Guidance1 for Industry and FDA Staff

Dental Composites – Premarket Notification

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

Dental Devices Branch
Division of Dental, Infection Control, and General Hospital Devices
Office of Device Evaluation

Preface

Public Comment:

Comments and suggestions may be submitted at any time for Agency consideration to Dr. Susan Runner, Branch Chief, Dental Devices Branch, HFZ-480, Office of Device Evaluation, Center for Devices and Radiological Health, U.S. Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, Phone: 301-827-5283, Fax: 301-480-3002. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Dr. Susan Runner at 301-827-5283.

Additional Copies:

World Wide Web/CDRH home page at http://www.fda.gov/cdrh/ode/642.pdf or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 642 when prompted for the document shelf number.

TABLE OF CONTENTS

1.0 INTRODUCTION 4

2.0 GENERAL INFORMATION 5

3.0 DEVICE DEFINITION 5

4.0 PRODUCT DESCRIPTION 6

5.0 CHEMICAL IDENTITY 6

6.0 PHYSICAL AND MECHANICAL PROPERTIES 7

7.0 BIOCOMPATIBILITY TESTING 7

8.0 LABELING 9

Guidance for the Preparation of Premarket Notifications for Dental Composites

1.0 INTRODUCTION

The purpose of this document is to provide guidance to the manufacturers of dental composites on the information desired for a more thorough and consistent preparation of a Premarket Notification submission (510(k)).

The development of this document is based on information recommended for a complete and adequate review by the Dental Devices Branch. The use of this document for the preparation of a 510(k) for dental composites does not ensure FDA clearance of a device, and certain 510(k) submissions may require additional information not contained in this document. However, use of this document will ensure that the basic elements are present to conduct an evaluation of substantial equivalence.

This guidance is subject to revision depending upon development of new technological information and/or changes in regulatory requirements.

Standards

Medical device manufacturers may elect to rely upon recognized consensus standards during the development and testing phase of their devices. We recognize that consensus standards, such as ISO standards, undergo periodic review and are subject to revision. FDA has published a document entitled "Guidance on the Recognition and Use of Consensus Standards" which provides guidance to industry and FDA reviewers on the use of recognized consensus standards, including declaration of conformity to the standards, during the evaluation of premarket submissions (**Federal Register**/Volume 63, No. 37/Wednesday, February 25, 1998). This document and related lists of recognized standards are on the Internet at FDA's web site:
http://www.fda.gov/cdrh/modact/modguid.html

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[1] This document is intended to provide guidance. 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 FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations or both.

2.0 GENERAL INFORMATION

510(k) Summary or 510(k) Statement. In accordance with the Safe Medical Devices Act of 1990 and 21 CFR Part 807.87(h), the applicant must submit either: (1)A summary of the safety and effectiveness information in the premarket notification submission upon which an equivalence determination could be based (i.e., a "510(k) Summary"); or (2)a statement that safety and effectiveness information will be made available to interested persons upon request (i.e., a "510(k) Statement"). The summary or statement should be clearly identified as a "510(k) Summary" or a "510(k) Statement".

Truthful and Accurate Statement. A statement must be provided that the applicant certifies and believes, to the best of his or her knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted. See 21 CFR Part 807.87(k).

Indications for Use Form. On January 1, 1996, FDA began requiring that all 510(k) submitters provide on a separate page and clearly marked "Indications for Use" the indications(s) for use of their device.

The New 510(k) Paradigm

On March 19, 1998, new procedures for the submission of 510(k)'s became effective. These procedures are collectively called the "New 510(k) Paradigm." More information on the New 510(k) Paradigm is available on the Internet at the following FDA web site: http://www.fda.gov/cdrh/ode/parad510.pdf.

3.0 DEVICE DEFINITION

Dental composites are class II prescription devices classified in the regulation as tooth shade resin materials intended to restore carious lesions or structural defects in teeth. See 21 CFR Part 872.3690. (FDA Product Code "EBF")

The traditional dental composites used for direct esthetic restorations consist mainly of a polymer matrix and dispersed reinforcing inorganic filler particles. The typical polymers used are based on dimethacrylate such as Bis-GMA or urethane dimethacrylate (UDMA). Quartz, lithium aluminum silicate, and barium, strontium, or zinc glasses have been commercially distributed as fillers. Dental composites can be classified also by the particle size and percentage distribution of the inorganic filler, which may contain fine irregularly shaped particles from 0.5 to 5 μm in diameter, microfine particles having a diameter of 0.04 to 0.2 μm, or blends (hybrids) of these particles sizes. Dental composites are usually supplied as a single-paste system in a syringe or in compules, and less often as a two-paste system supplied in two jars.

4.0 PRODUCT DESCRIPTION

A description of the dental composite system should clearly indicate specifically what you intend to market. This information includes:

- State the device classification name and the trade name of the composite material.
- Submit a detailed description of your product and its indication(s) for use, such as class III and V restorations.
- Specify whether the product is an anterior or posterior composite, as they have different intended uses and thus different information is needed to characterize each.
- Indicate whether the system is chemically cured, light cured, or dual cured.
- State whether a single-paste or two-paste (base/catalyst) system is employed.
- Specify whether the product is a fine particle or microfilled composite, a hybrid composite, or a flowable composite system.
- Provide a descriptive or table comparison of the similarities and differences to a legally marketed predicate dental composite in terms of intended use, chemical composition, physical characteristics and mechanical properties, safety and effectiveness.

5.0 CHEMICAL IDENTITY

- Provide the complete dental composite formulation, identifying the individual chemical components by percentage, to a sum of 100%.
    - Note the function of each chemical constituent.
    - Do not omit any chemical component nor submit generalizations under vague descriptions such as “composite resin.”
    - Provide the specific chemical name, and not proprietary or trade name, or abbreviated chemical name.
    - Disclose any pigments or other colorants used in the formulation.
    - Include the material safety data sheet (MSDS) for each chemical component, a diagram of the chemical structure and the molecular formula of the finished material, and the Chemical Abstracts Service (CAS) number if available.

6.0 PHYSICAL AND MECHANICAL PROPERTIES

The minimum tests needed for comparison to a predicate device:

- Compressive Strength (MPa)
- Polymerization Shrinkage (% by volume)
- Working and setting times (in minutes)
- Film Thickness (μm)
- Flow (mm^2/30 seconds)
- Wear (μm/10^5 cycles)
- Water Sorption (mg/cm^2) at 37°C after 7 days
- Thermal Expansion Coefficient (10^{-6}/°C)

Other tests which can be used for comparison to a predicate dental composite:

- Diametral Tensile Strength (MPa)
- Flexural (bending) Strength (MPa)
- Knoop Hardness (kg/mm^2)
- Young's Modulus (MPa)
- Radiopacity (mm of Aluminum)

In all cases, the test samples should be fully cured. A summary should be provided of the methodology and results of the bench testing that has been conducted. The quantitative results for the product testing should be compared to those of predicate dental composite materials. If the physical properties of the dental composite conform to a consensus standard for performance testing, the specific standard should be referenced, such as American Dental Association Specification No. 27 for Direct Filling Resins, International Organization for Standardization (ISO) ISO 4049 Dentistry-resin-based filling materials, etc.

If a dental composite contains a fluoride ion-releasing agent, such as sodium fluoride, sodium alumina-fluoro-silicate, etc., the release profile (ppm F-ions/cm^2 of sample vs. time in days) should be provided. The test should be performed at 37°C in distilled water. The test duration may range from one to four weeks. Fluoride release rates tend to drop precipitously after a few days and so seven days is generally sufficient to define the release profile. Claims of cavity prevention or other therapeutic benefits need to be supported with clinical studies. Such claims and the supporting clinical trials will be evaluated by both the Center for Devices and Radiological Health (CDRH) and the Center for Drug Evaluation and Research (CDER).

7.0 BIOCOMPATIBILITY TESTING

Biological evaluation of medical devices is performed to determine the potential toxicity resulting from contact of the component materials of the device with the body. The device materials should not, either directly or through the release of their material constituents: (1)Produce significant adverse local or systemic effects; (2)be carcinogenic; or (3)produce

adverse reproductive and developmental effects. Therefore, data from systematic testing should be evaluated to ensure that the benefits provided by the final product will exceed any potential risks produced by dental cement materials.

The ISO standard, ISO-10993, Part 1, uses an approach to test selection that is very similar to the Tripartite Guidance used in the past by FDA. It also uses a tabular format (matrix) for laying out the test requirements based on the various factors discussed above. The matrix consists of two tables, Initial Evaluation Tests for Consideration" and "Supplementary Evaluation Tests for Consideration." To harmonize biological response testing with the requirements of other countries, FDA has recognized the ISO standard. Reviewers in the Office of Device Evaluation will accept data developed according to ISO-10993, Part 1, with the matrix as modified and presented in Blue Book Memorandum #G95-1 entitled "Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part-1: Evaluation and Testing."

Manufacturers are advised to begin discussions with the Dental Devices Branch prior to the initiation of expensive, long-term testing of any new device materials to ensure that the proper testing will be conducted, and to avoid unnecessary tests.

Biocompatibility testing is indicated when the product contains a "new" or nonconventional chemical component is added for which the safety or effectiveness of the resulting formulation is in question. A material may be considered "new" based upon several factors, such as methods of manufacture, sterilization, duration of body exposure, etc. The biocompatibility testing should be performed on the finished product, i.e., in a form as close as possible to what the patient will be exposed to.

This is a list of the minimum testing which should be addressed in a regulatory submission.

- In Vitro Cytotoxicity
- Ames Test for Mutagenicity
- Mucous Membrane Irritation (hamster's pouch)
- Sensitization Test in Guinea Pigs
- Carcinogenicity (if tumorigenic potential previously documented)

For details on how to conduct these tests, refer to an appropriate international standard such as: American National Standard/American Dental Association Document No 41 for Recommended Standard Practices for Biological Evaluation of Dental Materials,1982; or ISO/TR: 1984(E), Biological Evaluation of Dental Materials, 1984.

8.0 LABELING

It is important to the consumer that the labeling for dental composites bear clear, accurate, and complete information for use concerning any relevant components, indications, method of preparation, hazards, contraindications, and precautions in their use.

As described in 21 CFR Part 801.109, labels should bear the statement "Caution: Federal law restricts this device to sale by or on the order of a dentist." Also, instructions for use of the product should bear the date of the issuance or the date of the latest revision.

Include in the 510(k) submission the proposed package labels and labeling, including available promotion and advertising information. Labeling refers to the package label plus other written, printed, or graphic material that accompanies the device or that is placed on either the device or any of its wrappers or containers. Advertising may be considered labeling, especially if it accompanies the product. See sections 201(k) and (m) and 502(f)(1) and (2) of the Federal Food, Drug, and Cosmetic Act.

If you wish specific advice on the applicability to your device of the FDA labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (301) 594-4618. Also, for questions on the promotion and advertising of your dental cement, please contact the Office of Compliance at (301) 594-4639. Additionally, note the regulation titled "Misbranding by reference to premarket notification" (21 CFR Part 807.97).