policies and procedures that establish uniform and objective standards to determine the need and amount of supplemental collateral or other credit enhancements that each OFI shall provide as a condition for obtaining funding, discount and other similar financial assistance from such Farm Credit bank.

(2) The amount, type, and quality of supplemental collateral or other credit enhancements required for each OFI shall be established in the general financing agreement and shall be proportional to the level of risk that the OFI poses to the Farm Credit Bank or agricultural credit bank.

§ 614.4580 Limitation on the extension of funding, discount and other similar financial assistance to an OFI.

(a) No obligation shall be purchased from or discounted for and no loan shall be made or other similar financial assistance extended by a Farm Credit Bank or agricultural credit bank to an OFI if the amount of such obligation added to the aggregate liabilities of such OFI, whether direct or contingent (other than bona fide deposit liabilities), exceeds 10 times the paid-in and unimpaired capital and surplus of such OFI or the amount of such liabilities permitted under the laws of the jurisdiction creating such OFI, whichever is less.

(b) It shall be unlawful for any national bank that is indebted to any Farm Credit Bank or agricultural credit bank, on paper discounted or purchased, to incur any additional indebtedness, if by virtue of such additional indebtedness its aggregate liabilities, direct or contingent, will exceed the limitation described in paragraph (a) of this section.

§ 614.4590 Equitable treatment of OFIs and Farm Credit System associations.

(a) Each Farm Credit Bank and agricultural credit bank shall apply similar objective credit underwriting standards to both OFIs and Farm Credit System direct lender associations.

(b) The total charges that a Farm Credit Bank or agricultural credit bank assesses an OFI through capitalization requirements, interest rates, and fees shall be comparable to the charges that the same Farm Credit bank imposes on its direct lender associations. Any variation between the overall funding costs that OFIs and direct lender associations are charged by the same funding bank shall result from differences in credit risk and administrative costs to the Farm Credit Bank or agricultural credit bank.

§ 614.4600 Insolvency of an OFI.

If an OFI that is indebted to a Farm Credit Bank or agricultural credit bank becomes insolvent, is in process of liquidation, or fails to service its loans properly, the Farm Credit Bank or agricultural credit bank may take over such loans and other assets that the OFI pledged as collateral. Once the Farm Credit Bank or agricultural credit bank exercises its remedies, it shall have the authority to make additional advances, to grant renewals and extensions, and to take such other actions as may be necessary to collect and service loans to the OFI's borrower. The funding Farm Credit bank may also liquidate the OFI's loans and other assets in order to achieve repayment of the debt.

PART 620—DISCLOSURE TO SHAREHOLDERS

6. The authority citation for part 620 continues to read as follows:

Authority: Secs. 5.17, 5.19, 8.11 of the Farm Credit Act (12 U.S.C. 2252, 2254, 2279aa–11); sec. 424 of Pub. L. 100–233, 101 Stat. 1568, 1656.

Subpart B—Annual Report to Shareholders

§ 620.5 [Amended]

7. Section 620.5 is amended by removing the words '', as defined in § 614.4540(e) of this chapter,'' and by removing the word ''financial'' and adding in its place the word ''financing'' in paragraph (a)(8).

PART 630—DISCLOSURE TO INVESTORS IN SYSTEMWIDE AND CONSOLIDATED BANK DEBT OBLIGATIONS OF THE FARM CREDIT SYSTEM

8. The authority citation for part 630 continues to read as follows:

Authority: Secs. 5.17, 5.19 of the Farm Credit Act (12 U.S.C. 2252, 2254).

Subpart B—Annual Report to Investors

§ 630.20 [Amended]

9. Section 630.20 is amended by removing the words '', as defined in § 614.4540(e) of this chapter,'' in paragraph (a)(1)(v).

Dated: July 14, 1997.

Floyd Fithian,

Secretary, Farm Credit Administration Board.

[FR Doc. 97–18827 Filed 7–16–97; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 872

[Docket No. 97N–0239]

Dental Devices; Effective Date of Requirement for Premarket Approval; Temporomandibular Joint Prostheses

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule; opportunity to request a change in classification.

SUMMARY: The Food and Drug Administration (FDA) is proposing to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the total temporomandibular joint (TMJ) prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis, and the interarticular disc prosthesis (interpositional implant). The agency is also summarizing its proposed findings regarding the degree of risk of illness or injury intended to be eliminated or reduced by requiring the devices to meet the statute's approval requirements as well as the benefits to the public from the use of the devices. In addition, FDA is announcing the opportunity for interested persons to request the agency to change the classification of the devices based on new information.

DATES: Submit written comments by October 15, 1997; requests for a change in classification by August 1, 1997. FDA intends that if a final rule based on this proposed rule is issued, PMA's or notices of completion of PDP's will be required to be submitted within 90 days of the effective date of the final rule.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Mary S. Runner, Center for Devices and Radiological Health (HFZ–480), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–827–5283.

SUPPLEMENTARY INFORMATION:

I. Background

Section 513 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c) requires the classification of medical devices into one of three regulatory classes: Class I (general controls), class II (special controls), and class III (premarket approval).

Generally, devices that were on the market before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976 (the 1976 amendments) (Pub. L. 94–295), and devices marketed on or after that date that are substantially equivalent to such devices, have been classified by FDA. For the sake of convenience, this preamble refers to the devices that were on the market before May 28, 1976, and the substantially equivalent devices that were marketed on or after that date as ''preamendments devices.''

Section 515(b)(1) of the act (21 U.S.C. 360e(b)(1)) establishes the requirement that a preamendments device that FDA has classified into class III is subject to premarket approval. A preamendments class III device may be commercially distributed without an approved PMA or notice of completion of a PDP until 90 days after FDA issues a final rule requiring premarket approval for the device, or 30 months after final classification of the device under section 513 of the act, whichever is later. Also, a preamendments device subject to the rulemaking procedure under section 515(b) of the act, is not required to have an approved investigational device exemption (IDE) (part 812 (21 CFR part 812)) contemporaneous with its interstate distribution until the date identified by FDA in the final rule requiring the submission of a PMA or a PDP for the device. At that time, an IDE must be submitted only if a PMA has not been submitted or a PDP completed.

Section 515(b)(2)(A) of the act provides that a proceeding to issue a final rule to require premarket approval shall be initiated by publication of a notice of proposed findings rulemaking containing: (1) The proposed rule, (2) proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved PMA or a declared completed PDP and the benefit to the public from the use of the device, (3) an opportunity for the submission of comments on the proposed rule and the proposed findings, and (4) an opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

Section 515(b)(2)(B) of the act provides that if FDA receives a request for a change in the classification of the device within 15 days of the publication of the notice, FDA shall, within 60 days of the publication of the notice, consult with the appropriate FDA advisory committee and publish a notice denying the request for change of classification or announcing its intent to initiate a proceeding to reclassify the device under section 513(e) of the act. If FDA does not initiate such a proceeding, section 515(b)(3) of the act provides that FDA shall, after the close of the comment period on the proposed rule and consideration of any comments received, issue a final rule to require premarket approval, or publish a notice terminating the proceeding. If FDA terminates the proceeding, FDA is required to initiate reclassification of the device under section 513(e) of the act, unless the reason for termination is that the device is a banned device under section 516 of the act (21 U.S.C. 360f).

If a proposed rule to require premarket approval for a preamendments device is made final, section 501(f)(2)(B) of the act (21 U.S.C. 351(f)(2)(B)) requires that a PMA or a notice of completion of a PDP for any such device be filed within 90 days of the date of issuance of the final rule or 30 months after final classification of the device under section 513 of the act, whichever is later. If a PMA or a notice of completion of a PDP is not filed by the later of the two dates, commercial distribution of the device is required to cease. The device may, however, be distributed for investigational use if the manufacturer, importer, or other sponsor of the device complies with the IDE regulations. If a PMA or a notice of completion of a PDP is not filed by the later of the two dates, and no IDE is in effect, the device is deemed to be adulterated within the meaning of section 501(f)(1)(A) of the act, and subject to seizure and condemnation under section 304 of the act (21 U.S.C. 334) if its distribution continues. Shipment of the device in interstate commerce will be subject to injunction under section 302 of the act (21 U.S.C. 332), and the individuals responsible for such shipment will be subject to prosecution under section 303 of the act (21 U.S.C. 333). In the past, FDA has requested that manufacturers take action to prevent the further use of devices for which no PMA has been filed and may determine that such a request is appropriate for total TMJ prostheses, glenoid fossa prostheses, mandibular condyle prostheses, and interarticular disc prostheses (interpositional implants).

The act does not permit an extension of the 90–day period after issuance of a final rule within which an application or a notice is required to be filed. The House Report on the amendments states that ''the thirty month 'grace period' afforded after classification of a device into class III * * * is sufficient time for manufacturers and importers to develop the data and conduct the investigations necessary to support an application for premarket approval'' (H. Rept. 94–853; 94th Cong., 2d sess. 42 (1976)).

A. Classification of Total TMJ Prostheses, Glenoid Fossa Prostheses, Mandibular Condyle Prostheses and Interarticular Disc Prostheses (Interpositional Implants)

In the **Federal Register** of December 20, 1994 (59 FR 65475), FDA issued a final rule classifying the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis, and the interarticular disc prosthesis (interpositional implant) into class III. The preamble to the proposal to classify these devices (57 FR 43165, September 18, 1992) included the recommendation of the Dental Products Panel (the Panel), an FDA advisory committee, which met on April 21, 1989, regarding the classification of the devices (Ref. 1), in particular, the total TMJ prosthesis and the interarticular disc prosthesis (interpositional implant). The preamble to the reproposed rule to classify the glenoid fossa prosthesis and the mandibular condyle prosthesis (59 FR 6935, February 14, 1994) included the recommendation of the panel that reconvened on February 11, 1993, (Ref. 2) regarding the classification of these two TMJ prostheses. The Panel recommended at the April 1989 meeting that the total TMJ prosthesis and the interarticular disc prosthesis (interpositional implant), and at the February 1993 meeting that the glenoid fossa prosthesis and the mandibular condyle prosthesis, be classified into class III, and identified certain risks to health presented by the devices. The Panel believed that the devices presented a potential unreasonable risk to health and that insufficient information existed to determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the devices or that application of performance standards would provide such assurance.

FDA agreed with the Panel's recommendations and, in the proposal (57 FR 43165) and in the reproposed rule (59 FR 6935), proposed that the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis and the interarticular disc prosthesis (interpositional implant) be classified into class III. The proposal and reproposal stated that FDA believed that general controls, either alone or in combination with the special controls applicable to class II devices, are insufficient to provide reasonable assurance of the safety and effectiveness of the devices. The proposal and

reproposal stated that premarket approval is necessary for the devices because the devices present potential unreasonable risks of illness or injury if there are not adequate data to ensure the safe and effective use of the devices.

The preamble to the final rule (59 FR 65475) classifying the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis and the interarticular disc prosthesis (interpositional implant) into class III advised that the earliest date by which PMA's or notices of completion of PDP's for the devices could be required was June 30, 1997, or 90 days after issuance of a rule requiring premarket approval for the devices. In the **Federal Register** of January 6, 1989 (54 FR 550), FDA published a notice of intent to initiate proceedings to require premarket approval for 31 class III preamendments devices. Among other items, the notice described the factors FDA takes into account in establishing priorities for proceedings under section 515(b) of the act for issuing final rules requiring that preamendments class III devices have approved PMA's or declared completed PDP's. FDA updated its priorities in a preamendments class III strategy notice of availability document published in the **Federal Register** of May 6, 1994 (59 FR 23731). Although the previous TMJ prostheses were not included in the lists of devices identified in the notice and the strategy paper, using the factors set forth in these documents, FDA has recently determined that the total TMJ prosthesis identified in § 872.3940 (21 CFR 872.3940), the glenoid fossa prosthesis identified in § 872.3950 (21 CFR 872.3950), the mandibular condyle prosthesis identified in § 872.3960 (21 CFR 872.3960), and the interarticular disc prosthesis identified in § 872.3970 (21 CFR 872.3970) have a high priority for initiating a proceeding to require premarket approval because the safety and effectiveness of these devices has not been established by valid scientific evidence as defined in § 860.7 (21 CFR 860.7). Moreover, FDA believes that insufficient information exists to identify the proper materials or design for the total TMJ, the glenoid fossa, and the mandibular condyle prostheses. Accordingly, FDA is commencing a proceeding under section 515(b) of the act to require that the previous four TMJ prostheses have an approved PMA or declared completed PDP.

B. Dates New Requirements Apply

In accordance with section 515(b) of the act, FDA is proposing to require that a PMA or a notice of completion of a PDP be filed with the agency for the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis, and the interarticular disc prosthesis (interpositional implant) within 90 days after issuance of any final rule based on this proposal. An applicant whose device was legally in commercial distribution before May 28, 1976, or whose device has been found by FDA to be substantially equivalent to such a device, will be permitted to continue marketing the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis, and the interarticular disc prosthesis (interpositional implant) during FDA's review of the PMA or notice of completion of the PDP. FDA intends to review any PMA for the device within 180 days, and any notice of completion of a PDP for the device within 90 days of the date of filing. FDA cautions that, under section 515(d)(1)(B)(I) of the act, FDA may not enter into an agreement to extend the review period of a PMA beyond 180 days unless the agency finds that '' * * * the continued availability of the device is necessary for the public health.''

FDA intends that, under § 812.2(c)(2), the preamble to any final rule based on this proposal will state that, as of the date on which a PMA or a notice of completion of a PDP is required to be filed, the exemption in § 812.2(c)(1) and (c)(2) from the requirements of the IDE regulations for preamendments class III devices will cease to apply to any total TMJ prosthesis, glenoid fossa prosthesis, mandibular condyle prosthesis, and interarticular disc prosthesis (interpositional implant) which is: (1) Not legally on the market on or before that date; or (2) legally on the market on or before that date but for which a PMA or notice of completion of PDP is not filed by that date, or for which PMA approval has been denied or withdrawn.

If a PMA, notice of completion of a PDP, or an IDE application for the total TMJ prosthesis, glenoid fossa prosthesis, mandibular condyle prosthesis, and interarticular disc prosthesis (interpositional implant) is not submitted to FDA within 90 days after the date of issuance of any final rule requiring premarket approval for the devices, commercial distribution for the devices must cease. FDA, therefore, cautions that for manufacturers not planning to submit a PMA or notice of completion of a PDP immediately, IDE applications should be submitted to FDA, at least 30 days before the end of the 90-day period after the final rule is published to minimize the possibility of interrupting all availability of the device. FDA considers investigations of the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis, and the interarticular disc prosthesis (interpositional implant) to pose a significant risk as defined in the IDE regulation.

C. Description of Devices

A total TMJ prosthesis is a device that is intended to be implanted in the human jaw to replace the mandibular condyle and augment the glenoid fossa to functionally reconstruct the TMJ.

A glenoid fossa prosthesis is a device that is intended to be implanted in the TMJ to augment a glenoid fossa or to provide an articulation surface for the head of a mandibular condyle.

A mandibular condyle prosthesis is a device that is intended to be implanted in the human jaw to replace the mandibular condyle and to articulate within a glenoid fossa.

An interarticular disc prosthesis (interpositional implant) is a device that is intended to be an interface between the natural articulating surface of the mandibular condyle and glenoid fossa.

D. Proposed Findings With Respect to Risks and Benefits

As required by section 515(b) of the act, FDA is publishing its proposed findings regarding: (1) The degree of risk of illness or injury designed to be eliminated or reduced by requiring the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis, and the interarticular disc prosthesis (interpositional implant) to have an approved PMA or a declared completed PDP; and (2) the benefits to the public from the use of the device.

E. Risk Factors

1. Total TMJ Prosthesis (§ 872.3940), Glenoid Fossa Prosthesis (§ 872.3950), and Mandibular Condyle Prosthesis (§ 872.3960)

The total TMJ prostheses, the glenoid fossa prostheses, and the mandibular condyle prostheses are associated with the following risks:

1. Implant loosening or displacement. The screws used to anchor the implant may loosen, resulting in implant loosening or displacement, causing changes in bite, difficulty in chewing, limited joint function and unpredictable wear on implant components (Refs. 3 through 6);

2. Degenerative changes to the natural articulating surfaces. Implant breakdown may result in erosion or resorption of the glenoid fossa, or the head of the mandibular condyle . The erosion or resorption may result in intense pain, changes in bite, difficulty in chewing, limited joint function and,

in the case of glenoid fossa prostheses, perforation into the middle cranial fossa (Refs. 3 through 6);

3. Foreign body reaction. Implant deterioration and migration may result in a foreign body reaction characterized by multinucleated giant cells (Refs. 3 through 6);

4. Infection. If the implant cannot be properly sterilized, infection may result;

5. Loss of implant integrity. If the implant materials are unable to withstand mechanical loading, the implant can be torn, worn, perforated, delaminated, fragmented, fatigued, or fractured, resulting in failure of the devices to function properly (Refs. 3 through 6);

6. Chronic pain. Degenerative changes within the articular surfaces and components of the TMJ due to implant breakdown may result in chronic pain (Refs. 3 through 6);

7. Corrosion. If the implant materials are subject to corrosion, toxic elements may migrate to various parts of the body;

8. Changes to the contralateral joint. Unilateral placement of the implant may result in deleterious effects to the contralateral joint; and

9. Malocclusion. Placement of the device may produce an improper occlusal relationship.

2. Interarticular Disc Prosthesis (Interpositional Implant) (§ 872.3970)

Interarticular disc prostheses (interpositional implants) are associated with the following risks:

1. Loss of implant integrity. If the implant materials are unable to withstand mechanical loading, the implant materials can be torn, perforated, delaminated, or fragmented, resulting in failure of the device to function properly (Refs. 5, 7 through 11, and 13 through 16);

2. Implant migration. Torn, worn, perforated, delaminated, and fragmented implant materials are capable of migrating to surrounding tissues, including the lymph nodes (Refs. 5 and 14);

3. Foreign body reaction. Implant deterioration and migration may result in a foreign body reaction characterized by multinucleated giant cells (Refs. 5 and 7 through 16);

4. Degenerative changes within the articular surfaces and components of the joint. Implant breakdown may result in severe resorption of the head of the mandibular condyle and glenoid fossa. The degenerative changes may result in joint noise, changes in bite, difficulty in breathing, severely limited joint function, erosion or perforation into the middle cranial fossa, crepitus, avascular necrosis and fibrous ankylosis (Refs. 5 and 7 through 15);

5. Implant displacement. Displacement of the implant may result in changes in bite, difficulty in chewing and limited joint function (Refs. 7 through 10, 12, and 13);

6. Infection. If the implant cannot be properly sterilized, infection may result;

7. Chronic pain. Degenerative changes within the articular surfaces and components of the joint due to implant breakdown may result in chronic pain (Refs. 7 through 9 and 12);

8. Calcification. Implant breakdown may result in the formation of scar tissue, leading to calcification (Refs. 11 and 16);

9. Granulomatous reaction. Implant particulate may produce a mass or nodule of chronically inflamed tissue with granulation (Refs. 13 through 16); and

10. Leaching of elements. Toxic elements may be leached from the implant materials and migrate to various parts of the body.

F. Benefits of the Devices

The total TMJ prosthesis, glenoid fossa prosthesis, mandibular condyle prosthesis, and interarticular joint prosthesis (interpositional implant) are implanted devices which are placed in the jaw either to functionally reconstruct the TMJ by replacing the mandibular condyle and augmenting the glenoid fossa; to augment a glenoid fossa, to substitute for the naturally occurring mandibular condyle or to provide an interface between the natural articulating surfaces of the mandibular condyle and glenoid fossa. The potential benefits intended from the use of these four TMJ prostheses are reconstruction of the articulation surface(s) for the restoration of jaw function and stability, and improvement in mastication, speech, esthetics, comfort, and pain relief.

II. PMA Requirements

A PMA for these TMJ prosthetic devices must include the information required by section 515(c)(1) of the act and § 814.20 (21 CFR 814.20) of the procedural regulations for PMA's. Such a PMA should include a detailed discussion of the risks as well as a discussion of the effectiveness of the device for which premarket approval is sought. In addition, a PMA must include all data and information on: (1) Any risks known, or that should be reasonably known to the applicant that have not been identified in the proposal (57 FR 43165) and in the reproposed rule (59 FR 6935); (2) the effectiveness of the specific TMJ prosthesis that is the subject of the application; and (3) full reports of all preclinical and clinical information from investigations on the safety and effectiveness of the device for which premarket approval is sought.

A PMA should include valid scientific evidence as defined in § 860.7 and should be obtained from well-controlled clinical studies, with detailed data, in order to provide reasonable assurance of the safety and effectiveness of the particular TMJ implant for its intended use. In addition to the basic requirements described in § 814.20(b)(6)(ii) for a PMA, it is recommended that such studies employ a protocol that meets the following criteria.

Applicants should submit PMA's in accordance with FDA's guideline entitled ''Guideline for the Arrangement and Content of a PMA Application.'' The guideline is available upon request from FDA, Center for Devices and Radiological Health, Division of Small Manufacturers Assistance (HFZ–220), 1350 Piccard Dr., Rockville, MD 20850.

A. General Protocol Requirements

The total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis, and the interarticular disc prosthesis (interpositional implant) should be evaluated in a prospective, randomized, clinical trial that uses adequate controls. The study must attempt to answer all of the questions concerning safety and effectiveness of the devices, including the risk to benefit ratio. The questions should relate to the pathophysiologic effects which the devices produce, as well as the primary and secondary variables analyzed to evaluate safety and effectiveness. Study endpoints and study success must be defined.

Biocompatibility testing for new material and/or the finished devices should be performed according to the Office of Device Evaluation blue book memorandum G95–1 entitled ''Use of International Standard ISO–10993, ''Biological Evaluation of Medical Devices Part–1: Evaluation and Testing.'' This memorandum includes the FDA-modified matrix that designates the type of testing needed for various medical devices. The following tests should be considered:

1. Cytotoxicity
2. Sensitization
3. Irritation or intracutaneous reactivity
4. Acute systemic toxicity
5. Sub-acute toxicity
6. Genotoxicity
7. Implantation
8. Hemocompatibility
9. Chronic toxicity

10. Carcinogenicity

Specific considerations include the following:

1. The selection of materials to be used in device manufacture and their toxicological evaluation should initially take into account a full characterization of the materials, such as chemical composition of components, known and suspected impurities, and processing. Any surface coatings to be applied are to be fully characterized, including materials, physical specifications, and application processes.

2. The materials of manufacture, the final product and possible leachable chemicals or degradation products should be considered for their relevance to the overall toxicological evaluation of the devices.

3. Any in vitro or in vivo experiments or tests must be conducted according to recognized good laboratory practices followed by an evaluation by competent informed persons.

4. Any change in chemical composition, manufacturing process, physical configuration or intended use of the devices must be evaluated with respect to possible changes in toxicological effects and the need for additional testing.

5. The biocompatibility evaluation performed in accordance with the guidance should be considered in conjunction with other information from other nonclinical studies and postmarket experiences for an overall safety assessment.

Examples of questions to be addressed by the clinical studies may include the following:

1. What morbidity (jaw dysfunction or limited range of motion, degenerative changes to the natural articulating surfaces, erosion or resorption of the glenoid fossa or mandibular condyle, intense pain, joint arthritis, perforation into the middle cranial fossa, foreign body or allergic reactions, multinucleated giant cells, infection, chronic pain, changes in the contralateral joint, malocclusion, joint noise, crepitus, avascular necrosis, fibrous ankylosis difficulty in chewing, calcification, granulomatous reaction, facial nerve and muscle weakness, paralysis, hearing problems, or hematoma formation) is associated with the subject device in the patient population and how does this compare to the control?

2. What impact do the devices have on the jaw function?

3. What are the long term effects of the devices on the oral tissue?

4. What changes in physical characteristics of the prostheses can take place over time?

5. What potential problems (such as prosthesis loosening or displacement, wear evidence and debris, cracking, or fracture) may be associated with the use of the devices over time?

6. Do the devices allow sufficient comfort for the user?

7. What criteria are used to select the correct size of TMJ prostheses for individual patients?

8. How is the individual occlusal plane determined to avoid traumatic occlusion?

9. Do the devices allow the patients to be able to masticate food, insofar as oral and psychologic conditions will permit?

10. Does use of the devices result in the individual patient presenting a normal individual appearance that satisfies esthetic requirements?

Statistically valid investigations should include a clear statement of the objectives, method of selection of subjects, nature of the control group, effectiveness and/or safety parameters, method of analysis, and presentation of statistical results of the study. Appropriate rationale, supported by background literature on previous uses of the particular TMJ prosthesis and proposed mechanisms for its effect, should be presented as justification for the questions to be answered, and the definitions of study endpoints and success. Clear study hypotheses should be formulated based on this information.

B. Study Sample Requirements

The subject population should be well defined. Ideally, the study population should be as homogeneous as possible in order to minimize selection bias and reduce variability. Otherwise a large population may be necessary to achieve statistical significance. Independent studies producing comparable results at multiple study sites using identical protocols are necessary to demonstrate repeatability. Justification must be provided for the sample size used to show that a sufficient number of TMJ disorder patients were enrolled to attain statistically and clinically meaningful results. Eligibility criteria for the subject population should include the subject's potential for benefit, the ability to detect a benefit in the subject, the absence of both contraindications and any competing risk and assurance of subject compliance. In a heterogeneous sample, stratification of the patient groups participating in the clinical study may be necessary to analyze homogeneous subgroups and thereby minimize potential bias. All endpoint variables should be identified, and a sufficient number of patients from each subgroup analysis should be included to allow for stratification by pertinent demographic characteristics.

The investigations should include an evaluation of comparability between treatment groups and control groups (including historical controls). Baseline (e.g., age, gender, etc.) and other variables should be measured and compared between the treatment and control groups. The baseline variables should be measured at the time of treatment assignment, not during the course of the study. Other variables should be measured during the study as needed to completely characterize the particular device's safety and effectiveness.

C. Study Design

All potential sources of error, including selection bias, information bias, misclassification bias, comparison bias, or other potential biases should be evaluated and minimized. The study should clearly measure any possible placebo effect. Treatment effects should be based on objective measurements. The validity of these measurement scales should be shown to ensure that the treatment effect being measured reflects the intended uses of the particular device.

Adherence to the protocol by subjects, investigators, and all other individuals involved is essential and requires monitoring to assure compliance by both patients and dental practitioners. Subject exclusion due to dropout or loss to follow up greater than 20 percent may invalidate the study due to bias potential; therefore, initial patient screening and compliance of the final subject population will be needed to minimize the dropout rate. All dropouts must be accounted for and the circumstances and procedures used to ensure patient compliance must be well documented.

Endpoint assessment cannot be based solely on statistical value. Instead, the clinical outcome must be carefully defined to distinguish between the evaluation of the proper function of the device versus its benefit to the subject. Statistical significance and effectiveness of the device must be demonstrated by the statistical results.

Observation of all potential adverse effects must be recorded and monitored throughout the study and the followup period. All adverse effects must be documented and evaluated.

D. Statistical Analysis Plan

The involvement of a biostatistician is recommended to provide proper guidance in the planning, design, conduct, and analysis of a clinical study. There must be sufficient

documentation of the statistical analysis and results including comparison group selection, sample size justification, stated hypothesis test(s), population demographics, study site pooling justification, description of statistical tests applied, clear presentation of data and a clear discussion of the statistical results, and conclusions.

In addition to this generalized guidance, the investigator or sponsor is expected to incorporate additional requirements necessary for a well-controlled scientific study. These additional requirements are dependent on what the investigator or sponsor intends to measure or what the expected treatment effect is based on each device's intended use.

E. Clinical Analysis

The analysis which results from the study should include a complete description of all the statistical procedures employed, including assumption verification, pooling justification, population selection, statistical model selection, etc. If any procedures are uncommon or derived by the investigator or sponsor for the specific analysis, an adequate description must be provided of the procedure for FDA to assess its utility and adequacy. Data analysis and interpretations from the clinical investigation should relate to the medical claims.

F. Monitoring

Rigorous monitoring is required to assure that the study procedures are collected in accordance with the study protocol. Attentive monitors, who have appropriate credentials and who are not aligned with patient management or otherwise biased, contribute prominently to a successful study.

III. Opportunity to Request a Change in Classification

Before requiring the filing of a PMA or a notice of completion of a PDP for a device, FDA is required by section 515(b)(2)(A)(i) through (b)(2)(A)(iv) of the act and 21 CFR 860.132 to provide an opportunity for interested persons to request a change in the classification of the device based on new information relevant to its classification. Any proceeding to reclassify the device will be under the authority of section 513(e) of the act.

A request for a change in the classification of the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis, and the interarticular disc prosthesis (interpositional implant) is to be in the form of a reclassification petition containing the information required by § 860.123 (21 CFR 860.123), including information relevant to the classification of the device, and shall, under section 515(b)(2)(B) of the act, be submitted by August 1, 1997.

The agency advises that, to ensure timely filing of any such petition, any request should be submitted to the Dockets Management Branch (address above) and not to the address provided in § 860.123(b)(1). If a timely request for a change in the classification of the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis or the interarticular disc prosthesis (interpositional implant) is submitted, the agency will, by September 15, 1997, after consultation with the appropriate FDA advisory committee and by an order published in the **Federal Register**, either deny the request or give notice of its intent to initiate a change in the classification of the device in accordance with section 513(e) of the act and 21 CFR 860.130 of the regulations.

IV. References

The following references have been placed on public display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Transcripts of the Dental Products Panel meeting, April 21,1989.

2. Transcripts of the Dental Products Panel meeting, February 11,1993.

3. Fontenot, M. G., and J. N. Kent, ''In-Vitro and In-Vivo Wear Performance of TMJ Implants,'' abstract, International Association of Dental Research, 1991.

4. Kent, J. N., and M. S. Block, ''Comparison of FEP and UPE Glenoid Fossa Prosthesis,'' abstract, International Association of Dental Research, 1991.

5. ''Clinical Information on the Vitek TMJ Interpositional (IPI) Implant and the Vitek-Kent (VK) Vitek-Kent 1 (VK–1) TMJ Implants,'' and ''Vitek Patient Notification Program,'' an FDA publication, 1991.

6. Kent, J. N., ''VK Partial and Total Joint Reconstruction,'' Current Concepts of TMJ Total Joint Replacement, University of Medicine and Dentistry of New Jersey, pp. 1–8, March 1992.

7. Primely, D., ''Histological and Radiological Evaluation of the Proplast™-Teflon Interpositional Implant in Temporomandibular Joint Reconstruction Following Meniscectomy,'' thesis, Masters degree in Oral Maxillofacial Surgery, University of Iowa, May 1987.

8. Westlund, K. J.,''An Evaluation Using Computerized Tomography of Clinically Asymptomatic Patients Following Meniscectomy and Temporomandibular Joint Reconstruction Using the Proplast™-Teflon Interpositional Implant,'' thesis, Masters Degree in Oral and Maxillofacial Surgery, University of Iowa, May 1989.

9. Wagner, J. D., and E. L. Mosby, ''Assessment of Proplast™-Teflon Disc Replacements,'' *Journal of Oral and Maxillofacial Surgery*, 48:1140–1144, 1990.

10. Florine, B. K. et al., ''Tomographic Evaluation of Temporomandibular Joints Following Discoplasty or Replacement of Polytetrafluoroethylene Implants,'' *Journal of Oral and Maxillofacial Surgery*, 48:183–188, 1988.

11. Heffez, L. et al., ''CT Evaluation of TMJ Disc Replacement with a Proplast™ Teflon Laminate,'' *Journal of Oral and Maxillofacial Surgery*, 45:657–665, 1987.

12. Ryan, D. E., ''Alloplastic Implants in the Temporomandibular Joint,'' Oral and Maxillofacial Surgery Clinics of North America, 1:427, 1989.

13. Valentine, J. D., ''Light and Electron Microscopic Evaluation of Proplast™ II TMJ Disc Implants,'' *Journal of Oral and Maxillofacial Surgery*, 47:689–696, 1989.

14. Logrotteria, L. et al., ''Patient with Lymphadenopathy Following Temporomandibular Joint Arthroplasty with Proplast™,'' *The Hour of Craniomandibular Practice*, vol. 4, No. 2:172–178, 1986.

15. Berarduci, J. P. et al., ''Perforation into Middle Cranial Fossa as a Sequel to Use of a Proplast™ Teflon Implant for Temporomandibular Joint Reconstruction,'' *Journal of Oral and Maxillofacial Surgery*, 46:496–498, 1990.

16. Berman, D. N., and S. L. Pronstein, ''Osteo Phytic Reaction to a Polytetrafluoroethylene Temporomandibular Joint Implant,'' Oral Surgery, Oral Medicine, Oral Pathology (continues the Oral Surgery Section of the American Journal of Orthodontics and Oral Surgery), 69:20–23, 1990.

V. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(8) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VI. 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). 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 consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the proposed rule is not a significant regulatory action as defined by the

Executive Order and so is not subject to review under 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. Because the total TMJ prosthesis, the glenoid fossa prosthesis, the mandibular condyle prosthesis and the interarticular disc prosthesis (interpositional implant) have been classified into class III since December 12, 1994, and manufacturers of such TMJ prostheses legally in commercial distribution before May 28, 1976, or found by FDA to be substantially equivalent to such devices, will be permitted to continue marketing during FDA's review of the PMA or notice of completion of the PDP, the Commissioner of Food and Drugs certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

VII. Comments

Interested persons may, on or before October 15, 1997, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Interested persons may, on or before August 1, 1997, submit to the Dockets Management Branch a written request to change the classification of the total TMJ prosthesis, glenoid fossa prosthesis, mandibular condyle prosthesis, or the interarticular disc prosthesis (interpositional implant). Two copies of any request are to be submitted, except that individuals may submit one copy. Comments or requests are to be identified with the docket number found in brackets in the heading of this document. Received comments and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

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 as follows:

PART 872—DENTAL DEVICES

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

Authority: Secs. 501, 510, 513, 515, 520, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351, 360, 360c, 360e, 360j, 371).

2. Section 872.3940 is amended by revising paragraph (c) to read as follows:

§ 872.3940 Total temporomandibular joint prosthesis.

* * * * *

(c) Date premarket approval application (PMA) or notice of completion of a product development protocol (PDP) is required. A PMA or a notice of completion of a PDP is required to be filed on or before (date 90 days after the effective date of a final rule based on this proposed rule), for any total temporomandibular joint (TMJ) prosthesis that was in commercial distribution before May 28, 1976, or that has on or before (date 90 days after the effective date of a final rule), been found to be substantially equivalent to a total TMJ prosthesis that was in commercial distribution before May 28, 1976. Any other total TMJ prosthesis shall have an approved PMA or a declared completed PDP in effect before being placed in commercial distribution.

3. Section 872.3950 is amended by revising paragraph (c) to read as follows:

§ 872.3950 Glenoid fossa prosthesis.

* * * * *

(c) Date premarket approval application (PMA) or notice of completion of a product development protocol (PDP) is required. A PMA or a notice of completion of a PDP is required to be filed on or before (date 90 days after the effective date of a final rule based on this proposed rule), for any glenoid fossa prosthesis that was in commercial distribution before May 28, 1976, or that has on or before (date 90 days after the effective date of a final rule), been found to be substantially equivalent to a glenoid fossa prosthesis that was in commercial distribution before May 28, 1976. Any other glenoid fossa prosthesis shall have an approved PMA or a declared completed PDP in effect before being placed in commercial distribution.

4. Section 872.3960 is amended by revising paragraph (c) to read as follows:

§ 872.3960 Mandibular condyle prosthesis.

* * * * *

(c) Date premarket approval application (PMA) or notice of completion of a product development protocol (PDP) is required. A PMA or a notice of completion of a PDP is required to be filed on or before (date 90 days after the effective date of a final rule based on this proposed rule), for any mandibular condyle prosthesis that was in commercial distribution before May 28, 1976, or that has on or before (date 90 days after the effective date of a final rule), been found to be substantially equivalent to a mandibular condyle prosthesis that was in commercial distribution before May 28, 1976. Any other mandibular condyle prosthesis shall have an approved PMA or a declared completed PDP in effect before being placed in commercial distribution.

5. Section 872.3970 is amended by revising paragraph (c) to read as follows:

§ 872.3970 Interarticular disc prosthesis (interpositional implant).

* * * * *

(c) Date premarket approval application (PMA) or notice of completion of a product development protocol (PDP) is required. A PMA or a notice of completion of a PDP is required to be filed on or before (date 90 days after the effective date of a final rule based on this proposed rule), for any interarticular disc prosthesis (interpositional implant) that was in commercial distribution before May 28, 1976, or that has on or before (date 90 days after the effective date of a final rule), been found to be substantially equivalent to an interarticular disc prosthesis (interpositional implant) that was in commercial distribution before May 28, 1976. Any other interarticular disc prosthesis (interpositional implant) shall have a PMA or a declared PDP in effect before being placed in commercial distribution.

Dated: July 3, 1997.

Joseph A. Levitt,

Deputy Director for Regulations Policy, Center for Devices and Radiological Health.

[FR Doc. 97–18831 Filed 7–16–97; 8:45 am]

BILLING CODE 4160–01–F

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 81

[LA–41–1–7342, FRL–5859–3]

Designation of Areas for Air Quality Planning Purposes; State of Louisiana; Correction of the Designation for Lafourche Parish

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed correction.

SUMMARY: This document announces EPA's proposal to correct the designation of Lafourche Parish, Louisiana, to nonattainment for ozone. Subsequent to publication, but prior to the effective date of the approval action in this matter, Lafourche Parish violated the ozone standard. Pursuant to the Clean Air Act (the Act), which allows