

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 872

DDM

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Certifier A. Corbun

[Docket No. 2002P-0520]

**Dental Devices; Tricalcium Phosphate Granules and Other Bone Grafting  
Material for Dental Bone Repair**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Proposed rule.

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**SUMMARY:** The Food and Drug Administration (FDA) is proposing to reclassify tricalcium phosphate (TCP) granules for dental bone repair from class III to class II (special controls); classify into class II (special controls) all other bone grafting material for dental indications, except those that contain drug or biologic components; and revise the classification name and identification of the device. Bone grafting materials that contain a drug or biologic component would remain in class III. The proposed classification identification includes materials such as hydroxyapatite, demineralized bone additives, collagen, and polylactic acids. After considering public comments on the proposed reclassification and classification, FDA will publish a final regulation, if appropriate. This action is being taken to establish sufficient regulatory controls that will provide reasonable assurance of the safety and effectiveness of this device. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice of availability of a draft guidance document that the agency proposes to use as a special control for the device.

**DATES:** Submit written or electronic comments by [*insert date 90 days after date of publication in the Federal Register*]. See section VI of this document for the proposed effective date of a final rule based on this document.

**ADDRESSES:** You may submit comments, identified by Docket No. 2002P-0520, by any of the following methods:

- Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.
- Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow the instructions for submitting comments on the agency Web site.
- E-mail: *fdadockets@oc.fda.gov*. Include Docket No. 2002P-0520 in the subject line of your e-mail message.
- FAX: 301-827-6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions]:  
Division of Dockets Management, 5630 Fishers Lane, rm. 1061,  
Rockville, MD 20852.

*Instructions:* All submissions received must include the agency name and Docket No. or Regulatory Information Number (RIN) for this rulemaking. All comments received will be posted without change to *http://www.fda.gov/dockets/ecomments*, including any personal information provided. For detailed instructions on submitting comments and additional information on the rulemaking process, see the “Comments” heading of the **SUPPLEMENTARY INFORMATION** section of this document.

*Docket:* For access to the docket to read background documents or comments received, go to *http://www.fda.gov/dockets/ecomments* and/or the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Michael E. Adjodha, Center for Devices and Radiological Health (HFZ-480), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850; 301-827-5283; e-mail: *mea@cdrh.fda.gov*.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

The Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 301 *et seq.*), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Public Law 94-295), the Safe Medical Devices Act of 1990 (Public Law 101-629), the Food and Drug Administration Modernization Act of 1997 (Public Law 105-115), and the Medical Device User Fee and Modernization Act of 2002 (Public Law 107-250) established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), generally referred to as preamendments devices, are classified after the following requirements are met: (1) FDA has received a recommendation from a device classification panel (an FDA advisory committee); (2) FDA has published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) FDA has published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Under section 520(l) of the act (21 U.S.C. 360j(l)), devices formerly regulated as new drugs are automatically classified into class III, unless the Secretary of Health and Human Services, in response to a reclassification petition, has classified the device into class I or II.

## **II. Recommendation of the Panel**

### *A. Identification of the Device*

In the **Federal Register** of August 12, 1987 (52 FR 30082), FDA issued a final rule codifying the classification of “tricalcium phosphate for dental bone repair” as a class III device under the 1976 amendments. At that time, FDA was not aware that bone grafting material, other than TCP, was a preamendments device and inadvertently omitted classifying it. Consistent with the act and regulations, FDA has since consulted with the Dental Products Advisory Panel (the panel), an FDA advisory committee, regarding classification of this device.

On November 12, 2002, Bicon, Inc., Boston, MA, submitted a petition to FDA to reclassify beta-tricalcium phosphate for dental indications from “Class III to Class Unclassified” (Ref. 1). On December 9, 2002, the petitioner amended its petition to make clear that it was requesting that FDA reclassify beta-tricalcium phosphate from class III to class II. Beta-tricalcium phosphate and all other forms of tricalcium phosphate for dental bone repair, including alpha and amorphous forms, are transitional devices and are currently regulated as class III devices under 21 CFR 872.3930, “Tricalcium phosphate granules for dental bone repair,” requiring premarket approval. Consistent with section 520(l)(2) the act and the regulations in 21 CFR 860.136, FDA consulted with the panel regarding reclassification of this device.

Other bone grafting materials in the form of synthetic hard tissue replacements have been used in dentistry since the 1970s (Ref. 2). Because they were inadvertently omitted from the August 12, 1987, final rule classifying most dental devices, these other bone grafting materials are unclassified preamendments devices. Although unclassified, they are nevertheless subject to general controls, such as premarket notification. TCP and other bone grafting materials share the same indications, risks, and recommended mitigation measures.

FDA believes that one classification identification that encompasses all bone grafting materials for dental indications would provide a more scientifically accurate and more administratively transparent regulation for these materials. Therefore, FDA is identifying bone grafting material as a naturally or synthetically derived material, such as hydroxyapatite, tricalcium phosphate, demineralized bone additives, collagen, or polylactic acids, that is intended to fill, augment, or reconstruct periodontal or bony defects of the oral and maxillofacial region.

#### *B. Recommended Classification of the Panel*

At the meeting of the Dental Products Advisory Panel held on May 22, 2003, the panel voted five to zero (with no abstentions) to recommend that TCP for dental indications be reclassified from class III to class II (special controls). The panel considered all forms of TCP, including beta-tricalcium phosphate, and concluded that special controls, in addition to general controls, would provide reasonable assurance of the safety and effectiveness of these bone grafting materials devices (Ref. 3).

In addition, on August 8 and 9, 1995, in accordance with the procedures set forth in 21 CFR 860.84, the panel considered classification of the non-TCP

materials. The panel recommended unanimously that non-TCP bone grafting materials be classified into class II, except when intended to be used alone in filling or repair of bony defects and/or augmentation of the alveolar ridge. For that indication, the panel recommended placing the device in class III, but with a low priority for establishing an effective date for the requirement for premarket approval (Ref. 4).

#### *C. Summary of Reasons for the Recommendation*

For TCP for dental indications and for bone grafting materials for certain dental indications, the panel believed that special controls, in addition to general controls, would provide reasonable assurance of the safety and effectiveness of these devices and that there is sufficient information to establish special controls to provide such assurance.

The panel recommended that TCP should remain in class III when used alone in filling or repair of bony defects and/or augmentation of the alveolar ridge because they believed that the materials present risks to health that cannot be addressed by special controls.

#### *D. Summary of the Data for the Recommendation*

For TCP for dental indications, the panel based its recommendation on the information provided by the petitioner and FDA, the presentations made by stakeholders and FDA at the panel meeting, the open discussion during the panel meeting, and the panel members' personal knowledge of and clinical experience with the device (Ref. 5). The panel did not discuss bone grafting materials containing a drug or biologic component.

For non-TCP materials, the panel based its recommendation on the information provided by FDA, presentations made by stakeholders who marketed bone filling and augmentation devices, the open discussion during

the panel meeting, and the panel members' personal knowledge of and clinical experience with the device.

### **III. Risks to Health**

The panel identified the following risks to health associated with bone grafting material: Ineffective bone formation, adverse tissue reaction, infection, and improper use.

#### *A. Ineffective Bone Formation*

The quality and physical properties of bone grafting material may be insufficient to support the required loads and lead to device failure. Device failure may result in ineffective treatment, revision, and permanent impairment for the patient.

#### *B. Adverse Tissue Reaction*

Inadequate biocompatibility of any of the components contained in bone grafting material may result in adverse tissue reaction and presents the potential for surgical revision (i.e., reoperation).

#### *C. Infection*

Implantation of an improperly sterilized device may result in an infection. Infection may result in revision or explantation of the device, which presents the potential for permanent impairment.

#### *D. Improper Use*

Inadequate labeling may result in improper use. Improper use may result in ineffective treatment and may cause permanent impairment.

### **IV. Proposed Rule**

FDA believes that bone grafting material that does not contain a drug or biologic component should be classified into class II and that TCP should be

reclassified into class II because special controls, in addition to general controls, would provide reasonable assurance of the safety and effectiveness of the device, and there is sufficient information to establish special controls to provide such assurance.

FDA disagrees with the (1995) panel's recommendation that bone grafting materials should remain in class III when used alone in filling or repair of bony defects and/or augmentation of the alveolar ridge. FDA believes that when used for these indications, the risks to health can be addressed by special controls and that all of these bone grafting material devices share the same risks and recommended mitigation measures. Accordingly, FDA has developed the draft guidance document entitled "Class II Special Controls Guidance Document: Dental Bone Grafting Material" to serve as the special control for TCP and other bone grafting material devices for dental indications. As noted previously, bone grafting material that contains a drug or biologic component would remain in class III and the special control guidance document would not apply.

## **V. Proposed Special Control**

FDA believes that the special controls guidance document entitled "Class II Special Controls Guidance Document: Dental Bone Grafting Material," in addition to general controls, can address the risks to health described in section III of this document. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of the draft guidance document.

If adopted, following the effective date of a final rule reclassifying and classifying the device, any firm submitting a 510(k) premarket notification for the device would need to address the issues covered in the special control guidance. However, the firm would need to show only that its device meets

the recommendations of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

The special controls guidance document contains recommendations with regard to the information and testing that should be included in a premarket notification. The guidance document addresses the following topics: Characterization, biocompatibility, sterilization, and labeling. Adequate characterization of the composition, physical properties, and in vivo performance can address the risk of ineffective bone formation. Adequate biocompatibility can address the risk of adverse tissue reaction. Sterilization can address the risk of infection, and labeling can address the risk of improper use.

The agency is not proposing to exempt this device from the premarket notification requirements of the act, as permitted by section 510(m) of the act (21 U.S.C. 360(m)). FDA believes that it needs to review information in a premarket notification submission that addresses the risks identified in the guidance document in order to assure that a new device is at least as safe and effective as legally marketed devices of this type.

## **VI. Effective Date**

FDA proposes that any final rule that may issue based on this proposal become effective 30 days after its date of publication in the **Federal Register**.

## **VII. Environmental Impact**

The agency has determined under 21 CFR 25.34(b) that this proposed classification is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, as categorically excluded, neither an environmental assessment nor an environmental impact statement is required.

## VIII. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is not a significant regulatory action as defined by the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Manufacturers of the preamendments devices that FDA is reclassifying are being relieved of the burden of eventually submitting a premarket approval application. Manufacturers of these devices are already subject to the premarket notification requirements. FDA has designated a guidance document as the special control. FDA believes that manufacturers, including small manufacturers, are already substantially in compliance with the recommendations in the guidance document, and they will not need to submit substantially more information in their premarket notification submissions in order to meet the recommendations in the guidance document or otherwise provide reasonable assurances of safety and effectiveness. FDA believes that any regulation based on this proposed rule will impose no significant economic impact on any small entities. The agency, therefore, certifies that this proposed rule will not have a significant impact on a substantial number of small entities. In addition, it will not impose costs of \$100 million or more

on either the private sector or State, local, and tribal governments in the aggregate, and therefore, a summary statement or analysis under section 202(a) of the Unfunded Mandates Reform Act of 1995 is not required.

#### **IX. Paperwork Reduction Act of 1995**

FDA tentatively concludes that this proposed rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520) is not required.

#### **X. Comments**

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

#### **XI. References**

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Petition from Bicon, Inc., Boston, MA to FDA, November 12, 2002.
2. Le Geros, R. Z., "Calcium Phosphate Materials in Restorative Dentistry: A Review," *Advances in Dental Research*, vol. 2, pp. 164–180, 1988.
3. Dental Products Panel of the Medical Devices Advisory Committee, meeting transcript, May 22, 2003.
4. Dental Products Panel of the Medical Devices Advisory Committee, meeting transcript, August 8 and 9, 1995.

5. Dental Products Panel of the Medical Devices Advisory Committee, information package, May 22, 2003.

### List of Subjects in 21 CFR Part 872

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 872 be amended in subpart D as follows:

### PART 872—DENTAL DEVICES

1. The authority citation for 21 CFR Part 872 continues to read as follows:

**Authority:** 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Section 872.3930 is revised to read as follows:

#### **§ 872.3930 Bone grafting material.**

(a) *Identification.* Bone grafting material is a naturally or synthetically derived material, such as hydroxyapatite, tricalcium phosphate, demineralized bone additives, collagen, or polylactic acids, that is intended to fill, augment, or reconstruct periodontal or bony defects of the oral and maxillofacial region.

(b) *Classification.* (1) Class II (special controls) if it contains no drug or biologic component. The special control for bone grafting materials that do not contain a drug or biologic component is FDA's "Class II Special Controls Guidance Document: Dental Bone Grafting Material." (See § 872.1(e) for the availability of this guidance document.)

(2) Class III (premarket approval) if it contains a drug or biologic component. Bone grafting materials that contain a drug or biologic component, such as biological response modifiers, require premarket approval.

(c) *Date PMA or notice of PDP is required.* For devices described in paragraph (b)(2) of this section, no effective date has been established for the requirement of premarket approval. (See § 872.3).

Dated: 5/4/04  
May 4, 2004.

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