PATIENT INFORMATION/INFORMED CONSENT

CLINICAL STUDY TITLE
CarboClear Pedicle Screw System

SPONSOR
CarboFix Orthopedics Inc., 506 Halle Park Drive, Suite 102, Collierville, TN 38017, USA

PROTOCOL NO.
CARBOCLEAR P_CLD 2492_US

PRINCIPLE INVESTIGATOR _____

SITE NAME _____

APPROVED BY INSTITUTIONAL REVIEW BOARD _____

Federal regulations require a written informed consent from participants prior to participation in a research evaluation, so that they know the nature and risks of participation and can decide to participate or not in a free and informed manner. You are asked to read the following material to ensure that you are informed of the nature of this research evaluation and of how you will participate in it if you consent to do so. Signing this form will indicate that you have been so informed and that you give your consent.

Dear Patient,

You are being asked to take part in this clinical investigation that involves collecting data on the clinical results of the CarboClear Pedicle Screw System, for the treatment of degenerative disc disease ("DDD") of the lumbar and/or sacral spine (the lower bones in your back).

Important: Before you agree to participate in this study, it is important that you understand the following explanation of the study and proposed procedures. Please take time to read this information carefully. If you have any questions regarding the study or your rights as a participant, be sure they are addressed before you agree to participate. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You should sign the Patient Informed Consent Form only after you have read and understood the entire document and after all of your questions have been answered. You should feel that signing this form is something you are doing voluntarily. If you feel that you are under pressure, we advise you to postpone your decision. If you decide to participate, you are free to withdraw your consent at any time. Signing this form will indicate that you have been informed and that you give your consent. Regardless of what you decide, you will continue to receive the best treatment for your condition at all times.

INTRODUCTION AND STUDY OBJECTIVE

You have been diagnosed with degenerative disc disease ("DDD") at your lumbar and/or sacral spine (the lower bones at your back, between the ribs and the pelvis), a condition clinically characterized by lower back pain and/or radicular leg pain. Your doctor would like to treat your condition using the CarboClear Pedicle Screw System. However, the CarboClear Pedicle Screw Device has not been cleared by the FDA. Although the CarboClear Pedicle Screw System is experimental for treating DDD, it is expected that implantation of the CarboClear Device could help resolve your symptoms. Your participation in this study will help us to test this hypothesis.

You are invited to participate in a clinical study in which you will undergo an implantation procedure utilizing the CarboClear Pedicle Screw System for your spine stabilization, as part of an operation for spinal fusion of adjacent vertebrae.
If you consent to participate in this study, you will undergo an implantation of the CarboClear Pedicle Screws and Rods. The implant components will be implanted in the back of your treated vertebrae, in order to provide for immobilization and stabilization of the treated spine. The procedure of implantation of pedicle screw system is commonly performed for stabilizing the spine in spinal fusion procedures. However, the use of this specific system – the CarboClear Pedicle Screw System – is experimental.
The procedure also includes removing of your disc from the treated lumbar/sacral vertebra/e, and placement of a device ("intervertebral body fusion device" or "cage") in between the lumbar vertebrae, in order to fuse and stabilize your degenerated vertebrae. This part of the operation is not experimental, and the cage that will be implanted between your vertebrae is cleared by the FDA.
As routinely done in spinal fusion procedures, the implantation of the cage and the CarboClear Device will be used in combination with bone taken from your body and/or bone derived from other human source and is cleared for such procedures by the FDA.
After surgery, bone is supposed to grow between the two treated vertebrae, fusing them into one, solid piece of bone.

The **purpose** of this study is to demonstrate the safety and effectiveness of the CarboClear Pedicle Screw System ("CarboClear System"), for DDD patients undergoing spinal fusion with a cage device, and requiring immediate, rigid, posterior immobilization and stabilization of the lumbar and/or sacral spine.

NUMBER OF PATIENTS PARTICIPATING IN THE STUDY

A total of up to 55 patients are expected to participate in the study.

STUDY DURATION

Your participation in the study is expected to last up to 2 years, as follow-up from the date of surgery will be for 12 months, and then will continue annually, until the last patient enrolled into the study has completed the 1-year follow-up.

DESCRIPTION OF CARBOCLEAR SYSTEM

The CarboClear System is composed of pedicle screws, rods, and locking elements.
During operation, two pedicle screws are inserted into each treated vertebra via the vertebral pedicles, in a posterior-anterior orientation (*i.e.*, from the back). The screws at each side of the vertebrae are longitudinally (*i.e.* along the spine) connected by a rod. Locking elements are placed at each screw-rod intersection, to firmly secure the screws and the rods together.
The pedicle screws, rods and locking elements are made of carbon fiber-reinforced polymer (CRF-PEEK), and include metal markers to enable their visualization under X-Rays. The threaded portion of the pedicle screw is encased within a thin layer of metal (titanium) shell.

It is noted, that the design and dimensions of this investigational pedicle screws and rods are similar to those of other, FDA cleared and market-available, pedicle screw systems, as is the implantation technique. The main difference between the investigational CarboClear pedicle screw system and cleared pedicle screw systems is the material – the implants of the investigational system are made of CFR-PEEK while those of cleared systems are typically made of metal (*e.g.*, stainless steel or titanium). The CRF-PEEK material has been cleared for use by the FDA in other spinal implants, but not in a pedicle screw system which will be investigated in this study.

STUDY REQUIREMENTS AND PROCEDURES

Prior to your enrollment to this study, your physician will verify that you are eligible to participate in the study by checking your compliance with the study inclusion criteria and exclusion criteria.
If you meet all enrollment criteria and have signed this Patient Informed Consent Form, you will be able to participate in the study.
Important: Women who are pregnant are excluded from this study. If you are a woman of child bearing potential, please discuss with your study doctor about your eligibility.

The surgery involving the investigational device and the related procedures/examinations which you will undergo if you take part in this study are detailed below.

Before surgery:

a. You will be interviewed regarding your current and past medical condition (including filling out dedicated patient questionnaires).
b. You will undergo physical and neurological examinations.
c. You will undergo radiographic evaluation (*e.g.*, fluoroscopy (X-Rays) and optionally CT/MRI scans).
d. Upon hospital admission, you will undergo the routine hospitalization processes in the medical center.

It is noted, that except for filling out questionnaires, the above pre-operative procedures are common to pedicle screw spinal surgeries, and are not unique to the investigational device.

During surgery:

a. You will receive anesthesia, as decided by your doctor.
b. Intraoperative imaging (such as fluoroscopy) will be used to visualize your spine and the implanted device throughout the surgical procedure.

c. Following conventional, open, posterior procedure steps (*i.e*., you will be laying prone), the surgeon will make an incision (up to 4 inches) in order to access the treated vertebra/e and prepare the implantation site by removing the disc (the non-bony tissue between two adjacent vertebrae) of the treated vertebra/e.
d. An FDA cleared intervertebral body device (also called a "cage") will be implanted into the space between the two vertebrae in order to help fuse and stabilize your degenerated vertebrae. This part of the operation is not experimental.
e. Prior to inserting the investigational pedicle screws, the surgeon will create pilot holes in the vertebral pedicles, as is routinely done in pedicle screws implantation procedures. Then, the surgeon will insert the investigational pedicle screws, while verifying their exact location, insertion angle, and final position using real-time fluoroscopy imaging. Once two pedicle screws are positioned at each side of the treated vertebrae, the surgeon will determined the correct rod shape and length, and insert two rods into the pedicle screw heads to longitudinally connect the pedicle screws in each vertebra. In order to lock the rods to the screws, the locking elements will be secured. The surgeon will verify, using fluoroscopy, the proper position of the device.
f. As routinely performed during spinal fusion procedures, bone graft from your body (pieces of bone taken from the surgical site or from your pelvis) and/or bone derived from other human sources will be placed between the two treated vertebrae in order to fuse them. In addition, the surgeon might decide to perform a decompression procedure such as laminectomy (*i.e*., removing a portion of the vertebral bone called the lamina, in order to allow more room for the nerve tissue). All procedures discuss in this step are common procedure in spinal fusion surgery (non-experimental).
g. The operation site will be closed and treated following conventional, non-experimental procedures for open posterior surgery such as metal clips and/or sutures.

<u>Following surgery</u>:

a. After the procedure, you will probably stay at the hospital for a few days, as is commonly done following pedicle screw surgery.
b. Prior to discharge from hospital, you will be examined (*e.g*., physical examination).
c. You will be asked to return for follow-up meetings at 6 weeks, 3 months, 6 months, and 12 months following the operation (and optionally at 24 months, until the last patient has completed a follow-up period of 12 months after operation). During these follow-up sessions, you will be questioned regarding your medical condition (including filling out dedicated patient questionnaires) and you will undergo physical and neurological examinations, and radiographic evaluation (X-rays, used to visualize your vertebrae and implants) in order to examine the condition of your treated vertebrae.
   Additional meetings and/or examinations might be required according to the physician's discretion. Your physician will guide you which additional meetings and/or examinations are required and for how long.

POTENTIAL RISKS AND DISCOMFORTS

As with every procedure of this nature, there are risks and discomforts may occur. The potential risks/complications and discomforts which may be associated with the use of CarboClear System are listed below. Please ask your physician to explain any of the following terms if they are not clear.

Risks Associated with Undergoing Surgery

- Infection/Sepsis.
- Development of respiratory problems, *e.g*. atelectasis, bronchitis, pneumonia, *etc*.
- Hemorrhage of blood vessels and/or hematomas occlusion, seroma, edema, hypertension, embolism, stroke, excessive bleeding, phlebitis, wound necrosis, wound dehiscence, damage to blood vessels, or other types of cardiovascular system compromise.
- Deep venous thrombosis, thrombophlebitis and/or pulmonary embolus.
- Damage to lymphatic vessels and/or lymphatic fluid exudation.
- Reactions to the drugs or anesthetic agent used during and after surgery.
- Ileus, gastritis, bowel obstruction or loss of bowel control or other types of gastrointestinal system compromise.
- Reactions to transfused blood.
- Incisional pain.
- Change in mental status.
- Death.

Risks Associated with Spine Surgery

- Loss of neurological function (e.g., sensory or motor), including paralysis (complete or incomplete), appearance of radiculopathy, dysesthesias, hyperesthesia, anesthesia, paresthesia, and/or the development or continuation of pain, numbness, neuroma, spasms, sensory loss, tingling sensation, and/or visual deficits.
- Cauda equina syndrome, neuropathy, neurological deficits (transient or permanent), paraplegia, paraparesis, reflex deficits, irritation, arachnoiditis, and/or muscle loss.
- Dural tear experienced during surgery could result in the need for further surgery for dural repair, a chronic cerebral spinal fluid leakage or fistula, and possible meningitis.
- Herniated nucleus pulposus, disc disruption or degenerative changes or instability at, above, or below the level of surgery.
- Loss of or decrease in spinal mobility or function.
- Loss of proper spinal curvature, correction, height and/or reduction.
- Bone fracture or bone loss or decrease in bone density, possibly caused by stress shielding at, above, or below the level of surgery.
- Tissue or nerve damage caused by improper positioning and placement of implants or instruments.
- Vascular damage due to surgical trauma or presence of the device could result in catastrophic or fatal bleeding. Malpositioned implants adjacent to large arteries or veins could erode these vessels and cause catastrophic bleeding in the late postoperative period.
- Bursitis.
- Scar formation possibly causing neurological compromise or compression around nerves and/or pain.

- Inability to resume activities of normal daily living.
- Reproductive system compromise, including sterility, retrograde ejaculation, and sexual dysfunction.
- Urinary retention or loss of bladder control or other types of urological system compromise.
- Risks of radiation exposure pre-operatively, during surgery and following operation, during follow-up sessions (*e.g.*, fluoroscopy, X-Rays, and optionally CT scan).

Risks Associated with Fusion Surgery of the Lumbar Spine

- Graft settling/displacement
- Non-union (or pseudarthrosis), delayed union or mal-union.
- Donor site pain
- Risks pertaining to the use of allograft (if applicable), including infection, fever, incomplete bone ingrowth, delayed fusion or non-union, hypercalcemia or transient hypercalcemia, disease transmission and undesirable immune response.

Risks Associated with The Use of The CarboClear Pedicle Screw System.

- Disassembly, loosening, bending or fracture of any or all of the implant components.
- Implant migration.
- Foreign body (allergic) reaction to the implants, debris, including possible staining, autoimmune disease, tumor formation and/or scarring.
- Pressure on the surrounding tissues or organs.
- Pressure on the skin from component parts in patients with inadequate tissue coverage over the implant, possibly causing skin penetration, irritation, fibrosis, neurosis, and/or pain.

Additional surgical intervention may be necessary to correct some of the possible adverse events. Surgical intervention may be a revision surgery, a removal procedure, re-operation, or supplemental fixation.

Please ask your physician, if you wish further information regarding the risks listed above.

POTENTIAL BENEFITS

In general, patients may not experience any direct benefits.
Based on the performance of other cleared pedicle screw systems that have successfully relieved symptoms of degenerative disc disease and clinical experience with the investigational device outside the United States, there is reason to believe that the CarboClear Pedicle Screw System could also relieve your symptoms. However, there is no guarantee of this and your symptoms could remain unchanged or worsen.

ALTERNATIVE THERAPIES

Your alternative is to not participate in this study and receive non-experimental treatment.
Non-surgical alternatives include, but are not limited to, conservative treatment without intervention, medications, injections, and/or physical therapy. However, if you are candidate to participate in this study, conservative treatment for at least six months has failed to help your condition.
Non-experimental surgical therapies to treat your condition primarily include vertebral fusion procedures using pedicle screw system and/or intervertebral fusion device, or total disc replacement.

Fusion

The following are the main types of spinal fusion procedures, which may be used in conjunction with each other:
Interbody fusion places the bone graft between the vertebrae in the area usually occupied by the intervertebral disc. In preparation for the spinal fusion, the disc is removed. A device (cage) may be placed between the vertebra to maintain spine alignment and disc height. This device may be made from either plastic (*e.g*., PEEK polymer) or metal (titanium). The fusion then occurs between the endplates of the vertebrae. Interbody fusion is performed using either anterior or posterior approaches (named ALIF and PLIF, respectively). The treated vertebrae may then be stabilized and fixed in place with screws, which are inserted via the pedicles of each vertebra and are connected longitudinally using a rod on each side of the vertebrae. The procedure is the same as described for the investigational device, but it uses metal screws and rods.
Posterolateral fusion places the bone graft between the vertebral transverse processes in the back of the spine. The treated vertebrae may then be stabilized and fixed in place with screws, which are inserted via the pedicles of each vertebra and connected longitudinally using a rod on each side of the vertebrae.
Fusion rates are slightly higher with interbody fusion, however it involves a more extensive surgery.
Minimally invasive techniques have also been introduced to reduce surgery-related complications and recovery time for spinal fusion.

Total Disc Replacement

In this surgical procedure, which is a more recent procedure as compared to spinal fusion, the degenerated intervertebral disc is removed and replaced with artificial disc. This procedure aims at preserving motion at the treated intervertebral segment.
Current evidences suggest that, compared with spinal fusion, total disc replacement for lumbar degenerative disc disease leads to equivalent outcomes two years after surgery. However, the longer-term clinical outcome of total disc replacement is still unclear.

CONFIDENTIALITY

This Informed Consent and another document called an "Authorization to Use and Disclose Health Information" control how your health information may be used and disclosed during and after this study.
The Authorization describes how your health information may be used and disclosed by your health care providers and the study investigator(s) as part of the study.

This section of the Informed Consent describes what the Sponsor and its representatives may do with the study data, including all of your health information received, collected or derived from you during, or produced during the course of, the study. The sponsor and its representatives may use and disclose this data:

- to conduct, monitor and/or audit the research and to confirm the research results;
- to evaluate and improve the performance of the CarboClear Pedicle Screw System;
- to assure the safety, effectiveness, and quality of research and of medical products and therapies, which may include, but is not limited to, the collection and reporting of adverse event information as permitted by law;
- to conduct new medical research and develop proposals for new medical products or therapies; *and*
- as required by law

Individuals from the **[*name of hospital/clinical trial site*]**, institutional review board (IRB), Clinical Trials Office, the U.S. Food and Drug Administration and other U.S. and foreign government agencies, and data safety monitoring board may look at and copy the health information created or collected about you as part of this study, to assure quality control, to analyze the information and as otherwise permitted by law, but they are bound by obligation not to reveal your identity to others.
The results of this study or other research conducted by the study investigator(s) and CarboFix Orthopedics may be published in journals and/or presented at scientific meetings; however, your identity will be held in strict confidence and not revealed.
To participate in this study, you must sign both this Informed Consent and the Authorization to Use and Disclose Health Information.

AVAILABILITY OF STUDY DATA ON THE INTERNET

A description of this clinical trial will be available on www.ClinicalTrials.gov as required by U.S. law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

COSTS OF STUDY PARTICIPATION

There will be no additional cost to you to participate in this study, compared to similar surgery which is not part of a clinical study.

PAYMENT FOR STUDY PARTICIPATION

You will not be paid for participating in this research.

TREATMENT OF RESEARCH RELATED INJURY

If you believe you have been injured while participating in this study, contact a member of the study staff at [***phone number***]. After hours or in case of emergency, you may call [***phone number***] [***hospital operator***] and ask the operator to page [***Dr's. Name***] [***principal investigator***]. In case of emergency, if you do not receive a response immediately, you should go to the emergency room. By signing this document, you verify that you understand that in the event of physical injury resulting from this study, only immediate, essential medical treatment, as determined by the hospital, will be available for the injury without charge.

PARTIES TO CONTACT

The investigator or his/her designee will answer all of your questions. If you have any other questions about this study, please contact **[*name and number of contact*].** During non-business hours, please contact **[*name and number of after-hours contact*]**.

INSTITUTIONAL REVIEW BOARD

If you have additional questions during the course of the study about your rights as a research participant, you may address them to **[*IRB name, address, and phone number*].**

VOLUNTARY PARTICIPATION/WITHDRAWAL

Your participation in this study is voluntary. If you wish, you may decline participation simply by telling your physician. Your refusal to participate will not affect your future medical care and treatment in any way, and will involve no penalty or loss of benefits to which you are entitled. You will receive the same standard of care that you normally would receive. If you decide to participate in this study, and later decide you do not wish to continue, you may withdraw from the investigation at any time, without any prejudice or effect on your future medical care treatment.

As a study participant, you must carefully follow all instructions given to you concerning the study, including adhering to follow-up sessions. You should also inform your physician if you have been sick or hospitalized for any reason during the study.

You will be informed of significant new findings or any changes in the nature of the study or the procedures that may relate to your willingness to continue participation in this study.

TERMINATION OF PARTICIPATION

The investigator/s may discontinue your study involvement at any time if it is felt to be in your best interests, if you do not comply with the study requirements, if the study is stopped, or for any other reason.

FINANCIAL INTERESTS OF THE STUDY DOCTOR IN CARBOFIX ORTHOPEDICS OR IN THE CARBOCLEAR SYSTEM

The institution running this study is being paid by CarboFix Orthopedics Inc. to cover the costs of conducting this study. Your doctor and institution do not have any other financial interest in the outcome of this study, does not have any ownership interest in the CarboClear Pedicle Screw System, and are not a stockholder in CarboFix Orthopedics Inc.

CONSENT TO PARTICIPATE IN THIS STUDY

CarboClear Pedicle Screw System

Date of Birth _____ / _____ / 20 _____

Day Month Year

Last Name: _____ First Name: _____

Address: _____

_____

Telephone Number: (_____)_____

I confirm that, after receiving both oral and written explanations, I agree to participate in the study described.

My participation is voluntary and I can withdraw my consent without jeopardizing my present or future treatment.

I will be given a copy of this signed consent form. By signing this form, I have not given up any of my legal rights as a research participant.

_____ _____ _____

(Date) (Signature of Participant) (Clinic Number)

_____ _____

(Date) (Signature of Investigator Obtaining Consent)