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IMPORTANT INFORMATION ON THE INFUSE/MASTERGRAFT™ Posterolateral Revision Device

PURPOSE

HUMANITARIAN DEVICE. INFUSE/MASTERGRAFT™ Posterolateral Revision Device is authorized by Federal law for the repair of symptomatic, posterolateral lumbar spine pseudoarthrosis. This device is intended to address a small subset of patients for whom autologous bone and/or bone marrow harvest are not feasible or are not expected to promote fusion; examples of these patients are diabetics and smokers. The effectiveness of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device for this use has not been demonstrated.

DESCRIPTION

INFUSE/MASTERGRAFT™ Posterolateral Revision Device consists of a 2-part bone graft replacement (INFUSE® Bone Graft + MASTERGRAFT® Granules) used as part of a 3 component system (INFUSE® Bone Graft + MASTERGRAFT® Granules + supplemental posterior fixation system, *e.g.*, the CD HORIZON® Spinal System). These components must be used as a system for the prescribed indication described below. The bone morphogenetic protein solution component must not be used without the carrier/scaffold component or with a carrier/scaffold component different from the one described in this document. The INFUSE® Bone Graft component must be used with the MASTERGRAFT Granules and must not be used with bulking agents different from the one described in this document.

Implied warranties of merchantability and fitness for a particular purpose or use are specifically excluded. See the MDT Catalog or price list for further information about warranties and limitations of liability.

INDICATIONS

The INFUSE/MASTERGRAFT™ Posterolateral Revision Device is indicated for the repair of symptomatic, posterolateral lumbar spine pseudoarthrosis. This device is intended to address a small subset of patients for whom autologous bone and/or bone marrow harvest are not feasible or are not expected to promote fusion. These patients are diabetics and smokers. This device is indicated to treat two or more levels of the lumbar spine.

DIRECTIONS FOR USE

The rhBMP-2 is provided as a lyophilized powder in a vial delivering 12mg of protein. After appropriate reconstitution, the concentration is (1.5mg/ml) of rhBMP-2. The solution is then applied to the provided absorbable collagen sponge. The INFUSE® Bone Graft component is prepared at the time of surgery and allowed a prescribed amount of time (no less than 15 minutes) before MASTERGRAFT® Granules are placed onto the absorbable collagen sponge. The ACS should then be rolled over the MASTERGRAFT® Granules until the ACS cannot be rolled any further.

A small amount of local bone may be added to the MASTERGRAFT® Granules as supplemental bulking material.

The INFUSE® Bone Graft component must not be sterilized by the hospital.

MASTERGRAFT® Granules are provided sterile and should be considered sterile unless the inner packaging has been opened or damaged. This product is never to be resterilized.

The Instructions for Preparation contain complete details on preparation of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device.

CONTRAINDICATIONS

- The INFUSE/MASTERGRAFT™ Posterolateral Revision Device is contraindicated for patients with a known hypersensitivity to recombinant human Bone Morphogenetic Protein-2, bovine Type I collagen or to other components of the formulation.
- The INFUSE/MASTERGRAFT™ Posterolateral Revision Device should not be used in the vicinity of a resected or extant tumor, in patients with any active malignancy or patients undergoing treatment for a malignancy.
- INFUSE/MASTERGRAFT™ Posterolateral Revision Device should not be used in patients who are skeletally immature (≤21 years of age or no radiographic evidence of epiphyseal closure).
- The INFUSE/MASTERGRAFT™ Posterolateral Revision Device should not be used in pregnant women. The potential effects of rhBMP-2 on the human fetus have not been evaluated.
- The INFUSE/MASTERGRAFT™ Posterolateral Revision Device should not be implanted in patients with an active infection at the operative site.

PHYSICIAN NOTE: Although the physician is the learned intermediary between the company and the patient, the important medical information given in this document should be conveyed to the patient.

WARNING(S)

- In an experimental rabbit study, rhBMP-2 has been shown to elicit antibodies that are capable of crossing the placenta. Reduced ossification of the frontal and parietal bones of the skull was noted infrequently (<3%) in fetuses of rabbit dams immunized to rhBMP-2; however, there was no effect noted in limb bud development. There are no adequate and well-controlled studies in human pregnant women. Women of child bearing potential should be warned by their surgeon of potential risk to a fetus and informed of other possible orthopedic treatments.
- Women of childbearing potential should be advised that antibody formation to rhBMP-2 or its influence on fetal development has not been completely assessed. In the clinical trial supporting the safety and effectiveness of the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device, 2/277 (0.7%) patients treated with INFUSE® Bone Graft component and 1/127 (0.8%) patients treated with autograft bone developed antibodies to rhBMP-2. The effect of maternal antibodies to rhBMP-2, as might be present for several months following device implantation, on the unborn fetus is unknown. Additionally, it is unknown whether fetal expression of BMP-2 could re-expose mothers who were previously antibody positive. Theoretically, re-exposure may elicit a more powerful immune response to BMP-2 with possible adverse consequences for the fetus. However, pregnancy did not lead to an increase in antibodies in the rabbit study. Studies in genetically altered mice indicate that BMP-2 is critical to fetal development and that a lack of BMP-2 activity may cause neonatal death or birth defects. It is not known if anti-BMP-2 antibodies may affect fetal development or the extent to which these antibodies may reduce BMP-2 activity.
- INFUSE® Bone Graft should not be used immediately prior to or during pregnancy. Women of childbearing potential should be advised not to become pregnant for one year following treatment with the INFUSE/MASTERGRAFT™ Posterolateral Revision Device.
- The safety and effectiveness of the INFUSE INFUSE/MASTERGRAFT™ Posterolateral Revision Device in nursing mothers has not been established. It is not known if BMP-2 is excreted in human milk.

- When degenerative disc disease was treated by a posterior lumbar interbody fusion procedure with cylindrical threaded cages (INTER FIX® devices), posterior bone formation was observed in some instances.

- When anterior cervical spinal fusions were performed using the INFUSE® Bone Graft component, some cases of edema have been reported within the first post-operative week. In some of these cases, this swelling has been severe enough to produce airway compromise, sometimes requiring emergency surgery.

- Placement of rhBMP-2/ACS can cause initial resorption of trabecular bone that may be transient.

- Nerve compression associated with ectopic bone formation has been reported in patients undergoing spine surgery with rhBMP-2/ACS. Surgical intervention may be required to address the symptoms.

PRECAUTION(S)

General

- The safety and effectiveness of repeat applications of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device has not been established.
- The INFUSE/MASTERGRAFT™ Posterolateral Revision Device should only be used by surgeons who are experienced in spinal fusion procedures and have undergone adequate training with this device, for posterolateral procedures.
- The INFUSE/MASTERGRAFT™ Posterolateral Revision Device is intended for single use only. Discard unused product and use a new device for subsequent applications.
- Prior to use, inspect the packaging, vials and stoppers for visible damage. If damage is visible, do not use the product. Retain the packaging and vials and contact a Medtronic representative.
- Do not use after the printed expiration date on the label.

Hepatic and Renal Impairment

- The safety and effectiveness of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device in patients with hepatic or renal impairment has not been established. Pharmacokinetic studies of rhBMP-2 indicate that the renal and hepatic systems are involved with its clearance.

Geriatrics

- Preliminary clinical results of the Pilot INFUSE® Bone Graft/ MASTERGRAFT® Granules/CD HORIZON® Spinal System study, did not include sufficient numbers of patients 65 years and older to determine whether they respond differently from younger subjects.

Bone formation

- The safety and effectiveness of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device has not been demonstrated in patients with metabolic bone diseases.
- While not specifically observed in a clinical study, the potential for ectopic, heterotopic or undesirable exuberant bone formation exists.

Antibody Formation/Allergic Reactions

- The safety and effectiveness of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device has not been demonstrated in patients with autoimmune disease.
- The safety and effectiveness of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device has not been demonstrated in patients with immunosuppressive disease or suppressed immune systems resulting from radiation therapy, chemotherapy, steroid therapy or other treatments.

Immunogenicity

- As with all therapeutic proteins, there is a potential for immune responses to be generated to the INFUSE® Bone Graft component. In a study evaluating a product which contained the rhBMP-2/ACS components of the HDE product to treat a population different from that of the HDE population, the immune response to the INFUSE® Bone Graft components was evaluated in 349 investigational patients and 183 control patients receiving lumbar interbody fusions.
  - *Anti-rhBMP-2 antibodies:* 2/349 (0.6%) patients receiving the INFUSE® Bone Graft component developed antibodies vs. 1/183 (0.5%) in the control group.
  - *Anti-bovine Type I collagen antibodies:* 18.1% of patients receiving the INFUSE® Bone Graft component developed antibodies to bovine Type I collagen vs. 14.2% of control patients. No patients in either group developed anti-human Type I collagen antibodies.
  - The presence of antibodies to rhBMP-2 was not associated with immune mediated adverse events such as allergic reactions. The neutralizing capacity of antibodies to rhBMP-2 is not known.

IMPORTANT INFORMATION CONCERING THE IMMUNOGENICITY AND ADVERSE EVENT DATA PRESENTED IN THE FOLLOWING SECTIONS

The device approved in this HDE has not been studied in human clinical trials. Several studies involving devices containing rhBMP-2, the signaling molecule present in this HDE device, have been performed. Although these devices and indications differ from device configuration and indication approved in this HDE, these data were used to support relative safety. As a result, all immunogenicity and adverse event data described below were from uses of products that are different from the HDE product and implanted in patients that were not identical to the HDE target population.

IMMUNOGENOCITY

INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device Clinical Trials

The immune response to the INFUSE® Bone Graft components (1.5mg/ml rhBMP-2) were evaluated in a study containing 277 investigational patients and 136 control patients receiving lumbar interbody fusions. The presence of antibodies was assessed preoperatively and at 3 months postoperatively using ELISA. If there was a positive response to bovine Type I collagen, the serum was also tested for antibodies to human Type I collagen. The screening ELISA cutpoint for positive antibody responses was set to 5 times the standard deviation of sera from normal human donors. Subjects were considered to have an elevated immune response if the preoperative test was negative (titer < 50) and postoperative test was positive (titer ≥ 50) or if the preoperative test was positive and the postoperative test was positive with a three-fold higher titer than the preoperative test.

INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device		
Antibody	**Investigational N=277**	**Control N=136**
Anti-rhBMP-2	2 (0.7%)	1 (0.7%)
Anti-bovine Type I Collagen	50 (18.1%)	16 (11.8%)
Anti-human Type I Collagen (tested only if positive to Anti-bovine Type I Collagen)	0 (0.0%)	0 (0.0%)

The presence of antibodies to rhBMP-2 was not associated with immune mediated adverse events such as allergic reactions. The neutralizing capacity of antibodies to rhBMP-2 is not known. An evaluation was performed on the impact of a positive antibody response on overall success and fusion success. There was very little difference in overall and individual success when antibody status was taken into consideration.

INFUSE® Bone Graft/MASTERGRAFT™ Granules/CD HORIZON® Spinal System Pilot Clinical Trial

The immune response to the INFUSE® Bone Graft components (1.5mg/ml rhBMP-2) were evaluated in a study containing 25 investigational patients and 21 control patients receiving posterolateral lumbar fusions. The presence of antibodies was assessed at the preoperative, 6 weeks, 3, 6, and 12 months visits using ELISA. If a positive response to bovine Type I collagen was exhibited, the serum was also tested for antibodies to human Type I collagen. The optical density (OD) of positive and negative control samples were analyzed and compared with the ELISA cutpoint OD to determine if antibodies specific for rhBMP-2 were present or absent in each subject sample. The ELISA cutpoint OD is defined as two times the mean of the negative control OD. Subjects were considered to have an elevated immune response if the preoperative test was negative (titer < 50) and postoperative test was positive (titer ≥ 50); or if the preoperative test was positive and the postoperative test was positive with a two-fold or higher titer than the preoperative titer for rhBMP-2 and a three-fold or higher titer than the preoperative titer for bovine Type 1 collagen and human Type 1 collagen.

INFUSE® Bone Graft/ MASTERGRAFT™ Granules/ CD HORIZON® Spinal System		
Antibody	**Investigational N=25**	**Control N=21**
Anti-rhBMP-2	1 (4.0%)	1 (4.8%)
Anti-bovine Type I Collagen	2 (8.0%)	3 (14.3%)
Anti-human Type I Collagen (tested only if positive to Anti-bovine Type I Collagen)	0 (0.0%)	0 (0.0%)

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The presence of antibodies to rhBMP-2 was not associated with immune mediated adverse events such as allergic reactions. The neutralizing capacity of antibodies to rhBMP-2 is not known. Those patients who exhibited an elevated antibody response to bovine type I collagen were further analyzed for antibodies to human type I collagen. All of these patients exhibited a negative antibody response to human type I collagen.

rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System Clinical Trial
The immune response to rhBMP-2 (2.0mg/ml) and a collagen based carrier has been evaluated in 451 patients involved in a study where 463 patients received lumbar posterolateral fusions. Of the 451 patients, 234 investigational patients were treated with rhBMP-2 and 217 control patients were treated with autogenous bone. The presence of antibodies was assessed at the preoperative, 6 weeks, 3, 6, and 12 month visits using ELISA. If there was a positive response to bovine Type I collagen, the serum was also tested for antibodies to human Type I collagen. The optical density (OD) of positive and negative control samples were analyzed and compared with the ELISA cutpoint OD to determine if antibodies specific for rhBMP-2 were present or absent in each subject sample. The ELISA cutpoint OD is defined as two times the mean of the negative control OD. Subjects were considered to have an elevated immune response if the preoperative test was negative (titer < 50) and postoperative test was positive (titer ≥ 50) or if the preoperative test was positive and the postoperative test was positive with a two-fold higher titer than the preoperative test.

rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System		
Antibody	**Investigational N=234**	**Control N=217**
Anti-rhBMP-2	15 (6.4%)	5 (2.3%)
Anti-bovine Type I Collagen	39 (16.7%)	46 (21.2%)
Anti-human Type I Collagen (tested only if positive to Anti-bovine Type I Collagen)	0 (0.0%)	0 (0.0%)

The presence of antibodies to rhBMP-2 was not associated with immune mediated adverse events such as allergic reactions. Patient samples which tested positive to anti-rhBMP-2 were also tested for their neutralizing activity. No patient samples demonstrated neutralizing activities.

ADVERSE EVENTS:

The adverse event data summarized below are associated with two uses of rhBMP-2. The first set of data describes the use of the HDE device to treat the HDE population. The first two studies described below fall into this category. While these studies were not specifically designed to evaluate the use of the HDE product in the HDE population, a retrospective analysis of the data revealed that a small number of patients met the definition of the HDE target population. The second set of data describes the use of products containing rhBMP-2 to treat other populations. These data are provided as additional clinical information to supplement the relative safety information associated with the HDE device. The last three studies described below fall into this category.

INFUSE® Bone Graft/MASTERGRAFT® Resorbable Ceramic Granules plus a supplemental posterior fixation device

The active ingredient in the INFUSE/MASTERGRAFT™ Posterolateral Revision Device is rhBMP-2, provided at a concentration of 1.5mg/mL. This formulation of INFUSE® Bone Graft has been used in previous studies. Adverse events observed in a retrospective collection of data on the use of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device in the indicated patient population are outlined below.

Adverse event rates presented are based on the number of patients having at least one occurrence for a particular adverse event divided by the total number of patients in that treatment group.

Data on the INFUSE/MASTERGRAFT™ Device was obtained in 7 patients. The only reported adverse event was back and/or leg pain, which occurred in 2 patients (28.6%), and ranged from 3 weeks to 3 years postoperatively. This incidence rate is similar to that observed in the INFUSE® Bone Graft/MASTERGRAFT® Granules/CD HORIZON® Spinal System Pilot Clinical Trial (32%) and the rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System (53.1%).

INFUSE® Bone Graft with MASTERGRAFT® Resorbable Ceramic Granules
"Retrospective Study of INFUSE® Bone Graft in Clinical Practice"

The active ingredient in the INFUSE/MASTERGRAFT™ Posterolateral Revision Device is rhBMP-2, provided at a concentration of 1.5mg/mL. This formulation of INFUSE® Bone Graft has been used in previous studies. Adverse events observed in a retrospective collection from the medical records on patients at least one year from the index surgery with the use of INFUSE® Bone Graft with MASTERGRAFT Resorbable Ceramic Granules, supplemental posterior fixation and local bone are discussed below.

In this "Retrospective Study of INFUSE® Bone Graft in Clinical Practice" there were a total of five patients that met the INFUSE/MASTERGRAFT™ Posterolateral Revision Device criteria. Of these five patients, there was only one adverse event reported. This patient had a revision surgery at the involved levels 2 months postoperatively. The reason for the revision surgery is unknown.

INFUSE® Bone Graft/ LT-CAGE Lumbar Tapered Fusion Device

The active ingredient in the INFUSE® Bone Graft kit is rhBMP-2, provided in a concentration of 1.5mg/mL. This formulation of INFUSE® Bone Graft has been used in previous studies. Adverse events observed in two studies which utilized this formulation of INFUSE® Bone Graft are outlined below.

Adverse event rates presented are based on the number of patients having at least one occurrence for a particular adverse event divided by the total number of patients in that treatment group.

The INFUSE® Bone Graft/LT-CAGE Lumbar Tapered Fusion Device was implanted in 288 investigational patients and compared to 139 control patients who received an LT-CAGE Lumbar Tapered Fusion Device filled with iliac crest autograft. The investigational patients were implanted with the device via either an open anterior surgical approach or a laparoscopic anterior surgical approach. The control patients were implanted only via the open anterior surgical approach.

ADVERSE EVENTS

(INFUSE® Bone Graft/LT-CAGE® Device data combined from all experience with the device)

	Surgery		Postoperative (1 day - <4 Weeks)		6 Weeks (≥4 Wks - <9 Weeks)		3 Months (≥9 Wks - <6 Months)		6 Months (≥6 Mos - <9Months)		12 Months (>9 Mos - <19Months)		24 Months (≥19 Mos - <30Months)		# of Patients Reporting & Total adverse events		48 Months (≥30 Mos - <60 Months)	72 Months (≥60 Mos - <84 Months)
Complication	Inves.	Control	Inves.	Control	Inves.	Control	Inves.	Control	Inves.	Control	Inves.	Control	Inves.	Control	Investigational # (% of 288) total events	Control #(% of 139) total events	Total # (% of 134) total events	Total # (% of 140) total events
Anatomical/Technical Difficulty	11	3	0	0	0	0	0	0	0	0	0	0	0	0	11 (3.8) 11	3 (2.2) 3	0 (0.0) 0	0 (0.0) 0
Back and/or Leg Pain	0	0	12	4	11	5	12	5	8	11	20	7	8	11	70 (24.3) 78	36 (23.0) 32	22 (16.4) 23	18 (12.9) 21
Cancer	0	0	0	0	0	0	0	1	1	0	1	0	1	0	2 (0.7) 2	1 (0.7) 1	4 (3.0) 4	1 (0.7) 1
Cardio/Vascular	1	0	6	5	5	2	1	3	1	1	4	2	1	1	17 (5.9) 20	12 (8.6) 14	7 (5.2) 7	4 (2.9) 4
Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 (0.0) 0	1 (0.7) 1	2 (1.5) 2	0 (0.0) 0
Dural Injury	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0 (0.0) 0	1 (0.7) 1	0 (0.0) 0	0 (0.0) 0
Gastrointestinal	1	0	40	22	2	0	5	1	7	5	10	3	7	5	56 (19.4) 72	27 (19.4) 32	14 (10.4) 17	6 (4.3) 8
Graft Site Related	0	0	0	8	0	0	0	0	0	0	0	0	0	0	0 (0.0) 0	8 (5.8) 8	0 (0.0) 0	0 (0.0) 0
Implant Displacement/ Loosening	0	0	1	1	3	0	1	0	0	0	0	0	0	0	5 (1.7) 5	1 (0.7) 1	0 (0.0) 0	0 (0.0) 0
Infection	0	0	19	9	8	4	5	1	0	2	3	0	0	2	36 (12.5) 40	16 (11.5) 17	4 (3.0) 4	3 (2.1) 3
Malpositioned Implant	5	0	0	0	0	0	0	0	0	0	0	0	0	0	5 (1.7) 5	0 (0.0) 0	0 (0.0) 0	0 (0.0) 0
Neurological	0	0	8	5	7	3	5	2	6	8	13	4	6	8	39 (13.5) 45	23 (16.5) 24	12 (9.0) 12	5 (3.6) 5
Non-Union*	0	0	0	0	0	0	0	0	1	1	4	0	1	1	6 (2.1) 6	3 (2.2) 3	0 (0.0) 0	0 (0.0) 0
Non-Union**	0	0	0	1	0	1	2	0	1	1	4	6	1	1	10 (3.5) 10	13 (9.4) 13	0 (0.0) 0	0 (0.0) 0
Other	5	6	18	11	9	2	3	4	20	7	15	8	20	7	64 (22.2) 81	37 (26.6) 42	22 (16.4) 29	17 (12.1) 18
Other Pain	0	0	3	1	2	1	4	2	10	3	11	8	10	3	33 (30.8) 36	14 (10.1) 1	14 (10.4) 19	12 (8.6) 13
Respiratory	0	0	3	2	1	0	0	0	0	1	0	1	0	1	5 (1.7) 5	4 (2.9) 4	1 (0.7) 1	0 (0.7) 1
Retrograde Ejaculation	0	0	5	1	4	0	1	0	0	0	2	0	0	0	11 (7.9)[1] 12	1 (1.4)[2] 1	0 (0.0) 0	0 (0.0) 0
Spinal Event	0	0	1	2	1	0	6	2	9	2	10	8	9	2	30 (10.4) 37	17 (12.2) 18	9 (6.7) 9	8 (5.7) 8
Subsidence	0	0	3	2	2	0	1	0	0	0	0	0	0	0	7 (2.4) 7	2 (1.4) 2	0 (0.0) 0	0 (0.0) 0
Trauma	0	0	4	5	5	3	11	7	19	8	28	11	19	8	69 (24.0) 81	34 (24.5) 39	21 (15.7) 23	20 (14.3) 22
Urogenital	0	0	24	5	3	0	2	3	7	2	3	1	7	2	41 (14.2) 45	13 (9.4) 14	2 (1.5) 2	3 (2.1) 3
Vascular Intra-Op	15	5	0	0	0	0	0	0	0	0	0	0	0	0	14 (4.9) 15	5 (3.6) 5	1 (0.7) 1	0 (0.0) 0
Vertebral Fracture	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1 (0.3) 1	0 (0.0) 0	0 (0.0) 0	0 (0.0) 0
Any Adverse Event															235 (81.6)	121 (87.1)	84 (62.7)	64 (45.7)

* Non-union adverse events that have not resulted in a second surgery.
** Non-union adverse events that have resulted in a second surgery.
[1] Percent of 140 males.
[2] Percent of 70 males.

In the IDE portion of the clinical study, the reported rates of several adverse events were high, but similar, in both the investigational and control groups. These events included back and leg pain, gastrointestinal events, neurological events, infection, and spinal events.

Urogenital events occurred with greater frequency in the investigational groups (14.2%) compared to the control group (9.4%). Retrograde ejaculation rates were greater in the investigational groups (11 subjects) compared to the control group (1 subject) with the majority of events occurring in the early postoperative period.

In the post-approval portion of the study, only investigational patients were followed at the 48 and 72 month timepoints. Patients continued to be monitored for all adverse events types. All adverse event rates, including those that were previously reported as high, did decrease throughout the extended follow-up periods.

Some of the reported adverse events required surgical interventions subsequent to the initial surgery. The number of subjects requiring a second surgical intervention was 8.7% (25/288) in the investigational groups and 10.8% (15/139) in the control group during the IDE phase of the trial. The majority of supplemental fixations were due to painful non-union.

The incidence of adverse events that were considered device related, including implant displacement/loosening, implant malposition and subsidence were all greater in the investigational groups compared to the control group. The rates of these events were low, however, and may be partially attributed to a learning curve associated with the laparoscopic surgical approach. The rate of non-union requiring secondary surgery in the investigational groups was comparable to that of the control group.

During the course of the study, 10 pregnancies were reported – one (1) in the control group and nine (9) in the investigational groups. There were seven (7) pregnancies in the laparoscopic approach group. Two (2) pregnancies in the IDE phase of the laparoscopic approach group resulted in first trimester miscarriages. The other five (5) pregnancies in the laparoscopic approach group resulted in live births with no reported complications. Two (2) of the five (5) pregnancies occurred during the post-approval phase of the study and were second pregnancies for both patients. There were two (2) pregnancies in the IDE phase of the open approach group that resulted in live births with no reported complications. There were no pregnancies reported in the post-approval phase of the open approach group. None of the pregnant subjects had antibody responses to rhBMP-2 or Type I collagen (bovine or human), that were detectable to the limits of the sensitivity of the assay. One (1) pregnancy was reported in the control group, resulting in a live birth with complications at approximately 24 months post-operatively. Control patients were not followed throughout the post-approval phase of the study.

Three (3) cases of cancer were diagnosed during the course of the IDE phase – two (2) in an investigational group (breast and pancreatic) and one (1) in the control group (breast). Five (5) additional cases of cancer were reported in the post-approval phase of the study (thyroid, melanoma of the leg, testicular, breast, squamous cell carcinoma of the scalp). No additional information is available on these subjects, *e.g.*, BMP-2 receptor expression.

One (1) death was reported in a control group subject with cardiovascular disease during the IDE phase of the trial. No investigational patients expired during the IDE phase. Two (2) investigational patient deaths were reported during the post-approval phase of the trial due to respiratory failure caused by pneumonia from diabetes mellitus and pancreatic cancer.

INFUSE® Bone Graft/MASTERGRAFT™ Granules/CD HORIZON® Spinal System Pilot Clinical Trial

The active ingredient in the INFUSE® Bone Graft kit is rhBMP-2, provided in a concentration of 1.5mg/mL. This formulation of INFUSE® Bone Graft has been used in previous studies. Adverse events observed in one study, which utilized this formulation of INFUSE® Bone Graft with MASTERGRAFT™ Granules, are outlined below.

Adverse event rates presented are based on the number of patients having at least one occurrence for a particular adverse event divided by the total number of patients in that treatment group.

The INFUSE® Bone Graft/ MASTERGRAFT™ Granules/ CD HORIZON® Spinal System was implanted in 25 investigational patients and compared to 21 control patients who received iliac crest autograft used in conjunction with the CD HORIZON® Spinal System. All patients were implanted with the device via posterolateral surgical approach.

INFUSE® Bone Graft/ MASTERGRAFT™ Granules/ CD HORIZON® Spinal System Pilot Clinical Trial																							
Adverse Event	**Operative**		**Postop** 1 Day- <1 Month		**6 Weeks** (≥1-<2 Months)		**3 Months** (≥2-<5 Months)		**6 Months** (≥5-<9 Months)		**12 Months** (≥9-<19 Months)		**24 Months** (≥19-<30 Months)		**36 Months** (≥30-<42 Months)		**Total Adverse Events**		**Total # Patients Reporting #(% of N)**			
	Inv N=25	Ctrl N=21	Inv N=25	Ctrl N=21	Inv N=25	Ctrl N=21	Inv N=25	Ctrl N=21	Inv N=25	Ctrl N=21	Inv N=25	Ctrl N=21	Inv N=25	Ctrl N=21	Inv N=25	Ctrl N=21	Inv N=25	Ctrl N=21	Inv N=25	%	Ctrl N=21	%
Accidental Injury/Muscle Strain	0	0	1	0	2	1	2	1	0	1	2	0	5	1	0	0	12	4	10	40.0	4	19.0
Allergic Reaction	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	1	4.0	0	0.0
Back &/or Leg Pain	0	0	1	1	1	0	2	0	2	2	2	1	1	1	0	0	9	5	8	32.0	5	23.8
Cancer	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	4.0	0	0.0
Cardiovascular	0	0	0	1	1	0	0	1	0	1	1	1	0	1	0	0	2	5	2	8.0	3	14.3
Cervical Spinal Event	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	1	1	1	4.0	1	4.8
Dural Injury	1	1	0	0	0	0	0	0	0	0	0	1	1	0	0	0	2	2	2	8.0	2	9.5
Electrolyte Imbalance	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0.0	1	4.8
Endocrine	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0.0	1	4.8
Gastrointestinal	0	0	1	4	0	1	1	1	0	0	1	4	1	0	0	1	4	11	3	12.0	8	38.1
Graft Site Related	0	0	0	1	0	0	0	0	0	1	0	1	0	1	0	0	0	4	0	0.0	4	19.0
Implant Displacement/ Loosening/ Breaking	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	1	4.0	0	0.0
Incision Related	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	4.0	1	4.8
Infection	0	0	1	1	0	1	0	0	0	2	2	1	1	0	1	1	5	6	4	16.0	5	23.8
Lower Extremity Pain Not of Back Etiology	0	0	1	1	0	0	0	0	1	1	4	0	0	0	1	0	7	2	6	24.0	2	9.5
Malpositioned Implant	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	4.0	0	0.0
Neck &/or Arm Pain	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0.0	1	4.8
Neurological	0	0	2	2	0	0	3	0	0	1	0	1	0	0	0	0	5	4	4	16.0	3	14.3
Non-Union (Pending)	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	2	0	0.0	2	9.5
Non-Union (Failure)	0	0	0	0	0	0	0	1	0	0	1	1	0	0	0	0	1	2	1	4.0	2	9.5
Other	0	0	1	3	0	0	0	0	1	0	0	0	2	2	0	1	4	6	3	12.0	6	28.6
Other Pain	0	0	1	0	0	0	2	0	0	0	2	0	0	0	1	0	6	0	4	16.0	0	0.0
Respiratory	0	0	0	1	0	0	0	0	0	1	1	0	1	0	0	0	2	2	2	8.0	2	9.5
Skin Disorder	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	2	0	0.0	2	9.5
Spinal Event at Other Lumbar Level(s)	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1	2	2	2	8.0	2	9.5
Spinal Event at Target Level	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	2	0	2	8.0	0	0.0
Spinal Event at Thoracic Level	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0.0	1	4.8
Trauma	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	1	4.0	0	0.0
Upper Extremity Pain Not of Neck Etiology	0	0	0	0	0	0	1	0	1	0	0	0	0	1	0	1	2	2	2	8.0	1	4.8
Urogenital	0	0	1	0	0	0	0	0	1	1	0	1	0	0	0	0	2	2	2	8.0	2	9.5
Any Adverse Event																	74	69	22	88.0	18	85.7

The reported rates of several adverse events were high, but similar, in both the investigational and control groups. These events included back and leg pain, infection, and neurological events.

Some of the reported adverse events required surgical interventions subsequent to the initial surgery which includes revisions and removals. The number of subjects requiring a second surgical intervention was 12.0% (3/25) in the investigational group and 9.5% (2/21) in the control group.

Gastrointestinal events occurred with greater frequency in the control group (38.1%) compared to the investigational group (12.0%). Lower extremity pain, not of back etiology, events occurred with greater frequency in the investigational group (24.0%) compared to the control group (9.5%).

The incidence of adverse events that were considered device or device/surgical procedure related were similar between the investigational and control group. The rate of non-union requiring secondary surgery in the investigational group (4.0%) was less than that of the control group (9.5%).

During the course of the study, there were no reported pregnancies.

One case of cancer was diagnosed during the course of the study. An investigational subject was found to have pancreatic cancer. No additional information is available on this subject, *e.g.*, BMP-2 receptor expression. One death was reported (4.0%). This occurred in an investigational patient secondary to pancreatic cancer.

rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System

The active ingredient in the rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System is rhBMP-2, provided in a concentration of 2.0mg/mL. This formulation of rhBMP-2 has not been used in previous studies. Adverse events observed in one pivotal study, which utilized this formulation of rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System, are outlined below.

Adverse event rates presented are based on the number of patients having at least one occurrence for a particular adverse event divided by the total number of patients in that treatment group.

The rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System was implanted in 239 investigational patients and compared to 224 control patients who received iliac crest autograft used in conjunction with the CD HORIZON® Spinal System. All patients were implanted with the device via posterolateral surgical approach.

rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System																				
EVENT	Operative		Postop 1 Day-<1 Month		6 Weeks (≥1-<2 Months)		3 Months (≥2-<5 Months)		6 Months (≥5-<9 Months)		12 Months (≥9-<19 Months)		24 Months (≥19-<30 Months)		Total Adverse Events		Total # Patients Reporting #(% of N)			
	Inv N=239	Ctrl N=224	Inv N=239	Ctrl N=224	Inv N=239	Ctrl N=224	Inv N=239	Ctrl N=224	Inv N=239	Ctrl N=224	Inv N=239	Ctrl N=224	Inv N=239	Ctrl N=224	Inv N=239	Ctrl N=224	Inv N=239	%	Ctrl N=224	%
Anatomical/Technical Difficulty	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0.4	0	0
Arthritis/Bursitis	0	0	3	1	1	1	7	2	4	3	6	6	1	6	23	19	22	9.2	19	8.5
Back &/or Leg Pain	0	0	19	7	10	5	15	13	19	29	33	29	31	23	135	111	127	53.1	106	47.3
Cancer	0	0	0	0	0	0	1	0	2	1	3	1	2	0	8	2	8	3.3	2	0.9
Cardiovascular	2	0	37	39	0	2	4	3	2	7	13	6	2	6	69	68	60	25.1	63	28.1
Carpal Tunnel Syndrome	0	0	0	0	0	0	0	0	2	1	4	3	3	2	9	7	9	3.8	6	2.7
Death	0	0	0	0	1	0	0	0	1	2	1	1	0	1	3	4	3	1.3	4	1.8
Dural Injury	13	18	1	0	0	0	0	0	0	0	0	0	0	0	14	18	14	5.9	18	8
Gastrointestinal	0	0	17	15	0	2	4	3	5	2	9	7	6	7	42	42	41	17.2	36	16.1
Graft Site Related	0	0	0	4	0	3	0	5	0	3	0	2	0	0	0	17	0	0	17	7.6
Implant Displacement / Loosening	0	1	0	0	0	0	0	1	0	0	1	1	0	0	1	3	1	0.4	3	1.3
Infection	0	0	19	24	3	6	4	2	4	1	11	9	6	6	52	51	47	19.7	48	21.4
Malpositioned Implant	1	0	3	1	0	1	1	0	0	0	0	0	0	0	5	2	5	2.1	2	0.9
Neurological	0	0	9	6	2	6	17	14	19	17	18	14	15	12	86	75	80	33.5	69	30.8
Non-Union Failure	0	0	0	0	0	0	1	7	0	4	5	5	0	1	6	17	6	2.5	17	7.6
Non-Union Outcome (Pending)	0	0	0	0	0	0	0	1	0	2	4	1	1	2	5	6	5	2.1	6	2.7
Other	1	0	35	26	7	3	6	8	5	10	14	11	16	15	99	92	84	35.1	73	32.6
Other Pain	0	0	2	3	2	0	1	1	6	5	12	4	8	16	31	30	31	13	29	12.9
Respiratory	0	0	8	7	0	1	1	1	0	1	4	3	2	0	16	13	15	6.3	13	5.8
Spinal Event	0	0	1	0	0	1	3	3	5	2	5	11	4	2	18	20	18	7.5	19	8.5
Trauma	0	0	3	3	2	8	8	7	11	15	33	16	23	18	87	70	80	33.5	67	29.9
Urogenital	0	0	10	6	2	2	5	3	4	3	5	4	1	5	27	24	27	11.3	23	10.3
Vertebral Fracture	3	3	0	0	0	0	0	0	0	1	0	0	0	1	3	5	3	1.3	5	2.2
Any Adverse Event															740	696	217	90.8	207	92.4

The incidence of adverse events that were considered device or device/surgical procedure related were similar between the investigational and control group. The rate of non-union requiring secondary surgery in the investigational group (2.5%) was less to that of the control group (7.6%). Seven deaths were reported (1.5%). Three deaths occurred in investigational treatment subjects (2 cancer events, 1 stroke) and four deaths occurred in control treatment subjects (2 cardiovascular events, 1 cancer event, 1 trauma). Ten cases of cancer were diagnosed during the course of this study – eight subjects in the investigational group and two in the control group. Cancers in the investigational group included basal cell carcinoma, laryngeal, lung, lymphatic, ovarian, pancreatic, prostate, squamous cell carcinoma, and breast. Cancers in the control group included colon and lymphatic.

Some of the reported adverse events required surgical interventions subsequent to the initial surgery which includes revisions and removals. The number of subjects requiring a second surgical intervention was 17.2% (41/239) in the investigational group and 25.4% (57/224) in the control group. Secondary surgical intervention information for investigational and control treatment groups is summarized in the Table below.

rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System						
EVENT	**Total Events through 24 Month Time point**		**# of Patients Reporting**			
	Inv N=239	**Ctrl N=224**	**Inv N=239**		**Ctrl N=224**	
Revisions	4	4	4	1.7%	3	1.3%
Removals	13	29	13	5.4%	28	12.5%
Supplemental Fixations	6	9	6	2.5%	9	4.0%
Reoperations	13	13	12	5.0%	11	4.9%

During the course of the study, three pregnancies were reported – one in the control group (reported 25 months postoperatively) and two in the investigational groups (reported 6 months and 24 months postoperatively). All pregnancies resulted in healthy births and there were no delivery or post-delivery complications. None of the pregnant subjects had antibody responses to rhBMP-2 or Type I collagen (bovine or human) that were detectable to the limits of the sensitivity of the assay.

POTENTIAL ADVERSE EVENTS

The following is a list of potential adverse events that may occur with spinal fusion surgery with the INFUSE/MASTERGRAFT™ Posterolateral Revision Device. Some of these adverse events may have been previously reported in the adverse events tables or have been reported to the manufacturer:

- Allergic reaction
- Anaphylactic reaction
- Bone fracture
- Bowel or bladder problems
- Cessation of any potential growth of the operated portion of the spine.
- Change in mental status
- Damage to blood vessels and cardiovascular system compromise
- Damage to internal organs and connective tissue
- Death
- Development of respiratory problems
- Disassembly, bending, breakage, loosening, and/or migration of components
- Dural tears
- Ectopic and/or exuberant bone formation
- Edema (swelling)
- Elevated erythrocyte sedimentation rate
- Erythematous tissue
- Fetal development complications
- Fluid–filled cysts, fluid collection, seromas
- Foreign body (allergic) reaction
- Gastrointestinal complications
- Hematoma
- Incisional complications
- Infection
- Inflammation
- Itching
- Loss of spinal mobility or function
- Neurological system compromise
- Non-union (or pseudoarthrosis), delayed union, mal-union
- Pain
- Postoperative change in spinal curvature, loss of correction, height, and/or reduction
- Scar formation
- Seroma
- Tissue or nerve damage

Note: Additional surgery may be necessary to correct some of these potential adverse events.

CLINICAL RESULTS:

INFUSE® Bone Graft/MASTERGRAFT™ Resorbable Ceramic Granules plus a supplemental posterior fixation device

Clinical data to support the safety and probable benefit of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device in the indicated patient population was collected in a retrospective manner. All patients had a compromising condition and were treated with INFUSE® Bone Graft and MASTERGRAFT® Granules in a multi-level, posterolateral revision procedure. No autograft bone was used to supplement the INFUSE/MASTERGRAFT™ Device. Supplemental posterior fixation was used in all cases.

Fusion status and clinical outcomes were obtained. Collection of patient outcome measures in a retrospective manner did not allow for success criteria to be defined prospectively. Chart reviews were used to determine patient outcomes. A radiographic success was defined as any patient stated to have fusion. A clinical success was defined as patients reported to be doing well or having improved pain. A clinical failure is defined as a patient continuing to have pain.

Primary Outcome Variable	INFUSE® Bone Graft/MASTERGRAFT™ Resorbable Ceramic Granules plus a supplemental posterior fixation device	
	Fusion Outcome	Clinical Outcome
Success	3/3	1/2
Failure	0/0	1/2
Not reported	1	2

INFUSE® Bone Graft with MASTERGRAFT® Resorbable Ceramic Granules
"Retrospective Study of INFUSE® Bone Graft in Clinical Practice"

"Retrospective Study of INFUSE® Bone Graft in Clinical Practice" was a retrospective study conducted to collect data on the clinical experience with INFUSE® Bone Graft when it is implanted as a substitute for or as a supplement to autogenous bone graft. Data was collected from the medical records on patients at least one year from the index surgery. The success of the surgical procedure was determined at the last available evaluation documented in the medical record. This retrospective study was conducted at multiple sites and all patients treated with INFUSE® Bone Graft were eligible for inclusion. For the purposes of the Humanitarian Device Exemption (HDE), a search of the database of these patients was performed to find patients meeting the HDE indications for use. The following clinical data are the result of this database query.

There were three (3) men and two (2) women ages 52 to 63 years old that met the HDE indications for use. There were three (3) two-level and two (2) three-level, revision surgeries. All patients were diabetics or smokers and also had a variety of other co-morbidities that are known to inhibit fusion, including osteoporosis/osteopenia and rheumatoid arthritis requiring chronic use of corticosteroids and NSAIDs. These patients underwent these multi-level lumbar posterolateral fusions using INFUSE® Bone Graft and MASTERGRAFT® Resorbable Ceramic Granules and posterior instrumentation. As would be expected, surgeons did not discard any local bone graft that was available to them from the surgical approach and exposure, and thus local bone graft was used in all cases. Surgeons used this local bone graft in order to add volume to the grafting materials ("void" or "space filling") and did not consider local bone graft alone to be sufficient to promote a successful fusion. The local bone alone would not be expected to stimulate spinal fusion in these patients and would be expected to function only as an osteoconductive material.

Latest documented assessment of patient outcomes and fusion success ranged from 2-48 months from the index revision procedure. Four out of five (4/5) patients had a successful fusion at the final evaluation. The final evaluation available for the patient whose fusion status was undetermined occurred at two (2) months postoperative, which was too early for a definitive fusion assessment. Thus, for those patients with sufficient follow-up to determine fusion, 4/4 patients were successfully fused.

The goal of pain relief was assessed in all five (5) patients. For this criteria, two (2) patients were graded as complete successes, two (2) were graded as partial successes, and one (1) patient was graded as unsuccessful at the 2-month time period. The goal of bone healing was assessed in three (3) patients. Two (2) patients were graded as complete successes, and one (1) was unsuccessful at 2 months postoperative. The goal of relief of neurological symptoms was assessed in one (1) patient and was graded as a complete success. There was only one adverse event reported. This patient had a revision surgery at the involved levels 2 months postoperatively. The reason for the revision surgery is unknown.

INFUSE® Bone Graft/MASTERGRAFT™ Resorbable Ceramic Granules plus autograft bone and a supplemental posterior fixation device			
Fusion Measures	Fusion Outcomes	Pain Relief Measures	Pain Relief Outcomes
Success	4/5	Complete Success	2/5
Failure	0/5	Partial Success	2/5
Undetermined	1/5	Unsuccessful	1/5

Three clinical studies have been conducted to support the safety and effectiveness of rhBMP-2 used in the lumbar spine evaluating both anterior interbody and posterolateral fusions. In these studies, neither the investigators nor the subjects were blinded to the treatment. Subject blinding was not possible due to the second surgical site resulting from the need to collect the iliac crest grafts in control subjects. The potential for investigator bias in the clinical outcome parameters was reduced by having the subjects rate their outcome using objective self-assessments. The radiographic outcome parameters were performed by independent radiologists who were blinded

to treatment. These were the only radiographic evaluations used for determining radiographic success.

Clinical and radiographic effectiveness parameters
Patients were evaluated preoperatively (within 6 months of surgery), intraoperatively, and postoperatively at 6 weeks, 3, 6, 12 and 24 months, and biennially thereafter until the last subject enrolled in the study had been seen for their 24 month evaluation. Complications and adverse events, device-related or not, were evaluated over the course of the clinical trial. At each evaluation time point, the primary and secondary clinical and radiographic outcome parameters were evaluated. Success was determined from data collected during the initial 12 or 24 months of follow-up.

Primary and secondary clinical and radiographic effectiveness outcome parameters were evaluated for all treated subjects at all follow-up evaluation time points identified above. The primary clinical parameters assessed were of pain, function, and neurological status or pain/disability status. The secondary clinical outcome parameters assessed were general health status, back and leg pain, donor site pain (control subjects only), patient satisfaction, and patient global perceived effect of the treatment. The primary radiographic outcome parameter consisted of evaluations of fusion.

In the anterior interbody study, fusion was evaluated at 6, 12 and 24 months post-op using plain radiographs (AP, lateral and flexion/extension films) and high resolution thin-slice CT scans. Fusion was defined as the presence of bridging bone connecting the inferior and superior vertebral bodies; a lack of motion on flexion/extension (≤ 3mm of translation and < 5° of angulation); and no evidence of radiolucencies over more than 50% of either implant. Fusion success was defined as the presence of all of these parameters plus the lack of a second surgical intervention resulting from a non-union. All assessments were made from the plain films except for the assessment of bridging bone, which was made using the CT scans only if bridging bone could not be visualized on the plain film.

In the posterolateral studies, fusion was assessed at 6, 12, and 24 months postoperatively using plain radiographs (AP, lateral and flexion/extension films) and high resolution thin-slice CT scans. Fusion was defined as evidence of bridging trabecular bone defined as bony continuous connection from the superior transverse process to the inferior transverse process on both sides; no evidence of motion (≤ 3mm of translation and < 5° of angulation between flexion and extension as seen on lateral flexion/extension radiographs), and the absence of cracking, as evidenced by radiolucent lines completely through the fusion mass. All assessments were made from the plain films except for the assessment of bridging bone, which was made using the CT scans only if bridging bone could not be visualized on the plain film.

Pain and function were measured in all studies using the Oswestry Low Back Pain Disability Questionnaire. Success was defined as a 15 point improvement in the Oswestry score from the pre-op baseline score.

Neurological status consisted of measurements of four parameters - motor, sensory, reflexes, and straight leg raise (SLR). Neurological status success was defined as maintenance or improvement of the pre-op baseline score for each parameter. Overall neurological status success required that each individual parameter be a success for that subject to be counted as a success.

Clinical and radiographic effectiveness evaluation
Individual subject success was defined as success in each of the primary clinical and radiographic outcome parameters. Success for these parameters included:

1. The presence of radiographic fusion;
2. An improvement of at least 15 points from the baseline Oswestry score;
3. Maintenance or improvement in neurological status;
4. The presence of no serious adverse event classified as implant-associated or implant/surgical procedure-associated; and
5. No additional surgical procedure classified as "Failure."

Success rate was expressed as the number of individual subjects categorized as a success divided by the total number of subjects evaluated. The summaries below describes the success rates for the individual primary outcome parameters and/or overall success. In completed pivotal studies, all success rates were based on the data from the 24 month follow-up evaluation and posterior probabilities of success were calculated using Bayesian statistical methods. In pilot studies or pivotal studies that are not yet complete, success rates were presented as general summary statistics.

INFUSE® Bone Graft/LT CAGE® Lumbar Tapered Fusion Device - Pilot and Pivotal Studies Results

In the anterior interbody fusion study, clinical data to support the safety and effectiveness of the INFUSE® Bone Graft/ LT-CAGE® Lumbar Tapered Fusion Device were collected as part of a prospective, multi-center pivotal study that consisted of randomized and non-randomized arms. The active ingredient in the INFUSE® Bone Graft kit is rhBMP-2, provided in a concentration of 1.5mg/mL. The randomized arm contained two groups, one investigational and one control. The control group was implanted with the LT-CAGE® Lumbar Tapered Fusion Device filled with iliac crest autograft bone, while the investigational group was implanted with the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device. In both cases, the surgical approach was an open anterior approach. The non-randomized arm contained only an investigational group, where subjects were implanted with the INFUSE® Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device through a laparoscopic anterior approach. The control group from the randomized arm was used as the control for the non-randomized arm.

The indication studied was degenerative disc disease (DDD) accompanied by back pain, with or without leg pain, at a single level between L4 and S1 confirmed by history and radiographic studies.

A total of 143 open approach investigational and 136 open approach control patients were enrolled in the randomized arm of the study and received the device. A total of 134 subjects were enrolled in the non-randomized, laparoscopic arm of the study and received the device. For the majority of the demographic parameters, there were

no significant differences between the open investigational and control treatment groups.

INFUSE® Bone Graft/LT CAGE® Lumbar Tapered Fusion Device – Summary of Pivotal Study Success at 24 Months			
	Posterior Probabilities of Success at 24 Months		
	Investigational		Control
Primary Outcome Variable	Open Surgical Approach	Laparoscopic Surgical Approach	Open Surgical Approach
	Posterior Mean (95% HPD Credible Interval)	Posterior Mean (95% HPD Credible Interval)	Posterior Mean (95% HPD Credible Interval)
Fusion	92.8% (88.5%, 96.9%)	93.0% (87.9%, 97.5%)	88.1% (82.6%, 99.3%)
Oswestry	71.0% (63.4%, 78.7%)	83.0% (75.6%, 90.5%)	70.9% (63.1%, 79.1%)
Neurologic	81.0% (74.5%, 87.9%)	89.0% (83.1%, 94.8%)	81.7% (74.9%, 88.7%)
Overall success	57.1% (49.2%, 65.7%)	68.0% (59.3%, 76.5%)	56.7% (48.3%, 65.0%)

The probability (also called the posterior probability) that the 24 month overall success rate for the investigational groups was equivalent to the 24 month success rate for the control group was 99.4% for the open surgical approach investigational group and almost 100% for the laparoscopic surgical approach investigational group.

For a patient receiving the INFUSE Bone Graft/LT-CAGE Lumbar Tapered Fusion Device via the open anterior surgical approach, the chance (the posterior probability) of overall success at 24 months would be 57.1% for the open surgical approach. Given the results of the trial, there is a 95% probability that the chance of success ranges from 49.2% to 65.7%. For a patient receiving the INFUSE Bone Graft/LT-CAGE Lumbar Tapered Fusion Device via the anterior laparoscopic surgical approach, the chance of overall success at 24 months would be 68.0%. Given the results of the trial, there is a 95% probability that the chance of success ranges from 59.3% to 76.5%. For a patient receiving the control treatment, the chance of overall success at 24 months would be 56.7%. Given the results of the trial, there is a 95% probability that the chance of success ranges from 48.3% to 65.0%.

INFUSE® Bone Graft/ MASTERGRAFT™ Granules/ CD HORIZON® Spinal System - Pilot Study Results

Clinical data to support the safety and effectiveness of the INFUSE® Bone Graft/ MASTERGRAFT™ Granules/ CD HORIZON® Spinal System were collected as part of a prospective, multi-center pilot, randomized study. The active ingredient in the INFUSE® Bone Graft kit is rhBMP-2, provided in a concentration of 1.5mg/mL. The investigational patients were implanted with the INFUSE® Bone Graft with MASTERGRAFT® Granules and the CD HORIZON® Spinal System. The control patients received iliac crest autograft used in conjunction with the CD HORIZON® Spinal System. Both arms were completed via a posterolateral fusion approach in which the implant was placed bilaterally across two adjacent transverse processes.

The indication studied was degenerative disc disease (DDD) accompanied by back pain, with or without leg pain, at a single level between L1 and S1 confirmed by history and radiographic studies.

A total of 25 investigational and 21 control patients were enrolled in the study and received the device. For the majority of the demographic parameters, there were no significant differences between the investigational and control groups.

Success rate was expressed as the number of individual subjects categorized as a success divided by the total number of subjects evaluated. The table below describes the success rates for the individual primary outcome parameters at 24 months postoperative.

INFUSE® Bone Graft/ MASTERGRAFT® Granules/ CD HORIZON® Spinal System – Summary of Pilot Study Success at 24 Months				
Primary Outcome Variable	Investigational		Control	
	Success	Failure	Success	Failure
Fusion	18 (94.7%)	1 (5.3%)	14 (70.0%)	6 (30.0%)
Oswestry Pain	22 (95.7%)	1 (4.3%)	15 (75.0%)	5 (25.0%)
Neurological	22 (95.7%)	1 (4.3%)	18 (90.0%)	2 (10.0%)
Overall Success	17 (81.0%)	4 (19.0%)	11 (55.0%)	9 (45.0%)

rhBMP-2/CRM/CD HORIZON® Spinal System - Pivotal Study Results

Clinical data to support the safety and effectiveness of the rhBMP-2/CRM/CD HORIZON® Spinal System were collected as part of a prospective, multi-center, randomized, pivotal study that consisted of two groups, one investigational and one control. The active ingredient in the rhBMP-2/Compression Resistant Matrix (CRM)/CD HORIZON® Spinal System is rhBMP-2, provided in a concentration of 2.0mg/mL. The investigational group was implanted with the rhBMP-2/CRM/CD HORIZON® Spinal System, while the control group received surgical treatment utilizing the CD HORIZON® Spinal System with autogenous bone derived from the iliac crest. Both arms were completed via a posterolateral fusion approach in which the implant was placed bilaterally across two adjacent

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transverse processes.

The indication studied was degenerative disc disease (DDD) at a single level between L1 and S1 accompanied by back pain, with or without leg pain, confirmed by subject history and radiographic studies.

As of October, 2006, a total of 463 patients were enrolled and treated in the study, 239 investigational and 224 control patients. There were no significant differences in demographics and preoperative evaluations between the two treatment groups. The patients were of an average age of 53 years.

Success rate was expressed as the number of individual subjects categorized as a success divided by the total number of subjects evaluated. The table below describes the success rates for the individual primary outcome parameters at 12 and 24 months postoperative.

rhBMP-2/CRM/CD HORIZON® Spinal System – Summary of Study Success at 12 and 24 Months

Primary Outcome Variable	12 Months				24 Months			
	Investigational		Control		Investigational		Control	
	Success	Failure	Success	Failure	Success	Failure	Success	Failure
Fusion	182 (87.5%)	26 (12.5%)	150 (82.4%)	32 (17.6%)	186 (95.9%)	8 (4.1%)	150 (89.3%)	18 (10.7%)
Oswestry Pain	159 (71.3%)	64 (28.7%)	150 (73.9%)	53 (26.1%)	152 (73.1%)	56 (26.9%)	133 (72.7%)	50 (27.3%)
Neurological	197 (87.6%)	28 (12.4%)	180 (88.7%)	23 (11.3%)	180 (87.0%)	27 (13.0%)	154 (84.2%)	29 (15.8%)
Overall Success	117 (54.7%)	97 (45.3%)	106 (53.8%)	91 (46.2%)	121 (60.5%)	79 (39.5%)	101 (55.5%)	81 (44.5%)

HOW SUPPLIED

INFUSE/MASTERGRAFT™ Posterolateral Revision Device is supplied in one kit containing all the components necessary to prepare the device (i.e., the collagen sponge(s), a vial with the lyophilized growth factor, a vial with sterile water for reconstituting the growth factor, MASTERGRAFT® Granules, syringes and needles).

Posterior supplemental fixation must be used with the INFUSE/MASTERGRAFT™ Posterolateral Revision Device but is not provided as part of the device.

STORAGE CONDITIONS

Store the INFUSE/MASTERGRAFT™ Posterolateral Revision Device at room temperature (15 – 30 degrees Centigrade (59° to 86°F).

PRODUCT COMPLAINTS

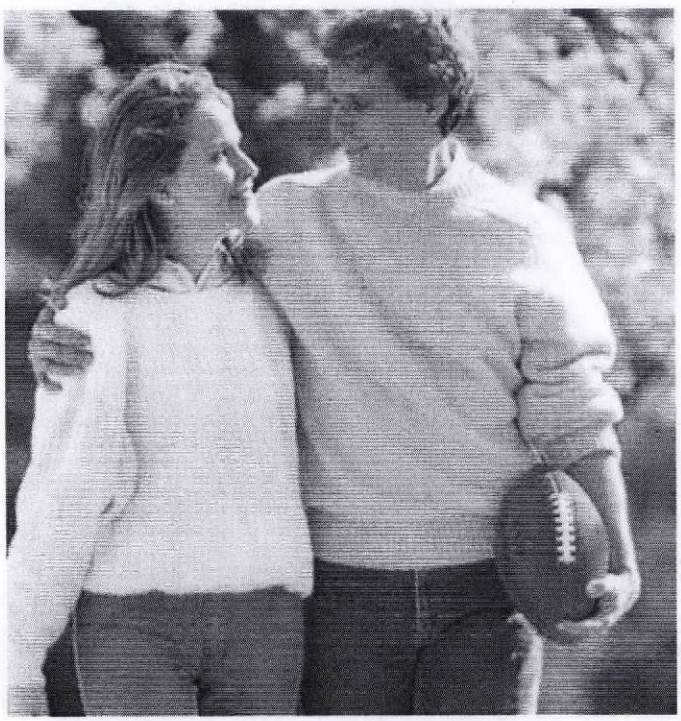
Any Health Care Professional (e.g., customer or user of this system of products), who has any complaints or who has experienced any dissatisfaction in the product quality, identity, durability, reliability, safety, effectiveness and/or performance, should notify the distributor or MEDTRONIC. Further, if any MEDTRONIC product ever "malfunctions," and may have caused or contributed to the death or serious injury of a patient, the distributor should be notified immediately by telephone, fax or written correspondence. When filing a complaint, please provide the component(s) name and number, lot number(s), your name and address, the nature of the complaint and notification of whether a written report from the distributor is requested.

FURTHER INFORMATION

Recommended directions for use of this system (surgical operative techniques) are available at no charge upon request. If further information is needed or required, please contact MEDTRONIC.

Patient
LABELING

INFUSE/MASTERGRAFT™
Posterolateral Revision Device

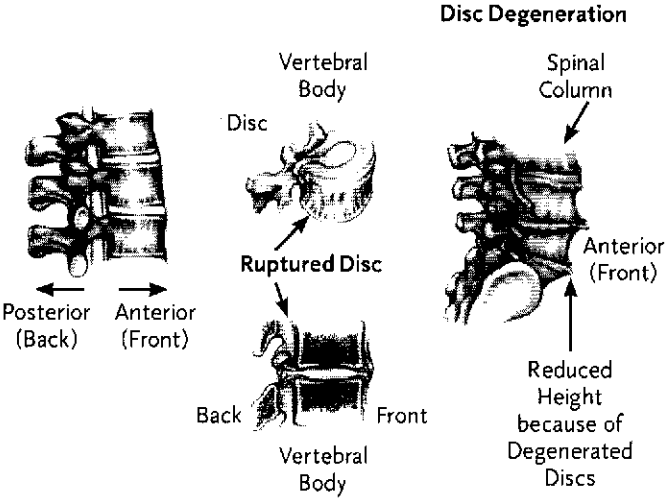


Patient Information Brochure

This Patient Guide is designed to help you make an informed decision about treatment for your back pain and related problems. Your doctor has proposed surgery to relieve your back pain and related problems using the INFUSE/ MASTERGRAFT™ Posterolateral Revision Device.

Your doctor has decided that you need additional spine surgery after carefully examining you, reviewing your history, X-rays, and taking into account the results of other diagnostic studies and previous surgical treatments. Specifically, your doctor has determined that you have a pseudarthrosis (your spine did not fuse after your previous surgery) and would benefit from having spinal repair surgery which provides lumbar stability and relieves the associated pain.

YOUR LOWER BACK



The bony vertebrae, which encircle and protect your spinal cord, are separated by shock-absorbing discs. The discs give your spine the flexibility to move. Each disc has a spongy center (nucleus) surrounded by tough outer rings. Nerves branching from the spinal cord pass through openings in the vertebrae to other parts of your body. Several of these nerves form the sciatic nerve, which runs down your leg.

As discs lose their water content because of disease or age, they lose their height, bringing the vertebrae closer together. As a result, the nerve openings in your spine become more narrow, and the discs don't absorb the shocks as well, particularly when you are walking, running, or jumping. Wear and tear, poor posture, and incorrect body movements can also weaken the disc, causing disc degeneration. Disc degeneration may cause back and/or leg pain, as well as functional problems such as tingling or numbness in your legs or buttocks, or difficulty walking. Doctors call this degenerative disc disease (DDD).

Currently, lumbar spinal fusion procedures are the only commonly performed option to treat these symptoms and improve your overall quality of life. However, successful fusion does not always occur in every patient, as was the case for you. For this condition (called pseudoarthrosis) additional fusion stability is required.

WHAT IS THE INFUSE/MASTERGRAFT™ POSTEROLATERAL REVISION DEVICE?

The INFUSE/MASTERGRAFT™ Posterolateral Revision Device was designed to aid in the treatment of pseudoarthrosis. It consists of a three component system—a bone graft replacement (the INFUSE® Bone Graft), a bone void filler (the MASTERGRAFT® GRANULES), and a posterior system of screws and rods used to stabilize the painful portion of your spine. A posterior stability system may already be present from your previous surgery or may be added during your revision procedure. All three of these components are required for your procedure.

The INFUSE® Bone Graft component is used to stimulate new bone formation and consists of two parts—a solution containing rhBMP-2 (recombinant human Bone Morphogenetic Protein-2) and the ACS (Absorbable Collagen Sponge). The protein is a manufactured (genetically engineered) version of a natural protein normally found in small quantities in the body. The purpose of the protein is to stimulate bone formation. During surgery, the protein solution soaks into the ACS. The ACS acts as a scaffold for the formation of the new bone that the protein stimulates. It is designed to resorb (disappear) over time.

The MASTERGRAFT® GRANULES component is intended to provide structural support to the ACS. These granules resorb more slowly than the ACS. The MASTERGRAFT® GRANULES are added to provide a scaffold for bone formation for a longer time period as compared to the ACS.

The INFUSE/MASTERGRAFT™ Posterolateral Revision Device will be supplemented with either an already existing posterior stability system or a new hook/rod/screw spinal system such as the CD HORIZON® Spinal System. For more information, ask your doctor.

WHAT ARE THE POSSIBLE BENEFITS?

A potential advantage of having a spinal fusion revision procedure using the INFUSE/MASTERGRAFT™ Posterolateral Revision Device is its ability to induce new bone formation and indirectly stimulate the formation of new blood vessels. Patients with pseudoarthrosis and compromising conditions (i.e., diabetes or smoking) may not have bone and/or bone marrow from the hip available to stimulate new bone growth.

WHAT ARE OTHER OPTIONS FOR TREATMENT?

Alternatives for treating pseudarthrosis in patients with diabetes and/or whom are smokers are listed below. Because your doctor is discussing the INFUSE/MASTERGRAFT™ Posterolateral Fusion Revision Device with you, he does not believe that these alternatives would work for you. Discuss each treatment with your doctor to determine the best option for you.

- Autograft bone or bone marrow – This is when bone or bone marrow is taken from one part of your body and placed at the part of the spine being fused. If your doctor has recommended the INFUSE/MASTERGRAFT™ Posterolateral Revision Device, then you probably have already been treated with autograft or are not a candidate for autograft or bone marrow. For those patients who have already been treated with autograft or bone marrow, obtaining bone or bone marrow from the same donor site or a new donor site may lead to increased risks, including but not limited to new or increased pain, fracture of the donor site bone because of larger bone loss, injury to the nerves or blood vessels in the donor site area because of scar tissue from the previous surgery, and complications from previous infection. Discuss this option with your doctor before being treated with the INFUSE/MASTERGRAFT™ Posterolateral Revision Device.
- Allograft bone – Instead of using your own bone, a revision spinal fusion could be performed using bone from a human donor. While not as good at forming a spinal fusion as your own bone, the use of allograft does not have the risks described above associated with autograft. Because allograft bone is from a donor, there is the risk of disease transmission.
- Bone graft substitutes – These are man-made materials that provide a guide for the formation of your own new bone. While they are not as good at forming a spinal fusion as your own bone, bone graft substitutes do not have the risks described above associated with autograft or allograft.
- Bone Growth Stimulators – These are devices that apply energy to the fusion site to promote healing.
- No surgical treatment – Some patients may choose to forego a second attempt at spinal fusion, in favor of pain management and non-surgical treatments.

WHO IS A CANDIDATE FOR THE INFUSE/MASTERGRAFT™ POSTEROLATERAL REVISION DEVICE?

The INFUSE/MASTERGRAFT™ Posterolateral Revision Device is indicated for spinal repair procedures for the treatment of posterolateral (the back of your spine and away from the middle line) pseudoarthrosis that are painful. This device

is intended to treat patients with compromised conditions (i.e., smokers and diabetics) for whom retrieval of bone or bone marrow from the hip is not feasible and have two or more painful motion segments of the lumbar spine. The effectiveness of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device has not been established.

WHO SHOULD NOT RECEIVE IT?

The INFUSE/MASTERGRAFT™ Posterolateral Revision Device should not be used if:

- you are pregnant or suspect that you might be pregnant
- you are sensitive to bovine (cow) Type I collagen or recombinant human Bone Morphogenetic Protein-2
- you have an infection near the area of the surgical incision
- you have a resected or extant tumor (existing tumor), an active malignancy (progressive and uncontrollable tumor) or are undergoing treatment for a malignancy
- your bones have not stopped growing

WARNINGS AND PRECAUTIONS

This device has not been tested to determine if it could harm a developing fetus. Women of childbearing age must not get pregnant for one year following treatment with the device.

This device has not been tested in pregnant women to determine if there is any effect on a developing fetus. This device has also not been studied in nursing mothers.

When tested in female rabbits that received the rhBMP-2, a component of the device, developed an immune response and later became pregnant, the following was seen:

- The antibodies developed by the mother were able to reach the developing rabbit fetus. The effect of these antibodies on the developing rabbit fetus is not currently known.
- Some bone formation abnormalities were observed in a small number of the rabbit fetuses tested. It is not known if these changes would disappear as the rabbit fetus continued to develop or at some time after birth.

This device should not be used immediately prior to or during pregnancy. Women of child-bearing potential should be advised not to get pregnant for one year following treatment with the device. Women of child bearing potential should be warned of potential risk to a fetus and should discuss other possible orthopedic treatments with their surgeon.

BMP-2 plays a critical role during fetal development in humans and other animals. It is not known whether a pregnant woman, previously exposed to BMP-2 by implantation with the device, might develop a second immune response to BMP-2 from the developing fetus with adverse effects for the woman or baby. In a rabbit pregnancy study to investigate this issue, no increase in anti-BMP-2 antibodies was observed.

In addition, this device has not been tested:

- to see if there are side effects by using it more than once in the same person
- in people with liver or kidney problems (this might be important because these organs are involved in removing any breakdown byproducts of the device as it resorbs)
- in people with metabolic bone diseases, such as osteoporosis
- in people with autoimmune or immunosuppressive disease, such as lupus or HIV/AIDS
- in people with immune deficiency due to other treatments, such as radiation therapy, chemotherapy, or steroid therapy

Although not seen in studies performed by the manufacturer, there is a possibility that too much bone may form at the implantation site (exuberant bone formation), bone may form at a location away from the implantation site (ectopic bone formation), or the bone that is formed may be abnormal.

Some patients may have an allergic reaction to the INFUSE® Bone Graft component.

Please talk with your doctor about any of the above warnings and precautions.

HOW IS THE SURGERY PERFORMED?

The INFUSE/MASTERGRAFT™ Posterolateral Revision Device can be implanted through an opening in your lower back. This is known as a posterior surgical approach. You should speak with your doctor about the risks and benefits of this technique prior to surgery.

During your surgery, your doctor will remove portions of the failed fusion site to allow the implants to be inserted. Rather than taking bone (autograft) from your hip or from the area in which the implants will be inserted, the surgeon will utilize the INFUSE/MASTERGRAFT™ Posterolateral Revision Device to help stimulate bone growth. Your surgeon will roll the INFUSE® Bone Graft around the MASTERGRAFT® GRANULES and implant these devices in the failed fusion area.

You should discuss this surgery with your surgeon before you make your decision.

WHAT CAN I EXPECT AFTER SURGERY?

Ask your doctor about your specific recovery plan following surgery. It is important to follow your doctor's instructions carefully to recover from surgery as quickly as possible and increase your chances of a successful outcome. Recovering from back pain and surgery is an ongoing process. How fast you recover depends on the type of surgery you had, your commitment to working closely with your physical therapist,

and moving and exercising correctly, as recommended by your surgeon.

In most cases, immediately after surgery, your heart and lung function will continue to be monitored, a drainage tube may have been left in your wound, and your doctor may prescribe medicines to control pain and nausea. The average hospital stay for a patient receiving the INFUSE/MASTERGRAFT™ Posterolateral Revision Device is estimated to be 4 days.

A nurse will show you how to care for your wound before you are sent home, and your doctor will discuss a program to gradually increase your activity. You may be required to wear a back brace after surgery, and you may be told to avoid repetitive bending, lifting, stooping, twisting, and athletic activities until fusion has occurred. You may also be cautioned to avoid vibrations, like you might experience when driving a car, for a period of time after your surgery.

Contact your doctor immediately if:

- you get a fever
- your wound starts leaking fluids
- you have trouble swallowing or breathing
- you have trouble urinating
- you have new or increased back or leg pain or numbness

Your doctor will schedule office visits to check on how you are doing and to see if anything else needs to be done.

After surgery, your surgeon may refer you to a physical therapist who will teach you exercises to improve your strength and increase your mobility. The goal of physical therapy is to help you become active as soon as possible, using safe body movements that protect your back. This often includes abdominal strengthening exercises. You may also be taught different ways of standing, sitting, or lifting to avoid reinjuring your back.

WHAT POSSIBLE COMPLICATIONS COULD OCCUR?

As with any surgery, spinal surgery is not without risk. A variety of complications related to the use of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device can occur. These may occur individually or in combination. Some of these may be severe, affecting your outcome. You may also need to have additional surgery to correct these complications. Some of the possible complications include:

- allergic reaction to the implant materials
- anaphylactic reaction (exaggerated allergic reaction to the protein)
- bone fracture
- bowel or bladder problems

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- cessation of any potential growth of the operated portion of the spine
- change in mental status
- damage to blood vessels and cardiovascular system compromise
- damage to internal organs and connective tissue
- death
- development of respiratory problems
- disassembly, bending, breakage, loosening, and/or migration of components
- ectopic and/or exuberant bone formation (displaced [ectopic] and/or profuse bone formation)
- edema (swelling)
- elevated erythrocyte sedimentation rate
- erythematous tissue (abnormal redness of the skin)
- fetal development complications
- fluid collection
- fluid-filled cysts
- foreign body (allergic) reaction
- gastrointestinal complications
- hematoma (localized swelling from an accumulation of blood)
- incisional complications
- infection
- inflammation
- itching
- loss of spinal mobility or function
- neurological system compromise
- nonunion (or pseudoarthrosis), delayed union, mal-union
- pain
- postoperative change in spinal curvature, loss of correction, height, and/or reduction
- scar formation
- seroma (localized swelling from an accumulation of fluid)
- tears of the dura (a layer of tissue covering the spinal cord)
- tissue or nerve damage

HAS INFUSE/MASTERGRAFT™ POSTEROLATERAL REVISION DEVICE BEEN STUDIED IN HUMANS?

The INFUSE/MASTERGRAFT™ Posterolateral Revision Device has not been previously tested in controlled human clinical trials for the intended indication. Data supporting its use in symptomatic, multi-level posterolateral revision procedures has been obtained from a small number of patients who were smokers and/or diabetics. In this analysis, no new adverse events were observed. All 3 patients with fusion data were determined to have a solid fusion outcome. Additionally, 4 patients received the INFUSE/MASTERGRAFT™ Posterolateral Revision Device and a small amount of their own bone. Fusion success was achieved in all cases with sufficient follow-up. This provides insight into the safety and probable benefit of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device in its approved indication.

The combination of INFUSE® Bone Graft and MASTERGRAFT® Resorbable Ceramic Granules with spinal instrumentation has also been evaluated in a different study. This study was intended for patients suffering from single level disease requiring surgical intervention at the operative level for the first time. The data, shown in the table below, provides further evidence supporting the safety and probable benefit of the INFUSE/MASTERGRAFT™ Posterolateral Revision Device.

INFUSE® Bone Graft
MASTERGRAFT® GRANULES
CD HORIZON® Spinal System
Summary of Pilot Study Success at 24 Months

Primary Outcome Variable	Investigational		Control	
	Success	Failure	Success	Failure
Fusion	18 (94.7%)	1 (5.3%)	14 (70.0%)	6 (30.0%)
Oswestry Pain	22 (95.7%)	1 (4.3%)	15 (75.0%)	5 (25.0%)
Neurological	22 (95.7%)	1 (4.3%)	18 (90.0%)	2 (10.0%)
Overall Success	17 (81.0%)	4 (19.0%)	11 (55.0%)	9 (45.0%)

INFUSE® BONE GRAFT COMPONENT

The INFUSE® Bone Graft component of this device has been evaluated in several other human clinical studies resulting in FDA approval for various indications. These indications include: the treatment of acute, open tibial shaft fractures that have been stabilized with intramedullary nail fixation and spinal fusion bone grafting procedures. Specifically, these procedures ("Indications for Use") include:

Tibial Fracture
Intramedullary (IM) nail fixation is a surgical procedure that involves placing a metal rod down the center of the tibia and affixing it in place with bone screws. To aid in the treatment, INFUSE® Bone Graft is then placed around the fractured bone. The goal of the procedure is to stabilize the fracture and allow the bone to heal.

Anterior Lumbar Intervertebral Body Fusion
Anterior lumbar interbody fusion (ALIF) is a surgical procedure that involves approaching the spine from the front (anterior) of the body to remove all or part of a diseased or damaged disc in the lumbar spine. INFUSE® Bone Graft/Interbody Fusion Device is then implanted between the vertebral bodies. The INFUSE® Bone Graft/ Interbody Fusion Device helps maintain normal disc height. As the body heals, the vertebral bone eventually grows together and stabilizes the spine.

MASTERGRAFT® RESORBABLE CERAMIC GRANULES COMPONENT

The MASTERGRAFT® Resorbable Ceramic Granules component of this device has been proven to be substantially equivalent to other previously cleared products. The MASTERGRAFT® Resorbable Ceramic Granules have been marketed for use in humans since 2002.

TALK TO YOUR DOCTOR.

While this brochure has hopefully provided you with the information you need to make an informed decision about your treatment options, it is not intended to replace professional medical care or provide medical advice. If you have any questions or need additional information about the INFUSE/ MASTERGRAFT™ Posterolateral Revision Device, please call or see your doctor, who is the only one qualified to diagnose and treat your back. As with any surgical procedure, you should find a surgeon who is experienced in performing the specific surgery that you are considering.

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