DE NOVO CLASSIFICATION REQUEST FOR OGMEND® IMPLANT SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Screw sleeve bone fixation device: A screw sleeve bone fixation device is intended to be implanted in conjunction with a non-resorbable, metallic bone screw where the screw has lost purchase due to loosening, backout, or breakage. The device fits between the screw threads and surrounding bone, and provides increased surface area to create an interference fit to restore stability of the implant construct.

NEW REGULATION NUMBER: 21 CFR 888.3043

CLASSIFICATION: Class II

PRODUCT CODE: QAC

BACKGROUND

DEVICE NAME: OGmend® Implant System

SUBMISSION NUMBER: DEN180065

DATE DE NOVO RECEIVED: December 13, 2018

SPONSOR INFORMATION:

Woven Orthopedic Technologies, LLC
63 E. Center Street
Manchester, Connecticut 06040

INDICATIONS FOR USE

The OGmend® Implant System is indicated as follows:

The OGmend® implant system is for the use with screws as part of a fracture fixation plate system in long bones in rescue scenarios where the screw has lost purchase due to screw loosening, back out, or breakage and the stability of the plate construct is at risk. The OGmend® Implant System is for use in skeletally mature patients.

LIMITATIONS

The sale, distribution, and use of the OGmend® Implant System is restricted to prescription use in accordance with 21 CFR 801.109.

The safety and effectiveness of the OGmend® Implant System has not been established for use with non-metallic, resorbable, or self-tapping screws.

The OGmend® Implant System should not be used with stand-alone screws, joint arthroplasty systems, and spinal fixation procedures.

The OGmend® Implant System should not be used in a situation where other rescue techniques (i.e., rescue screw, repositioning of bone plating system or stand-alone screw) will provide a better patient outcome.

The OGmend® Implant System has not been tested in patients with osteoporosis, osteopenia, diabetes, nor in patients who smoke or who have any other metabolic bone diseases.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The OGmend® Implant System is a sterile, single-use device intended to provide supplemental fixation to restore stability if the screw/bone interface of a plate and screw system becomes mechanically compromised. When inserted into a prepared bone pilot hole, the OGmend® Implant System is designed to use the principles of interference fit to serve as a rescue technology to secure a bone screw and stabilize the fracture construct. The OGmend® Implant System is manufactured from woven polyethylene terephthalate (PET), with an inner diameter of 6.5mm and an outer diameter of 7.5mm, and can be used with screws ranging in diameter from 3.5mm to 6.5mm. The OGmend® Implant System is 100mm in length and is cut intra-operatively to the appropriate length.

Figure 1: View of OGmend® Implant System on sample screw

When a screw loses stability due to loosening, backout, or breakage, the OGmend® Implant System is intended to restore stability. The device is placed into a prepared hole after removal of the failed screw, and a new screw is inserted though the inner diameter of the OGmend® Implant

System, in order to generate mechanical interferences and improve the stability of the screw and bone-plate construct.

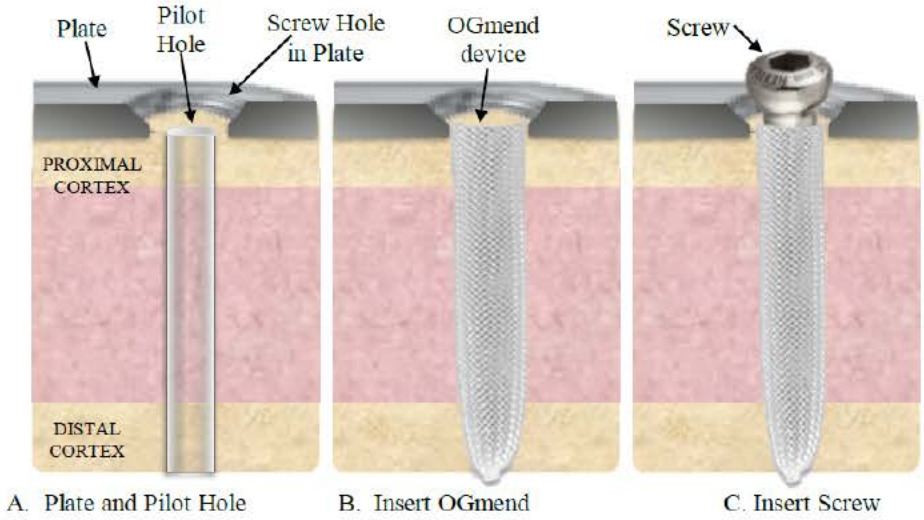


Figure 2: Illustration of placement of OGmend® Implant System in hole during the repair of a failed screw on a bone plate system.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The OGmend® Implant System is manufactured from the following materials:

Table 1: Device Materials

Description	Material	Direct Patient Contact	Contact Duration
OGmend® Implant System	Polyethylene Terephthalate	Yes	(b)(4)
Inserter Instrument	(b)(4)	Yes	(b)(4)

Biocompatibility Testing is described in the table below.

Table 2: Biocompatibility Testing

ISO 10993 Endpoint	Test Performed	Endpoint Met
Cytotoxicity	Yes	Yes
Sensitization	Yes	Yes
Irritation / Intracutaneous Reactivity	Yes	Yes
Acute Systemic Toxicity	Yes	Yes
Material-Mediated Pyrogenicity	Yes	Yes

Subacute / Subchronic Toxicity	Yes	Yes
Genotoxicity	Yes	Yes
Implantation	Yes	Yes
Chronic Toxicity	Yes	Yes
Carcinogenicity	Yes	Yes

Additional *in vivo* studies data were leveraged to address biocompatibility of the OGmend® Implant System (See Animal Testing section below). In conjunction with the CDRH Guidance *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process*", the *in vivo* testing and ISO 10993 testing provided, was used to demonstrate the biocompatibility of the device.

SHELF LIFE/STERILITY

The subject device is a single use device and is provided sterile to the end user. The sterilization method is gamma radiation at a dose of 25 kGy. Sterilization was validated using the VD_{max} method as per ISO 11137, and achieved a Sterility Assurance Level (SAL) of 10^{-6}. The subject device and instruments are packaged together in sealed double-blister Tyvek pouches.

Sterilized samples accelerated-aged to (b)(4) months, and real-time aged to (b)(4) months were used to determine the shelf life of the device. Distribution testing and package integrity testing (bubble/leak test, ASTM F2096), and seal strength testing (ASTM F88/F88M) were used to validate the sterile shelf life of device. Non-clinical performance testing of the implant (See Table 3) was used to assess the performance shelf life of the device. The testing confirmed a (b)(4) shelf life.

The following standards were utilized in the validation of the sterilization and shelf-life:

- ANSI/AAMI/ISO 11137-1:2006: Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices
- ANSI/AAMI/ISO 11137-2:2012: Sterilization of Health Care Products -Radiation - Establishing the Sterilization Dose - Method VD_{max}^{25}
- ISO 11737-1 2006/(R)2011 Sterilization of medical devices - Microbiological methods - Part 1: determination of a population of microorganisms on products
- ANSI/AAMI/ISO 11737-2:2009 Sterilization of medical devices – Microbiological methods – Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process
- ASTM F88/ F88M–15: Standard Test Method for Seal Strength of Flexible Barrier Materials
- ASTM F1886/ F1886M-09 (2013): Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection

- ANSI/AAMI/ISO11607-1:2006: Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems, and packaging systems
- ANSI/AAMI/ISO11607-2:2006: Packaging for terminally sterilized medical devices – Part 2: Validation requirements for forming, sealing, and assembly processes
- ASTM F1980, Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
- ASTM F 1140:2007, Standard Test Methods for Internal Pressurization Failure Resistance of Unrestrained Packages.
- ASTM F2096-2004, Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)
- ASTM D-4332/1991, Standard practice for conditioning containers, packages, or packaging components for testing
- ISTA 2A-2011, Partial Simulation Performance Tests

MAGNETIC RESONANCE (MR) COMPATIBILITY

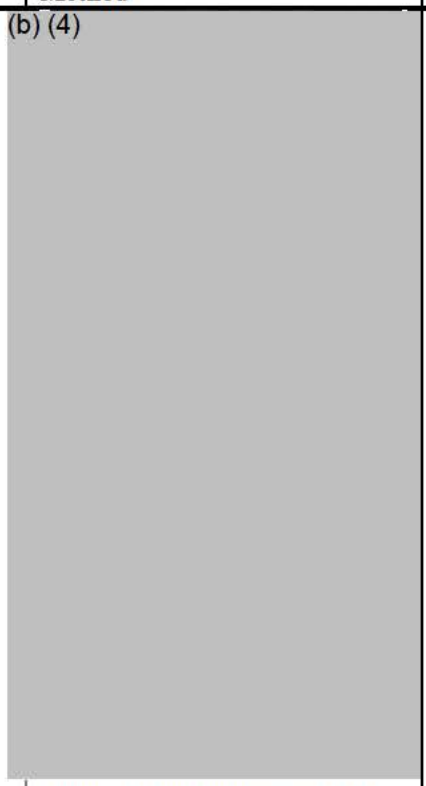
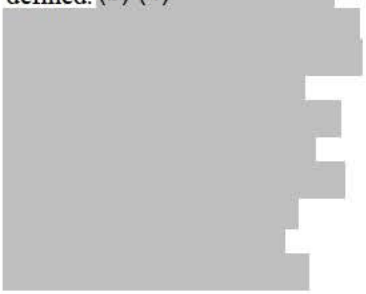
The subject device was not evaluated for safety in a (b)(4) Environment. The device is manufactured from a non-ferromagnetic, non-metallic, and radiofrequency transparent material, PET; however, as it is intended to be used with metallic bone plate and screw systems, the following precaution is included in the labeling:

- There may be concerns regarding the MR safety of the metallic hardware (i.e., plates and screws) used in conjunction with the OGmend® Implant System.

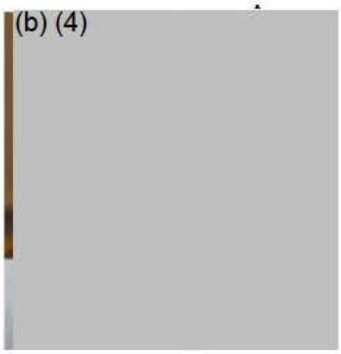
PERFORMANCE TESTING - BENCH

Table 3: Summary of Bench Testing

Test	Purpose	Method	Acceptance Criteria	Results
Screw Axial Pullout	This test is intended to assess if the subject device provides improved stability compared to an alternate treatment for a failed screw.	To simulate a rescue scenario, a 3.5 mm pilot hole was made in 20 pcf Sawbone. The device was then implanted in combination with a 3.5 mm screw. The screw was then pulled axially until failure as per ASTM F543. 4.0 mm screws were inserted into 3.5 mm pilot holes to simulate placing a larger screw in a failed screw hole as a control.	The axial pullout force of the screw in combination with the sleeve must be equivalent to or greater than the pullout force for a rescue screw alone.	Test results show that the force required to pull out a 3.5 mm screw with the OGmend® Implant System in place exceeded the force required to pull out a 4.0 mm screw without the OGmend® Implant System. The acceptance criteria were met.

Test	Purpose	Method	Acceptance Criteria	Results
		(b) (4)  **Figure 3: Test setup for Axial Pullout**		
Sleeve Dynamic Axial Loading, Pullout and Removal/ Extraction Torque	This test is intended to assess if dynamic loading would damage the implant and/or cause a reduction in pullout strength.	A control group (without the OGmend® Implant System) and treatment group (with the OGmend® Implant System) were defined. (b) (4)  Axial loading is considered to constitute the worst-case clinical loading scenario as compression plates are designed to generate axial loading on the screw, and the resultant force on the screw would be reduced by transfer of some load to the plate. Each screw was sinusoidally loaded between (b) N and (b) % of the pullout force determined from	After (b) (4) cycles, there should be no decrease in pullout values or damage to the device.	The test results showed no decrease in axial pullout force or removal torque in either the control group or in the OGmend® Implant System treatment group. This testing demonstrated that cyclic loading did not negatively affect the mechanical strength of the device or the stability of the interference fit.

Test	Purpose	Method	Acceptance Criteria	Results
		static testing for a total of (b) (4) cycles at a rate of (Hz. For reference, the pullout force was re-evaluated during this testing to determine the correct (b % value. The (b % pullout force value for the subject device was (b) N and was (b) N for the control. At the completion of (b) (4) cycles, removal torque and pullout testing were conducted per ASTM F543.		
Sleeve Insertion Force	This test is intended to evaluate the force required to insert the sleeve compared to the force required to insert the sleeve manually during a surgical procedure.	The axial force needed to push the sleeve into a pilot hole using an inserter tool in (b) pcf bone foam was measured. Testing was performed with both a 3.5 mm and 6.5 mm pilot hole to represent the smallest and largest potential holes compatible with the device. To assess the load needed to cause damage to the sleeve, a probe was pressed through the sleeve against the distal tip at a constant rate until failure of the sleeve occurred. (b) (4) **Figure 4: Test setup for sleeve mechanical strength test**	No more than (b) N should be required to insert the OGmend® Implant System. This was based on an assessment of load needed to damage the device with a margin of safety.	For both a 3.5 mm and a 6.5 mm pilot hole, it required less than (b N to insert the device (b) (4) N in the 3.5 mm hole, and (b) (4) N in the 6.5 mm hole). This compares to an average force of (b) .1 N needed to rupture the distal end of the sleeve. This demonstrated that the device can be successfully inserted into bone using the provided surgical technique and instruments without damage to the device.
Screw Removal/ Extraction Torque	This test is intended to assess the ability of the screw to be inserted and extracted when used with the OGmend® Implant System compared to a traditional, fully threaded bone screw used without the	The investigational cohort, consisting of the OGmend® Implant System and screw, was tested with two screw diameters (3.5mm and 6.5mm) in 20 pcf sawbone. Pilot holes were made in the sawbone, and the sleeve and screw were implanted following the surgical technique. During insertion, torque was measured using a load cell. After	The torque required to insert and remove the screw with the OGmend® Implant System in place must be less than the torsional strength of the screw	The OGmend® Implant System did increase the torque needed to insert and remove the screw. The torque to insert the screw increased from 0.025 Nm to

Test	Purpose	Method	Acceptance Criteria	Results
	OGmend® Implant System. The intent of the test is to demonstrate that the interference generated by the implant did not increase the insertion/removal torque sufficiently that it could lead to breakage of the screw during implantation or removal, or not allow for proper implantation of the screw.	insertion, the screw was then removed while measuring torque, as per ASTM F543-17. The torsional strength of the screw was assessed by torqueing the screw until failure as per ASTM F543.  **Figure 5: Test setup for insertion torque testing.**		0.133 Nm (3.5 mm) and from 0.123 Nm to 0.651 Nm (6.5 mm screw). Similarly, the torque to extract the screw increased from 0.025 Nm to 0.180 Nm (3.5 mm) and from 0.137 to 0.803 Nm (6.5 mm screws) While there was an increase in the torque required to implant and remove the screw, the torque was still significantly less than the yield torque of the screws being tested, indicating there is no risk of screw failure during insertion and removal.
Durability of Sleeve during Screw Implantation	This test is intended to assess if the OGmend® Implant System can be inserted into the bone without damage of the device, using the provided instruments, in preparation for the placement of a screw.	(b) (4)	Screw pullout force following repeated insertions must not be reduced compared to prior axial pullout testing.	Testing showed no reduction in pullout strength of a screw compared to baseline. This indicates the device can withstand the handling of surgery without damage that could affect its mechanical performance.
Wear Particle Generation	This test is intended to assess if the sleeve can withstand screw insertion and cyclic loading	(b) (4)	The device should not sustain damage such that it fails to perform its intended function, and wear	Assessment of images found no significant damage occurred to the structural

Test	Purpose	Method	Acceptance Criteria	Results
	without damage. There is potential for the screw threads to generate wear particles during insertion, or during toggling during cyclic loading.	layer was used. The device was implanted following the surgical technique, and a 325 N load was applied at R = 10 at 5 Hz for 1 million cycles. Following testing, the test block and specimens were assessed for particulate generation, and high-resolution photographs of the sleeve were taken to assess if damage occurred to the device.	particles generated should be fully characterized.	integrity of the device. A total particulate measure of 0.12 ± 0.24 (range 0.005 to 0.661) mg of PET was recorded in the dynamically loaded samples, compared to 0.21 ± 0.23 (range 0.026 to 0.654) in the control group. Total particle count was different between groups, with an average of 3.26E4 ± 2.70E4 particles in the toggle group and 1.26E6 ± 1.64E6 in the control group.

PERFORMANCE TESTING - ANIMAL AND/OR CADAVER

The sponsor conducted and provided a total of four (4) animal studies to support safety and effectiveness of the subject device. Three of these studies were conducted in sheep metatarsals, and the fourth study was conducted in the sheep lumbar spine to evaluate vertebral pedicle screw fixation for spinal fusion. While the sponsor is not proposing any spinal indications or sleeve compatibility with pedicle screws in this submission, they included this animal study for further evaluation of bony response to PET in a load-bearing scenario.

The high-level protocol information for each of these animal studies is shown in the table below:

Table 4: Overview of Animal Studies

	Screw Model	Osteotomy Model	Osteotomy Model	Spine Model
Animal Model	Ovine Metatarsal	Ovine Metatarsal with Osteotomy	Ovine Metatarsal with Osteotomy	Ovine Lumbar Spine Fusion
Sample Size	10 Animals	4 Animals	18 Animals + 6 Cadaveric	54 Animals
Construct	Screw only (6 Cortical and 2 Cancellous screws per animal)	9-Hole Plate (7 Cortical and 2 Cancellous screws per plate)	9-Hole Plate (7 Cortical and 2 Cancellous screws per plate)	L2-L3 Fusion (4 pedicle screws and 2 rods)

	Screw Model	Osteotomy Model	Osteotomy Model	Spine Model
Cohorts	**Control**: Bone Screw (n=5) **Treatment:** Screws with OGmend® Implant System (n=5)	**Control**: Plate and Screw Alone (n=2) **Treatment**: Plate and Screw with OGmend® Implant System (n=2)	**Control**: Cadaveric Sheep (n=6) **Treatment**: Plate and Screw with OGmend® Implant System(n=18)	**Positive Control** (n = 18) **Negative Control** (n=18) **Treatment** (Negative Control with OGmend® Implant System, n= 18)

For the Spine model, the positive control consisted of a standard screw, in which a 4.5 mm screw was placed in a 3.5 mm pilot hole. The negative screw represented a "failed" screw, in which a 4.5 mm screw was placed in a 4.5 mm pilot hole. The treatment group were also prepared with a 4.5 mm pilot hole and 4.5 mm screw, however the OGmend® Implant System was used in conjunction with the screw. Data from the pivotal spine study was used in the final safety and efficacy determination. The sponsor provided assessment of six animals at 0, 12, and 24 weeks. The final determination of the safety and effectiveness of the device was based upon data generated by the Spine Model study. Data provided in the Spine Model Study used to determine the safety and efficacy of the device included:

- Axial Pullout force of screws at each time point to assess the fixation strength of the implant compared to controls.

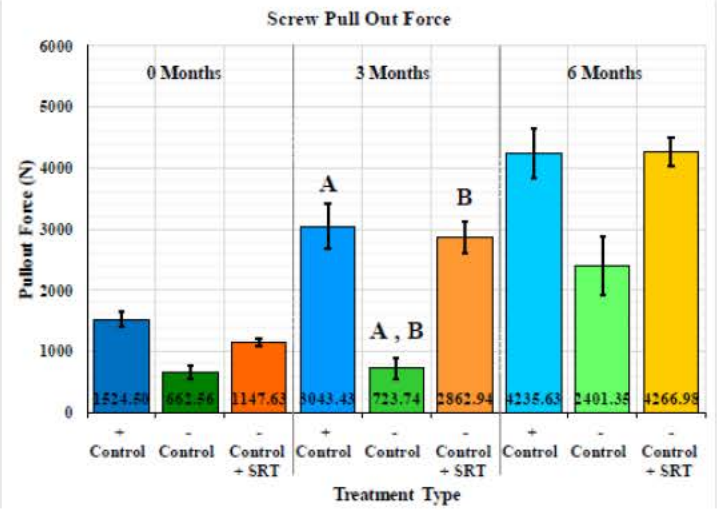


Figure 6: Screw pullout force test results. For this test, the OGmend® Implant System is labeled as "-Control + SRT". The +Control and -Control groups represent the positive and negative controls described above.

- Insertion Torque at the time of implantation, to validate bench models so as to ensure the sleeve does not excessively increase the torque needed in implant screws.

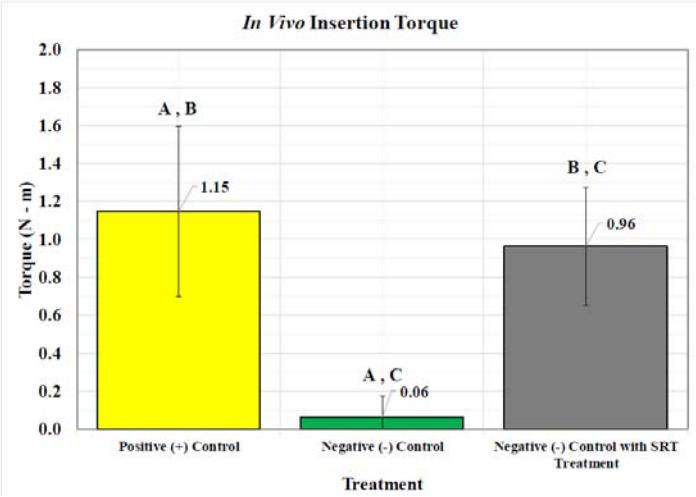


Figure 7: Insertion Torque results, measured at baseline

- Extraction Torque at each time point, to assess the stability of the implant over time compared to controls.

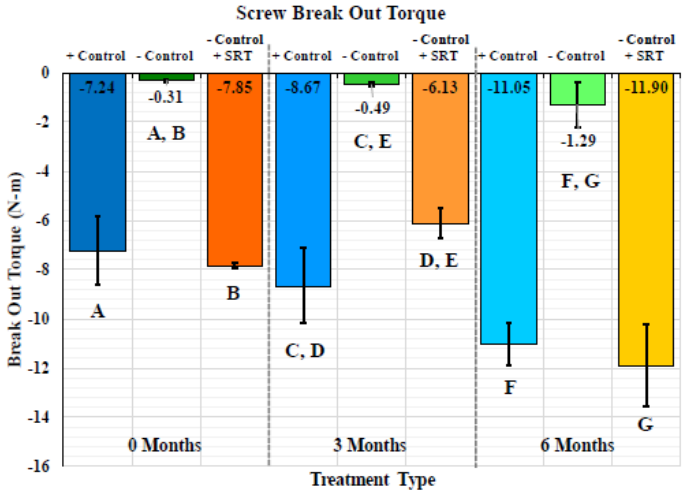


Figure 8: Extraction Torque results, measured at each time point

- Pullout Stiffness was measured at each time point, to assess the mechanical stability of the implant compared to controls.

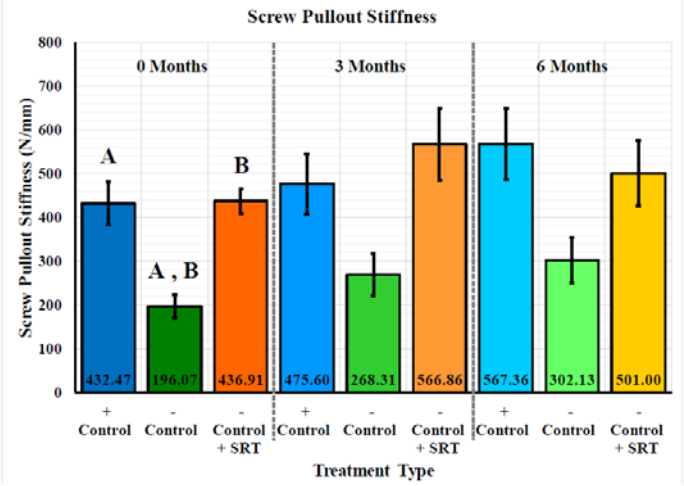


Figure 9: Pullout Stiffness data at each timepoint

- Kinematics of the fusion site to demonstrate that the device provided sufficient stability to allow for clinically relevant healing of the fusion site, as an analog for fusion of a fracture. Assessment included range of motion and bending stiffness in Flexion/Extension, Lateral bending, and Axial Rotation.

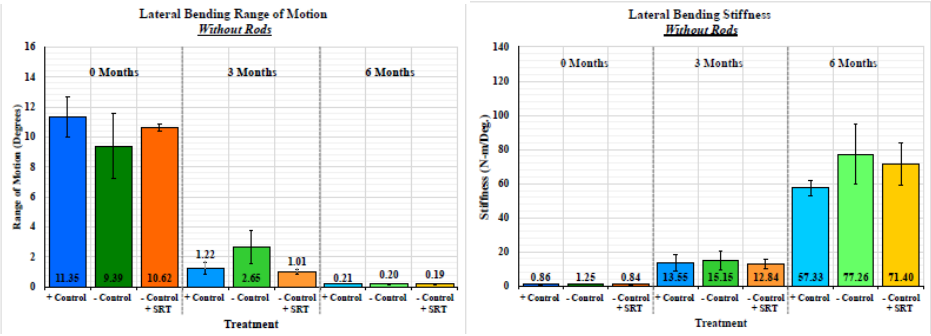


Figure 10: Lateral Bending Range of Motion, and Lateral Bending Stiffness results

- Histological, Histopathological, and Histromorphometric assessment of the tissue around the implant at each time point. This data was analyzed to determine if the implant or wear particles generated by the implant resulted in a negative biologic reaction which may be detrimental to the long-term health of the tissue.

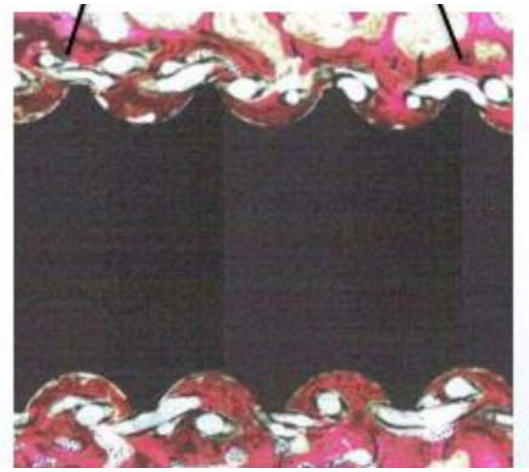


Figure 11: Example histology image of screw and OGmend® Implant System in the Ovine Spine at 24 weeks. Image above shows the bone screw (black) imbedded in bone (stained red). The OGmend® Implant System can be seen as the colorless fibers around the screw (black arrows).

- Radiographic review of the fusion site to confirm that fusion occurred.

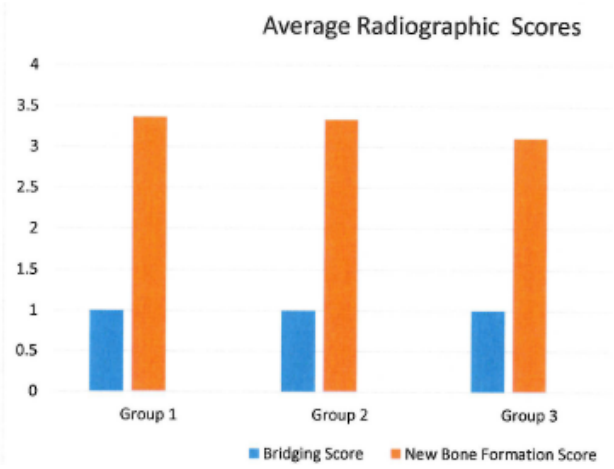


Figure 12: Results of radiographic assessment. Bridging score was an assessment of the percentage of bone bridge formed across the fusion site, with a score of 1 indicating the highest bridging (76-100%). Group 1 represents the Positive Control group, Group 2 represent the Negative Control group, and Group 3 represents the Treatment group (Negative Control plus the OGmend Implant System). New bone formation score was an assessment of the amount of bone formed, with a score of 4 representing the best score. There was no significant difference observed between groups.

Overall, it was determined that the data provided were sufficient to demonstrate that the device provided sufficient mechanical stability for healing, and that the observed biologic response at 12 and 24 weeks was not significant enough to cause long term adverse biological reaction.

LABELING

The safety and effectiveness of the device was evaluated with respect to the use with metallic plate and screw systems in long bones, and was not evaluated in conditions in which the sleeve crossed a fracture site. To clarify the use of the device with respect to the supporting data provided to demonstrate safety and effectiveness, the device labeling was revised to including the following:

- The device description states the material used for the implant (PET).
- The Indications for Use statement states the device is for use in skeletally mature patients.
- The device is contraindicated for patients with insufficient bone quality or quantity to permit stabilization of a plate and screw system.
- There is a warning that the device should not be used in stand-alone screw systems, joint arthroplasty systems, and spinal fixation procedures.
- There is a warning that the device should not be used with non-metallic or resorbable screws.
- While the material of the device is a pure polymer and contains no metallic components, and there are no safety concerns regarding the presence of the sleeve in a Magnetic Resonance (MR) environment, it is only intended to be used with metallic bone screws, and therefore the labeling includes precautions that the MR safety of the plates and screws should be considered.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with the use of a screw sleeve bone fixation device and the measures necessary to mitigate these risks.

Table 4: Identified Risks to Health and Mitigation Measures

Identified Risks to Health	**Mitigation Measures**
Loss of function / mechanical integrity resulting from: ▪ Device malposition ▪ Device breakage ▪ Damage to screw during insertion ▪ Deterioration due to aging ▪ Insufficient restoration of screw fixation	*In vivo* performance testing Non-clinical performance testing Shelf life testing Labeling
Revision	*In vivo* performance testing Non-clinical performance testing Labeling
Adverse tissue reaction	Biocompatibility evaluation

	In vivo performance testing Non-clinical performance testing Labeling
Infection	Sterilization validation Shelf life testing
Febrile response due to endotoxins	Pyrogenicity testing

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the screw sleeve bone fixation device is subject to the following special controls:

(1) *In vivo* performance testing under anticipated conditions of use must demonstrate:
   (i) The device provides sufficient stability to allow for fracture healing; and
   (ii) A lack of adverse biologic response to the implant through histopathological and histomorphometric assessment.
(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. Testing must:
   (i) Assess the stability of the device in a rescue screw scenario;
   (ii) Demonstrate that the device can be inserted and removed without damage to the implant or associated hardware;
   (iii) Demonstrate the device can withstand dynamic loading without device failure; and
   (iv) Characterize wear particle generation.
(3) The device must be demonstrated to be biocompatible.
(4) The device must be demonstrated to be non-pyrogenic.
(5) Performance data must demonstrate the sterility of the device.
(6) Performance data must support the labeled shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the established shelf life.
(7) Labeling must include:
   (i) A detailed summary of the device technical parameters;
   (ii) Information describing all materials of the device;
   (iii) Instructions for use, including device removal; and
   (iv) A shelf life.

BENEFIT-RISK DETERMINATION

The sponsor has collected adequate data to assess the safety profile of the subject device and has identified that there are benefits. The known or probable risks of the device include biologic responses to polymeric surgical implants, specifically polyethylene terephthalate implants, documented in the published literature or observed in the animal studies conducted for this device, as well as mechanical failure modes either anticipated or observed in the mechanical testing of the device as described above. While there was an ongoing foreign body reaction at the

final time point in the animal spine model study, it was determined that the degree of reaction would not lead to unacceptable risk to patients.

Patient Perspectives

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

Benefit/Risk Conclusion

In conclusion, given the available information above, the data support that for the following indications for use statement:

> The OGmend® Implant System is intended for use with screws as part of a fracture fixation plate system in long bones in rescue scenarios where the screw has lost purchase due to screw loosening, back out, or breakage and the stability of the overall construct is at risk. The OGmend® Implant System is for use in skeletally mature patients.

the probable benefits outweigh the probable risks for the OGmend® Implant System. The device provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the OGmend® Implant System is granted and the device is classified as follows:

> Product Code: QAC
> Device Type: Screw sleeve bone fixation device
> Regulation Number: 21 CFR 888.3043
> Class: II