

**DE NOVO CLASSIFICATION REQUEST FOR
ORTHOBOND MARINER PEDICLE SCREW SYSTEM**

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Spinal fusion device with quaternary ammonium compound coating. A spinal fusion device with quaternary ammonium compound coating is a rigid metallic implant device or system comprised of single or multiple components intended to facilitate fusion in skeletally mature patients. The device includes a quaternary ammonium compound coating that is covalently bonded to the device. Where applied, the coating is intended to reduce microbial contamination on the surface of the device prior to implantation. The device does not contain antimicrobial agents that act within or on the body and this device type does not include combination products.

NEW REGULATION NUMBER: 21 CFR 888.3071

CLASSIFICATION: Class II

PRODUCT CODE: QZY

BACKGROUND

DEVICE NAME: Orthobond Mariner Pedicle Screw System

SUBMISSION NUMBER: DEN220015

DATE DE NOVO RECEIVED: February 28, 2022

SPONSOR INFORMATION:

Orthobond Corporation
1 Deerpark Drive, Suite A
Monmouth Junction, New Jersey 08852

INDICATIONS FOR USE

The Orthobond Mariner Pedicle Screw System is indicated as follows:

The intended use of the Orthobond Mariner Pedicle Screw System in a posterior or anterolateral approach is to provide immobilization and stabilization of spinal segments in skeletally mature patients as an adjunct to fusion in the treatment of the following acute and chronic instabilities or deformities of the thoracic, lumbar, and sacral spine.

The indications for use are as follows:

- Degenerative disc disease (DDD) as defined by back pain of discogenic origin with degeneration of the disc confirmed by patient history and radiographic studies,
- Spondylolisthesis,
- Trauma (i.e., fracture or dislocation),
- Spinal stenosis,
- Deformities or curvatures (i.e., scoliosis, kyphosis, and/or lordosis),
- Spinal tumor,
- Pseudarthrosis, and/or
- Failed previous fusion.

The Orthobond coating is intended to reduce bacterial contamination prior to implantation resulting from deposition in the operating room on the surface of the device. The clinical impact associated with the Orthobond coating, including prevention of infection or reduction of infection risk in patients, has not been evaluated in human clinical trials. The Orthobond coating is not intended to treat existing infections and does not act within or on the body.

LIMITATIONS

The sale, distribution, and use of the Orthobond Mariner Pedicle Screw System are restricted to prescription use in accordance with 21 CFR 801.109.

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

DEVICE DESCRIPTION

The device is a pedicle screw system, with instrumentation for implantation and removal, intended for spinal fusion as shown in **Figure 1**. The Ti6Al4V ELI implants are coated with 12-Methacryloyloxydodecyl Pyridinium Bromide (MDPB), a type of quaternary ammonium compound, which is intended to reduce bacterial contamination on the surface of the implant prior to implantation which may occur from deposition in the operating environment. Based on in vitro testing, this coating may result in immobilization and/or lysis of some challenge organisms. The pedicle screw system is comprised of screws, rods, connectors, and hooks of various sizes. The instruments included in the Mariner Pedicle Screw System facilitate the placement, adjustment, final locking, and removal, if necessary, of the system implants, and accessories to the system include trays and caddies for storage, protection, and organization prior to and during the steam sterilization process.



Figure 1 - Orthobond Mariner Pedicle Screw System

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Orthobond Mariner Pedicle Screw System is manufactured from Ti6Al4V ELI coated with MDPB.

Biocompatibility evaluation on the subject implant device has been completed according to FDA's Guidance, "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process.'" Biocompatibility testing for the permanent implant included cytotoxicity (ISO 10993-5), intracutaneous reactivity (ISO 10993-10), sensitization (ISO 10993-10), material-mediated pyrogenicity (ISO 10993-11), acute systemic toxicity ISO 10993-11), genotoxicity (ISO 10993-3; bacterial reverse mutation assay, mouse lymphoma assay). All results and test methods were found acceptable.

A 26-week ovine study was conducted to evaluate systemic toxicity per ISO 10993-11:2017, and local implantation per ISO 10993-6:2016. The test articles did not produce systemic toxicological effects and resulted in minimal local tissue reactivity.

Chemical characterization with exhaustive extraction in polar, mid-polar, non-polar solvents, and under acidic (pH 4) conditions, was performed per ISO 10993-18 with toxicological risk assessment per ISO 10993-17 to evaluate extractables.

The instruments included in the Orthobond Mariner Pedicle Screw System are made from various materials with limited (less than 24 hour) contact to tissue/bone. The instruments were adequately evaluated for biocompatibility in prior marketing submissions.

STERILITY/PACKAGING AND SHELF-LIFE/PYROGENICITY

Sterility:

The Orthobond Mariner Pedicle Screw System is a single-use device provided clean and sterile to the end user. Gamma sterilization of the device has been validated to provide a Sterility Assurance Level (SAL) of 10^{-6} based on the VDMax^{17.5} method as recommended by FDA Recognized Consensus Standard series ANSI/AAMI/ISO 11137-1 (“Sterilization of health care products – Radiation – Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices”)/-2 (“Sterilization of health care products – Radiation – Part 2: Establishing the sterilization dose”).

Packaging and Shelf-Life:

Implants are packaged in a sterile Nylon pouch configuration consisting of an inner pouch, outer pouch, and pouch carton. The pouches are manufactured from multiple sealed, co-extruded layers of biaxially oriented Nylon/low density polyethylene/peelable sealant. Non-clinical performance testing established a shelf-life of 3 months. Antibacterial performance testing was evaluated over the proposed shelf-life.

Pyrogenicity:

Bacterial endotoxins testing was performed to determine whether the Orthobond Mariner Pedicle Screw System met pyrogen limit specifications. All tested devices passed with a reported value of less than or equal to 1 EU/device, meeting the recommended endotoxin limits per ANSI/AAMI ST72:2011 (“Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing”).

Reprocessing:

The instruments included in the Orthobond Mariner Pedicle Screw System are intended to be reprocessed. The reprocessing validation was evaluated in prior marketing submissions.

PERFORMANCE TESTING – BENCH

A summary of non-clinical mechanical performance evaluations is provided in **Table 1:**

Table 1: Summary of Non-clinical Mechanical Performance Evaluations

Test	Purpose	Method	Performance Criteria	Results
Static Compression Bending	Evaluate mechanical properties of the coated Spinal Fusion Device under Static	The device was tested under static compression bending until failure. The yield load and stiffness	Acceptable performance was determined to be equivalent in yield loads, stiffness values,	The tested device resulted in acceptable yield loads, stiffness values, and failure modes compared to

Test	Purpose	Method	Performance Criteria	Results
	Compression Bending Loading	values were compared to the untreated device. The test methodology is in accordance with ASTM F1717 ("Standard Test Methods for Spinal Implant Constructs in a Vertebrectomy Model").	and failure modes compared to the uncoated device.	the untreated device. Representative pre- and post-test images were provided along with the force-displacement graphs. The linear equations used to calculate stiffness was also provided.
Dynamic Compression Bending	Evaluate mechanical properties of the coated Spinal Fusion Device under Dynamic Compression Bending Loading	The device was tested under dynamic compression bending to (b)(4) cycles at 6 Hz. The run-out load and failure modes were compared to the untreated device. The test methodology is in accordance with ASTM F1717.	Acceptable performance was determined to be equivalent run-out load values and failure modes compared to the uncoated device.	The tested device attained acceptable run-out load and post-test dimensions. Mass loss measurements were provided under the applied load compared to the pre-test dimensions and mass. Representative pre- and post-test images were provided along with the cycle-displacement table.
Static Torsion	Evaluate mechanical properties of the coated Spinal Fusion Device under Static Torsion Loading	The device was tested under torsion until failure. The yield load and stiffness values were compared to the untreated device. The test methodology is in accordance with ASTM F1717.	Acceptable performance was determined to be equivalent yield loads, stiffness values, and failure modes compared to the uncoated device.	The tested device resulted in yield loads, stiffness values, and failure modes compared to the untreated device. Representative pre- and post-test images were provided along with the force-displacement graphs. The linear equations used to calculate stiffness was also provided.

Antimicrobial Performance:

The subject device's MDPB coating was evaluated for its antimicrobial performance based on a simulated use *in vitro* test method that demonstrated antibacterial activity. The subject device's MDPB coating was also evaluated for its antimicrobial resistance risk profile.

Information was provided establishing reasonable evidence to support the understanding that the antimicrobial action of the MDPB coating is neutralized in the body and would

not be expected to have meaningful antimicrobial activity in or on the body following implantation.

Corrosion Performance:

The subject device's corrosion performance was evaluated through dynamic compression bending in (b)(4)% PBS runout to (b)(4) million cycles at a load of (b)(4) N and frequency of (b)(4) Hz.

MDPB Coating Physicochemical Characterization:

The subject device's MDPB coating was characterized and evaluated for assessment of coating physicochemical properties such as coating chemistry, thickness, density, and uniformity. Information to establish these characteristics included a detailed description of the substrate morphology and coating process, a validated fluorescein method to determine the MDPB coating density on the surface of the subject device, micro-imaging and spectroscopy techniques to determine the coating thickness and elemental compositions, appropriate visual inspections to demonstrate sufficient uniformity of the MDPB coating on the surface of the subject device, and a final product release strategy containing appropriately established product specification and sampling plan. The sponsor demonstrated that the biocompatibility and antimicrobial performance testing are representative of worst-case performance of the subject device based on the coating characterization.

SUMMARY OF FUNCTIONAL ANIMAL STUDY

Study Objective: The purpose of the study was to demonstrate that MDPB surface treatment of a pedicle screw system does not affect the function of the device for spinal stabilization and fusion.

Study Design: The subject device and the uncoated Mariner Pedicle Screw System were implanted in a two-level posterior lumbar fusion model in skeletally mature sheep with sacrifice timepoints of 4, 12, and 26 weeks.

Study Endpoints: *In vivo* evaluations included radiographs and computed tomography (CT) imaging. *Ex vivo* evaluations included radiographs, manual palpation, destructive biomechanical pedicle screw pull-out testing, microCT analysis, histology, and histomorphometry.

Study Outcomes: CT, microCT, histopathology, and manual palpation assessments showed similar fusion rates between the two groups, the subject device and the uncoated Mariner Pedicle Screw System. Histology showed a decrease in reactivity over time.

Conclusion: Overall, there was progression of fusion over time for both groups with a lack of significant inflammatory response.

LABELING

The labeling consists of the following: device description, indications for use, instructions for use including surgical steps, principles of device operation, identification of device materials, intended levels of fixation, detailed removal instructions, contraindications, warnings, precautions, and a list of potential adverse effects. Furthermore, the sterile packaging includes a shelf-life for the device. The labeling meets the requirements of 21 CFR 801.109 for prescription devices.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a spinal fusion device with quaternary ammonium compound coating and the measures necessary to mitigate these risks.

Risks to Health	Mitigation Measures
Antimicrobial resistance	Antimicrobial resistance analysis
Implant failure leading to non-fusion or pain	Animal performance testing Non-clinical performance testing Labeling
Adverse tissue reaction	Biocompatibility evaluation Non-clinical performance testing Pyrogenicity testing
Infection	Non-clinical performance testing Sterilization validation Shelf life testing Reprocessing validation Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the spinal fusion device with quaternary ammonium compound coating is subject to the following special controls:

- (1) Animal performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The study must assess fusion, bone formation, and tissue response at relevant timepoints over the course of healing. Evaluation methods must include imaging, histology, histomorphometry, and biomechanical testing.
- (2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use and include the following:
 - (i) Evaluation of the static and dynamic mechanical performance of the implant;
 - (ii) Evaluation of fretting and corrosion;

- (iii) Evaluation of antimicrobial performance with clinically relevant microbial species; and
 - (iv) Coating characterization, including a detailed description of the coating process and evaluation of coating physiochemical properties, such as density, thickness, chemistry, and uniformity.
- (3) An analysis must be provided that identifies and evaluates any contribution to the development and spread of antimicrobial resistance.
 - (4) An analysis or information must be provided to support that the antimicrobial does not act within or on the body.
 - (5) The patient-contacting components of the device must be demonstrated to be biocompatible.
 - (6) Performance data must support the sterility and pyrogenicity of the device components intended to be provided sterile.
 - (7) Performance data must validate the reprocessing instructions for the reusable instrumentation to be used with the device.
 - (8) Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.
 - (9) Labeling must include the following:
 - (i) Identification of device materials;
 - (ii) Intended levels of fixation;
 - (iii) A shelf life; and
 - (iv) Detailed device removal instructions.

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 antimicrobial performance testing demonstrated a reduction of *in vitro* bacterial contamination as discussed in the non-clinical studies section. The risks to health, which include antimicrobial resistance, implant failure leading to non-fusion or pain, adverse tissue reaction, and infection have been mitigated by various animal and benchtop non-clinical studies outlined in the section above. In conclusion, the benefits of using the subject device for its intended use/indications for use outweigh the risks to health.

BENEFITS: The probable primary benefit of the subject device is to provide immediate fixation and stabilization of the spine as an adjunct to fusion. Secondly, as demonstrated by the pre-clinical evaluations described above, the subject device reduced bacterial contamination on the surface of the device under specific *in vitro* test methods. Bacterial contamination may occur from deposition in the operating environment prior to implantation.

RISKS: The risks of the subject device, listed in the Risks to Health section above, are antimicrobial resistance, implant failure leading to non-fusion or pain, adverse tissue reaction, and infection. These risks have been mitigated by the listed pre-clinical Mitigation Measures above, which include animal performance testing, biocompatibility evaluation, non-clinical performance testing, pyrogenicity testing, reprocessing validation, sterilization validation, shelf-life validation, and labeling.

To address potential safety concerns related to the MDPB coating stability and effect in humans, a 522 Order for a Postmarket Surveillance Study will be issued for this device.

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, for the following indication statement:

The intended use of the Orthobond Mariner Pedicle Screw System in a posterior or anterolateral approach is to provide immobilization and stabilization of spinal segments in skeletally mature patients as an adjunct to fusion in the treatment of the following acute and chronic instabilities or deformities of the thoracic, lumbar, and sacral spine.

The indications for use are as follows:

- Degenerative disc disease (DDD) as defined by back pain of discogenic origin with degeneration of the disc confirmed by patient history and radiographic studies,
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- Pseudarthrosis, and/or
- Failed previous fusion.

The Orthobond coating is intended to reduce bacterial contamination prior to implantation on the surface of the device which may occur from deposition in the operating environment. The clinical impact associated with the Orthobond coating, including prevention of infection or reduction of infection risk in patients, has not been evaluated in human clinical trials. The Orthobond coating is not intended to treat existing infections and does not act within or on the body.

The probable benefits outweigh the probable risks for the Orthobond Mariner Pedicle Screw 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 Orthobond Mariner Pedicle Screw System is granted and the device is classified as follows:

Product Code: QZY

Device Type: Spinal fusion device with quaternary ammonium compound coating

Regulation Number: 21 CFR 888.3071

Class: II