low. Insert a new battery, and properly dispose of the old battery.

If the audible alarm and red light are intermittent, the continuity of the circuit may have been interrupted. Confirm that the electrode lead is properly connected to the electrodes and the stimulator. Check that the electrodes are making proper contact with the skin, and reapply the electrodes if necessary. If the alarm and red light continue, replace the electrode lead. If the alarms stop, the original electrode lead may be defective. If the alarms continue, there may be a problem with the stimulator. Use a new stimulator.

Do not attempt to fix the stimulator. Please contact Bioelectron at 1-800-524-0677 or your sales representative.

An On/Off Switch on the stimulator controls the audible alarm, but not the visual alarm. The patient may elect to turn the audible alarm off if it would be disruptive, but the alarm should be re-activated as soon as practicable.

4. The Physician Test Meter

The health care professional may use the Physician Test Meter to monitor the number of days of device use, and to evaluate the stimulator's treatment voltage and current levels.

Before using the Physician Test Meter, make sure the stimulator has a new battery and the electrodes are properly placed on the patient's skin.

Remove the stimulator's battery compartment cover. Insert the Test Meter into the jack located inside the battery compartment of the stimulator, as shown in Figure 3.

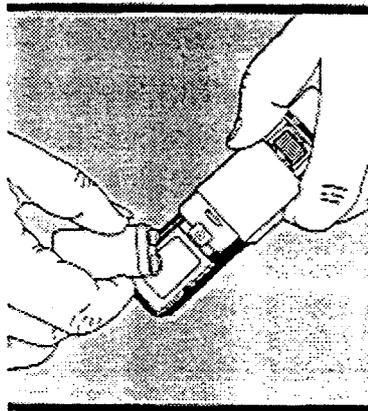


Figure 3

The voltage (VOLTS) is read first, then the current in milli-amperes (mAMPS), and then days (DAYS) by pressing the appropriate button on the front of the test meter. The test meter is operating only when the buttons are depressed.

The chart below describes the appropriate action to be taken based upon the meter readings.

BUTTON	VOLTAGE (VOLTS)	CURRENT (mAMPS)	APPROPRIATE ACTION
Reading	Between 3 & 6.3	Between 5 & 10	1. Normal treatment range.*
	Less than 3 or greater than 6.3**	Between 5 & 10	1. Check and correct the application of electrodes. 2. Insert a new battery. 3. If the voltage reading is still less than 3 volts or greater than 6.3 volts, proceed with treatment as current is within treatment range.
	"88.8"***	Less than 5 or greater than 10	1. Check and correct the application of the electrodes. 2. Insert a new battery. 3. If the current (mA) reading is still outside the range of 5 to 10 mA; the stimulator may be defective. Try a new stimulator.

* The essential requirement of the treatment signal is between 5 and 10 mA of current. The voltage is simply the driving force for the delivery of the current (mA).

** A value greater than 6.3 will be displayed as a flashing "88.8."

When the device has recorded 270 days of accumulated therapy, the SpinalPak® Fusion Stimulator will automatically cease to function. The red/green light indicators and the audible alarm will also cease to function.

PATIENT COUNSELING INFORMATION

The patient should be thoroughly instructed on how to properly use and care for the SpinalPak® Fusion Stimulator, and receive the patient labeling, which provides detailed instructions. A summary of the key points in the patient labeling is provided below.

Compliance - The patient should be instructed that compliance with device use and care is critical to assure the proper function of the device and effective treatment.

Battery - The patient should be instructed to insert a new battery in the stimulator every 24 hours.

Electrodes - The patient should be instructed to replace the electrodes every five to seven days, and to clean thoroughly the electrode sites with soap and water prior to applying the electrodes.

Skin Irritation - The patient should be instructed to examine the skin for irritation when replacing the electrodes. If irritation is present, the patient should be instructed to relocate the electrodes immediately above or below the original sites and to contact the physician within 48 hours. The patient should be evaluated periodically to assess the skin for sensitivity.

Alarms - The patient should be instructed to replace the battery if a continuous audible alarm and red light appear. If the audible and visual alarms are intermittent, the patient should be instructed to check that the electrode lead is connected, and to check that the electrodes are properly applied to the skin and to reapply if necessary. If the alarms continue after these checks, the patient should be instructed to contact Bioelectron at 1-800-524-0677 or the sales representative.

On/Off Switch for the Audible Alarm - The patient should be instructed to keep the audible alarm system in the "On" position as often as practical, and to reset the alarm system if it has been switched to the "Off" Position as soon as practicable.

Bathing - The patient should be instructed to disconnect the stimulator unit during bathing, showering or swimming. It should be reconnected as soon as practical following these activities. The patient should also be instructed to either remove the electrodes, or to cover the electrodes with the protective adhesive covers (available through Bioelectron), during bathing and showering.

STORAGE AND HANDLING

The SpinalPak® Fusion Stimulator should be stored in a cool and dry place. Do not use cleaning agents or solvents on any of the device components. The stimulator and electrode leads may be cleaned using a damp cloth.

The device components should be handled with care. Damage may occur if the device is inappropriately handled or abused.

The stimulator must not be submerged or exposed to water.

**If you have any questions regarding the
SpinalPak® Fusion Stimulator, please call one of our
customer service representatives at 1-800-524-0677.**

**Bioelectron, Inc.
25 Commerce Drive
Allendale, NJ 07401**

Bioelectron, Inc.

SpinalPak® Patient Education Brochure

COVER

HEAD: SpinalPak® Fusion Stimulator

SUBHEAD: A Patient's Guide

LOGO: Bioelectron

NOTE Caution: Federal law restricts this device to sale by or on the
INSIDE: order of a physician.

Why Your Doctor Has Prescribed SpinalPak®

Following your spine fusion (back) surgery, your doctor has prescribed the SpinalPak® Fusion Stimulator as an added treatment to your surgery. The SpinalPak® Fusion Stimulator delivers an electrical signal to the area of your surgery. This booklet provides instructions on how to use and care for your SpinalPak®. Please read this information carefully before using the device. The safe and effective use of SpinalPak® depends upon following the instructions and care described below.

How SpinalPak® Works

SpinalPak® delivers an electrical signal that is intended to help your back to heal. The signal operates at a high frequency, therefore you should not feel the signal during your treatment with the SpinalPak®. Two lightweight electrodes (conductors of electrical signals), which look like round Band-Aids®, are placed on your spine, four to six inches apart from one another, at the level of your back surgery. These dermal (skin) electrodes are easy to apply, are extremely lightweight, and are a necessary component in delivering the electrical signal to your surgery site. The stimulator is battery operated. Upon insertion of the 9-volt battery, the unit is automatically activated (turned-on), and is always "on" as long as the battery is not used up, and the electrodes are placed on the skin.

Your SpinalPak® Kit consists of:

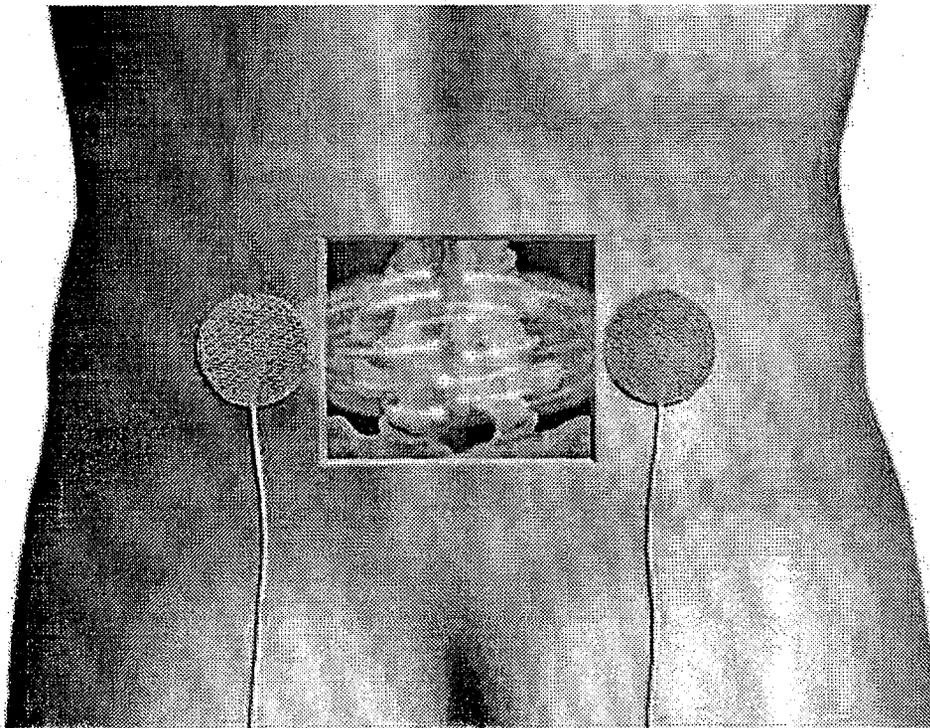
- SpinalPak® Fusion Stimulator
- Extra Electrodes
- Additional adhesive electrode covers to enhance electrode security (if needed)
- Electrode lead wires (to connect the electrodes to the SpinalPak® device)
- 9-volt batteries.

* Band-Aids® is a Registered Trademark of Johnson and Johnson

Wearing SpinalPak®

- SpinalPak® has been designed so that it is convenient to use, comfortable to wear, and safe to operate. You should begin using SpinalPak® immediately after you have read the instructions for use.
- Place two electrodes on your skin, the first two to three inches to the left of the area of your surgery, and another two to three inches to the right of the area of your surgery. Depending on your ability to move after your surgery, it may be helpful to ask another person to help you place these electrodes on your back. With your fingertip, wet the entire gel area of the electrode with tap water. Consult your doctor should you have questions about proper electrode placement.

Make sure you apply the electrodes after your skin has been cleaned and dried. If your skin becomes abnormally red at the electrode sites, the electrodes should be moved either immediately above or below the original sites. If the redness does not go away after 48 hours after moving the electrodes, you should call your doctor.



- Connect the electrodes to the stimulator using the lead wires provided. Choose the shortest lead wires possible to connect to the SpinalPak® Fusion Stimulator where you wish to wear the stimulator on your body. Put the electrode lead plug carefully into the jack at the top of the stimulator, and turn it clockwise, see Figure 1.

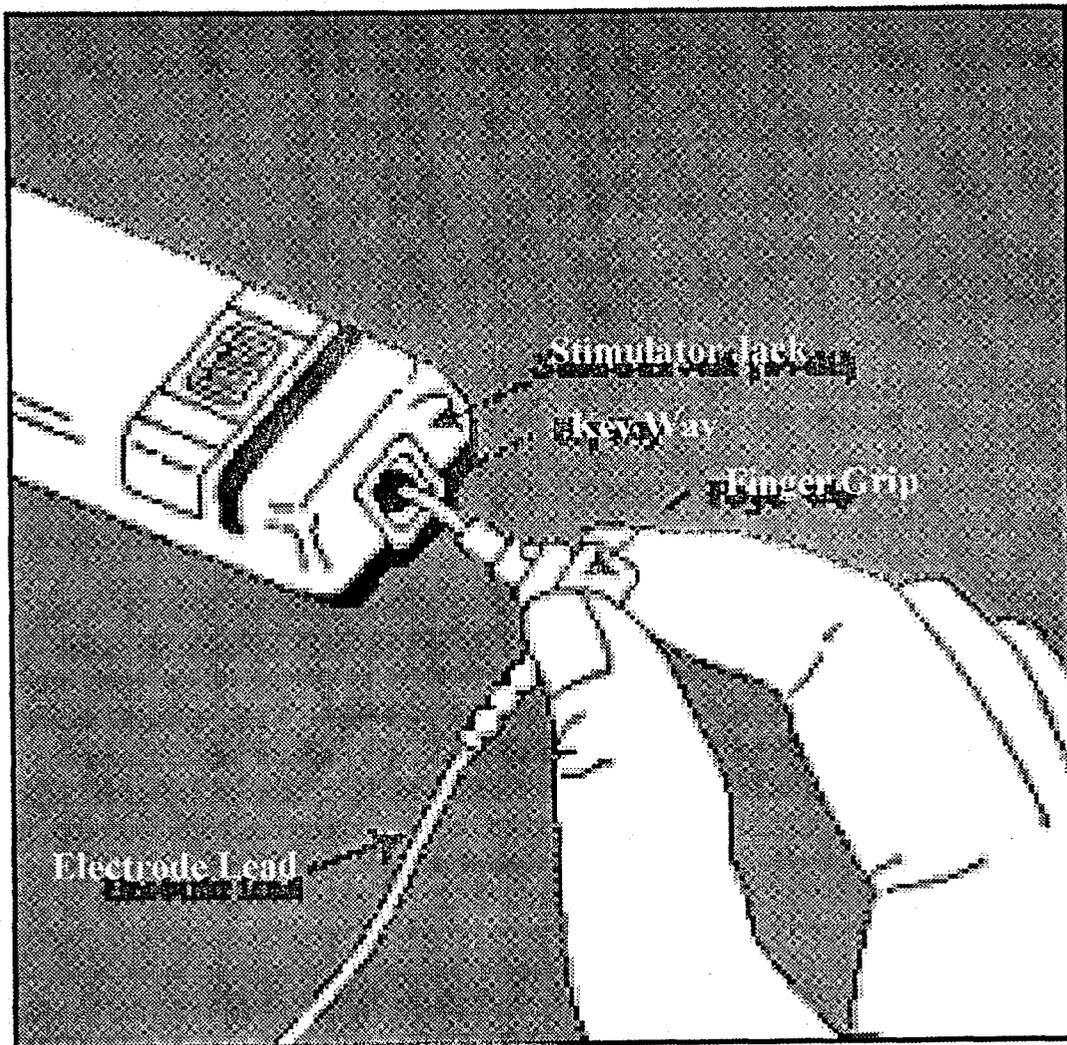


Figure 1

- Insert a new 9-volt alkaline battery every day.

Each day, (preferably at the same time), you should:

- Remove the battery compartment cover as shown in Figure 2.
- Insert one of the supplied, new 9-volt batteries, and throw away or recycle the old battery.
- Replace the cover by pressing it down. It will snap into place.
- Check to see that the stimulator's indicator light is flashing "green" on the front of the unit. This shows that the unit is operating properly, and that the

device is sending the therapeutic signal. If the indicator light flashes "red", see the "Warning Section" to try to figure out what is wrong.

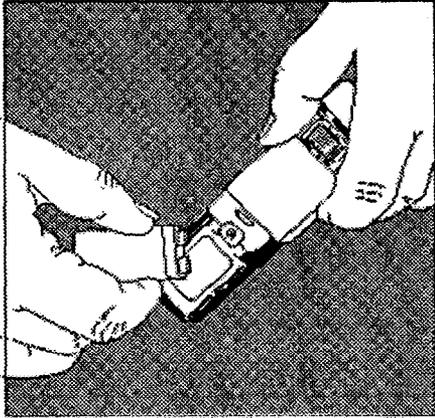


Figure 2

- Change your electrodes every five to seven days. Different skin types will provide for longer or shorter life of the electrodes. If the indicator starts and stops flashing "red" it is likely that either the lead wire connection is incomplete or the adhesive (gel) on the electrode is no longer working, and the electrodes need changing. Check all lead wire connection points, to make sure that the lead wire is tightly plugged into the top of the SpinalPak® device, and that the lead wire connectors are completely inserted into both electrode connectors. If all the connections are made and the indicator light continues to flash "red," it is probably time to change the electrodes.
 - Remove the old electrodes from your skin by wetting your fingertips with tap water, and gently peeling back the electrode. DO NOT abruptly tear the electrode off the skin.
 - Wash your skin gently with soap and water and pat dry.
 - Remove two new electrodes from the packaging.
 - Thoroughly moisten the entire gel area of each electrode with tap water applied with your fingertip.
 - Gently press the electrodes on your skin in same place as before. You may need help putting the electrodes on your back. Ask another person for help if you cannot reach your back easily. If your skin is very red, place the electrodes slightly above or below the original sites, and call your doctor if the redness does not go away in 48 hours. It is normal to note a slight pinkness of the skin after removal of the previous pair of electrodes. This pinkness will fade within minutes.
- Use SpinalPak® up to 24 hours per day. Your doctor will tell you when to stop using it. After 270 days of use, your SpinalPak® will automatically turn off.

NOTE:

The SpinalPak® Spine Fusion Stimulator accurately records the number of days you receive treatment. A special monitor records and displays this information for your doctor. This helps your doctor track your treatment.

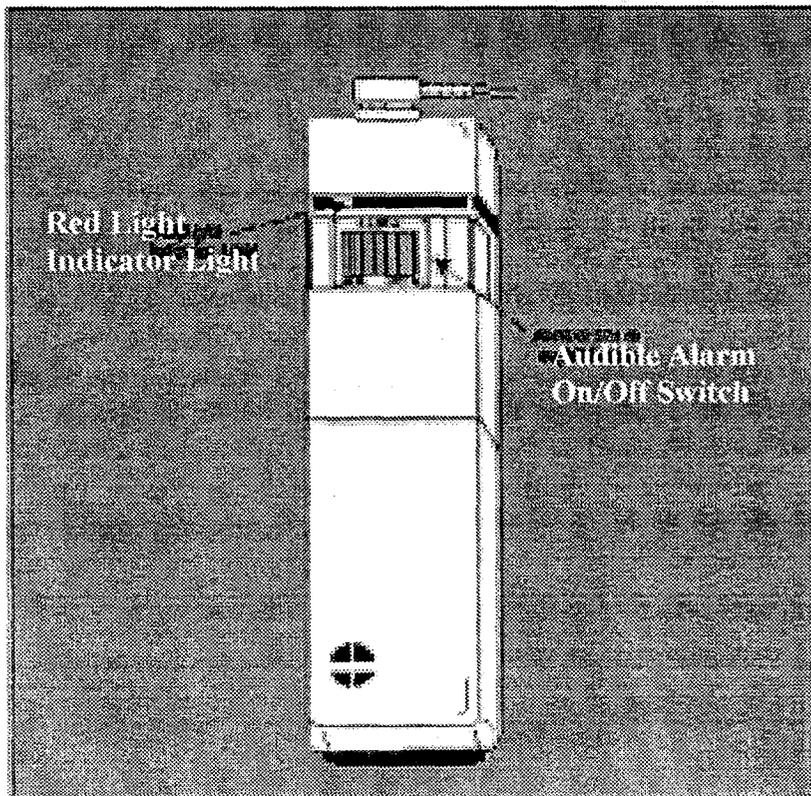
Indicator Light:

- A flashing green light indicates that the device is working properly. A flashing or constant “red” light and an audible alarm signal (a signal that you can hear) alert you to any problems. The alarm you can hear can be turned off using the “ON/OFF” switch on the front of the device. This switch does not affect the indicator light, see Figure 3.
- If the red light and audible alarm do not go away, first try replacing the wire to your electrodes. If the alarms stop, your electrode wire may have been defective. If the alarms do not stop, there may be a problem with your SpinalPak® stimulator. Do not try to fix the stimulator. Call Bioelectron 1 (800) 524-0677.

Tip:

Keep the audible alarm system in the “On” position as much as possible. This alarm will help warn you to any problems with the device. During special occasions when you would like the device not to tell you audibly about stimulator problems, you may set the switch to the “Off” position. It is recommended that you turn the unit back “On” as soon as possible.

- Remove your SpinalPak® when you bathe, shower or swim. You should also either remove the electrodes, or cover them with the additional adhesive covers provided if



you prefer to leave the electrodes attached to the skin during bathing and showering.

Figure 3

Caring for Your SpinalPak®

- Don't use cleaning products or detergents on any part of SpinalPak®. You just need a damp cloth.
- Do handle SpinalPak® carefully. Dropping or rough handling can cause damage.
- Store SpinalPak® in a cool and dry place when you are not wearing it.
- Contact Bioelectron at 1 (800) 524-0677 if you believe that the device has been damaged or is operating improperly.

Warning Signals

- Flashing green light: the stimulator is working properly
- Constant Red light and Constant audible beeping: Replace battery.
- Flashing Red light and intermittent beeping: The circuit is incomplete, check all connection points, including electrode to skin interface.

Tip:

Loose Electrodes – Make sure that both electrodes are in complete contact with your skin. Remoisten or replace worn electrodes if necessary.

Incomplete Circuit – Check all connection points, insuring tight fit of lead wire into top of SpinalPak® device, and adequate touching of lead wire pin into electrode wire receptacle.

Broken Electrode Lead – If you have checked the electrodes and the connections and the flashing red light and audible alarms continue, a break in the lead wire may be responsible. Remove the old electrode lead. Turn the lead counterclockwise and then pull out. Attach a new electrode lead into the jack. An extra electrode lead is provided in the kit.

If the alarm still continues, please call Bioelectron at 1-800-524-0677.

If You Have Questions

If you have questions about your SpinalPak® contact Bioelectron Customer Service toll-free at (800) 524-0677 24 hours a day, seven days a week.

IMPORTANT: Any/All medical questions must be directed to your doctor.

INDICATIONS FOR USE

The SpinalPak® Fusion Stimulator is a noninvasive bone growth stimulator indicated for use adjunct electrical treatment to primary lumbar spinal fusion surgery for one or two levels.

WARNINGS

- Cardiac pacemakers or cardioverters may be adversely affected by the SpinalPak® Fusion Stimulator. The concomitant use of the device and a pacemaker or cardioverter must be assessed on an individual basis, such as with an electrocardiogram, prior to use. The patient should be referred to a cardiologist for monitoring of pacemaker function while wearing the active SpinalPak® device. If there are any observable adverse changes in the pacemaker rhythm or output, the SpinalPak® device should not be used.
- The safety and effectiveness of the SpinalPak® Fusion Stimulator in pregnant women have not been studied, and the effects of the device on the mother or the developing fetus are unknown. A patient who is either pregnant or is intending to become pregnant should be referred to her doctor prior to treatment with the SpinalPak® device.

PRECAUTIONS

- The safety and effectiveness of the SpinalPak® Fusion Stimulator in individuals with the following conditions have not been studied, and therefore the safety and effectiveness of the device in these individuals is therefore unknown:
 - spondylitis, infection, Paget's disease
 - cancer, diabetes mellitus, renal disease
 - trauma of the lumbar spine
 - osteoporosis
- Apply the electrode after the skin has been cleaned and dried. If erythema develops at the electrode sites, the electrodes should be relocated either immediately above or below the original sites. If the reaction does not resolve after 48 hours after relocating the electrodes, the patient should be instructed to consult with the physician.
- Do not submerge or expose the SpinalPak® Fusion Stimulator to water. The patient should be instructed to remove the stimulator during bathing, showering or swimming.

- Compliance with the treatment schedule, daily battery changes, proper maintenance of the device, and replacing the electrodes every five to seven days are essential for proper device function.
- Patients should be able to use the device in accordance with the instructions for use. If a patient cannot comply with these instructions for any reason, use of the device is not recommended.
- This system should only be used with components and parts recommended by Bioelectron, Inc. Other components and parts may not be compatible, and may damage the device.
- If any component does not function properly, contact Bioelectron, Inc. at 1 (800) 524-0677. No attempt should be made to modify or repair the device.

ADVERSE EVENTS

During a multi-center clinical study of 349 patients treated with the SpinalPak® Fusion Stimulator for the indication listed above, skin irritation was the most common adverse effect associated with the use of the SpinalPak® device. It occurred in 9 patients (2.6% of the trial population) – 4 patients treated with the active device and 5 patients treated with the placebo device.

LOGO: Bioelectron
Pathways to Healing

ADDRESS: 25 Commerce Drive, Allendale, NJ 07401
(800) 524-0677 • (201) 760-6400