Class II Special Controls Guidance Document: Resorbable Calcium Salt Bone Void Filler Device; Draft Guidance for Industry and FDA

Draft Guidance – Not for Implementation

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Restorative Devices Branch
Division of General, Restorative, and Neurological Devices
Office of Device Evaluation

Preface

Public Comment

For 90 days following the date of publication in the Federal Register of the notice announcing the availability of this guidance, comments and suggestions regarding this document should be submitted to the Docket No. assigned to that notice, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852.

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This document is intended to provideguidance. It represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind the Food and Drug Administration (FDA) or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations.

Background

This guidance document was developed as a special controls guidance to support the classification of the resorbable calcium salt bone void filler device into class II. This guidance will be issued in conjunction with a Federal Register notice proposing to classify this device type. This guidance is issued for comment purposes only. If a final rule to classify this device type is not issued, this guidance document will not be issued as a special control.

FDA believes that special controls, when combined with the general controls, will be sufficient to provide reasonable assurance of the safety and effectiveness of the resorbable calcium salt bone void filler device. If the device is classified into class II, a manufacturer who intends to market a device of this generic type must (1) conform with the general controls of the Food, Drug & Cosmetic Act, including the 510(k) requirements described in 21 CFR 807.81, (2) address the specific risks to health associated with the resorbable calcium salt bone void tiller device, and (3) receive a substantial equivalence determination from FDA prior to marketing the device.

This special control guidance document identifies the risks to health and serves as the special control that, when followed and combined with the general controls, will generally address the risks associated with this generic device type. It is not intended to address general or specific requirements of a 5 1 O(k).

Scope

FDA identifies this generic type of device as a physical medicine device classified under 21 CFR 888.XXXX (to be determined), product code MVQ. A resorbable calcium salt bone void filler device is a resorbable implant intended to fill bony voids or gaps caused by trauma or surgery that are not intrinsic to the stability of the bony structure.

Risks to Health

FDA has identified the following risks to health associated with the use of the resorbable calcium salt bone void filler device:

1. infection of the soft tissue and/or bone (osteomyelitis) and fever
2. adverse tissue reaction
3. transient hypercalcemia
4. incomplete bone ingrowth, delayed union, and non-union
5. fracture of the newly formed bone
6. disease transmission and undesirable immune response associated with use of a device material derived from a biological source

Controls

FDA believes that the controls below, when combined with general controls, will address the above identified risks to health associated with the use of the device. Manufacturers should demonstrate that their device complies with either the specific recommendations of this guidance or with an alternate means to address the above identified risks to health and to provide reasonable assurance of the safety and effectiveness of the device.

Manufacturers who reference recognized standards as part of their 5 1 O(k) submission should provide statements regarding conformance or "Declarations of Conformity" under the FDA Modernization Act of 1997. Because statements afford greater flexibility for device developers than "Declarations of Conformity," submitters of 5 1 0(k)s should consider using guidance documents and consensus standards in this manner. For information regarding declarations of conformity, refer to FDA's "Guidance on Recognition and Use of Consensus Standards," which is available on our website at http://www.fda.gov/cdrh/modact/k982.html.

1. FDA Guidance Documents

a. "510(k) Sterility Review Guidance K90-1" dated 2/12/90

b. "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part I: Evaluation and Testing"'

2. Voluntary Consensus Standards

United States Pharmacopoeia (U.S.P.) official monographs or American Society for Testing and Materials (ASTM) standards for the specification of the chemical composition of the calcium salt should be considered. Examples of voluntary consensus standards that may be used, depending on the specific calcium salt, include:

a. U.S.P. National Formulary (NF) "Official Monograph for Calcium Sulfate"

b. ASTM F1185-88, "Standard Specification for Composition of Ceramic Hydroxylapatite for Surgical Implants"

3. Material Characterization - Calcium Salt

a. Chemical Composition:

(1) For calcium carbonate or calcium sulfate salts, X-ray diffraction (XRD) testing and Fourier transform infrared spectroscopy (FTIR) should be provided.

(2) The specific crystal structure of each crystalline compound present in the calcium salt and the percentage of each compound based on the XRD spectra should be identified. The percentage of total crystalline material should also be identified.

(3) For calcium phosphate salts, data confirming the phase(s) of the material and the calcium-to-phosphate ratio should be provided. If the calcium phosphate salt is a mixed phase system, XRD and FTIR should be used to quantify the relative contributions of the components.

(4) The XRD spectra requested above should be presented along with individually superimposed standards as given for the relevant calcium salt in the powder diffraction files of the JCPDS (Joint Committee on Powder Diffraction Standards).

b. Physical Properties:

The following physical property data should be provided:

(1) Porosity (surface, internal and interconnectivity) characterization

(2) Size, shape, and surface area specifications

(3) Mass to volume ratio measurements (i.e., relative mass of calcium salt per unit volume of bone void)

4. Material Characterization – Biological Source Material

a. For a calcium salt or calcium salt additive derived from a biological source, e.g., either animal or human tissue, reasonable assurance that the implant material has been appropriately sourced, adequately processed (i.e., for inactivation of viruses, bacteria, and fungi), and immunologically inactivated should be provided.

b. Information on sourcing and processing of any component from a biological source should be provided.

5. Performance Testing

a. The following performance tests should be performed on final, sterilized devices and should simulate the intended clinical use environment:

(1) pH measurements

(2) *In vitro* solubility and dissolution testing

(3) Setting reaction temperature, if the calcium salt is intended to set *in vivo*

b. Animal testing to evaluate bone formation, device resorption and the biomechanical properties of the newly formed bone over the time required for complete resorption of the device material may be necessary. Radiographic and histomorphometric analysis should be used to evaluate bone formation and device resorption. Appropriate biomechanical testing (e.g., torsion or three-point bending tests) should be used to characterize the strength of the newly formed bone.

6. Instructions for Use

Instructions for use should include adequate information (contraindications, warnings, and precautions) to address the identified risks to health.

The following is a description of how the controls above address the identified risks to health:

(1) Adherence to the FDA guidance documents will help to:
- assure that the device is safe for long-term implantation;
- control the risk of infection by assuring that only a sterile device is implanted,
- minimize the additional risk of eliciting a fever response; and
- assure that only a biocompatible material is used.

(2) Adherence to the voluntary consensus standards will help to assure that a material with appropriate composition and purity is used.

(3) Adherence to the material characterization controls will help to:
- assure that the device has appropriate physicochemical properties for bone ingrowth and device resorption; and
- control the risks of disease transmission, including virus transmission, and an undesirable immune response associated with the implantation of a calcium salt or calcium salt additive derived from a biological source, e.g., either animal or human bone, that is inadequately deproteinated or immunologically inactived.

(4) Adherence to the performance testing will help to:
- assure that implantation of the material permits an adequate environment for bony ingrowth and that its dissolution properties are as intended;
- assure that a calcium salt intended to set *in vivo* will not result in a temperature increase that may cause tissue necrosis; and
- assure that use of the device results in adequate bone formation and material resorption, and the formation of bone that is sufficiently strong.

(5) Adherence to our recommendations for the instructions for use will help to ensure that the appropriate patients are treated and that the device is prepared correctly and used as intended.