Special Control Guidance Document on Encapsulated Amalgam, Amalgam Alloy, and Dental Mercury Labeling; Draft Guidance for Industry and FDA

Draft Guidance – Not for Implementation

This guidance document is being distributed for comment purposes only.
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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:

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 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 and regulations.

INTRODUCTION

This guidance document represents the agency's current thinking on the content and format of labeling for Encapsulated Amalgam Alloy and Dental Mercury (hereinafter referred to as Encapsulated Amalgam), Amalgam Alloy, and Dental Mercury. This guidance is intended as a special control for these devices. It does not 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 an approach satisfies the requirements of the applicable statute, regulations, or both.

Amalgam alloy is a Class II device. The Agency is currently proposing to classify encapsulated Amalgam into Class II, to amend the classification regulation for amalgam alloy to provide for special controls, and to reclassify Dental Mercury into Class II. As class II medical devices, these products will be subject to special controls as defined in section 513 (a)(1)(B) of the Food, Drug and Cosmetic Act (the act) (21 USC 360c(a)(1)(B) and 360d(a)(2)(c)). Special controls may include, among other things, recommendations and guidance for the form and content of product labeling. This guidance document describes a means by which manufacturers of encapsulated amalgam, amalgam alloy, and dental mercury may comply with the requirements of class II special controls. Designation of this guidance document as a special control means that manufacturers of encapsulated amalgam, amalgam alloy, and dental mercury, who follow the recommendations listed in this document before introducing their device into commercial distribution in the United States, will be able to market their device after they have submitted a premarket notification submission, referred to as a 510(k), and received a finding of "substantial equivalence" for their device. Manufacturers should comply with either the recommendations of this guidance or some alternate means that provide

equivalent assurance of safety and effectiveness.

The Office of Device Evaluation (ODE), Center for Devices and Radiological Health, Food and Drug Administration (FDA), has prepared this guidance as part of an effort of the Public Health Service to provide adequate information about dental products for dental professionals and patients. The guidance is intended (1) to assist manufacturers who are required to submit a premarket notification for Encapsulated Amalgam, Amalgam Alloy, and Dental Mercury products, and (2) to guide FDA reviewers to ensure that decisions regarding new amalgam products will be consistent with agency policy. As regulatory requirements, technology, and public health needs change, this guidance may be subject to revision.

CONTENT

1: ADMINISTRATIVE GUIDANCE

1.1 REGULATORY AUTHORITY/STATUTORY LABELING PROVISIONS

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 amendments) (Pub. L. 94-295), and the Safe Medical Devices Act of 1990 (the SMDA) (Pub. L. 101-629), 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 (general controls plus special controls), and Class III (premarket approval).

Pursuant to section 513 (a)(1)(B) of the act (21 U.S.C. 360c(a)(1)(B), a device can be classified into Class II if the Agency concludes that general controls alone will not provide reasonable assurance of the safety and effectiveness of the device. Special controls include, among other things, the development and dissemination of a labeling guidance.

The purpose of a guidance document is to provide assistance to the regulated industry by clarifying requirements that have been imposed by Congress or issued in regulations by the FDA. A guidance document may explain how industry may comply with those statutory and regulatory requirements, and provides specific review and enforcement approaches to help ensure that the agency's mandate is applied in an effective, fair, and consistent manner.

1.2 LABELING REQUIREMENTS FOR PRESCRIPTION DEVICES

Encapsulated Amalgam, Amalgam Alloy, and Dental Mercury products are prescription devices under 21 CFR 801.109, and are exempt from section 502(f)(1) of the act pertaining to misbranding, provided the labeling bears:

1. The statement "Caution: Federal law restricts this device to sale by or on the order of a _____" The blank to be filled with the word "physician", "dentist", "veterinarian" or with the descriptive designation of any other practitioner licensed by the law of the State in which he practices to use or order the use of the device."

2. Information for use, including indications, effects, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions under which the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury can safely be used;

3. The date of issuance or date of the latest revision in a location other than the outside package label and carton; and,
4. Labeling that meets other requirements for prescription devices under 21 CFR 801.109.

2: GENERAL INFORMATION

2.1: DEFINITIONS

Label: As defined in section 201(k) of the act (21 U.S.C. 521(k)), the term "label" means a display of written, printed, or graphic matter upon the outside of the immediate container or packaging of a device. The term labeling as defined in section 201(m) of the act (21 U.S.C. 321 (m)), however, means all labels and other written, printed, or graphic matter upon a device or any of its containers or wrappers, or accompanying the device.

Ingredient: The term "ingredient" applies to any component in the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury, whether added to the formulation as a single component or in an admixture with other substances.

2.2 USE OF ENGLISH LANGUAGE

All words, statements, and other information to appear on the label or labeling must appear in the English language. If, however, the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury is distributed only in the Commonwealth of Puerto Rico or in a Territory where the predominant language is one other than English, the predominant language may be substituted for English. 21 CFR 801.15(c)

2.3 LABELING TO SUBMIT IN 510(k)

In accordance with the Premarket Notification requirements in 21 CFR 807.87(e), each 510(k) submission must contain proposed labels, labeling, and advertisement sufficient to describe the device, its intended use, and the directions for its use.

A copy of all of the proposed labels and labeling should be included in the 510(k) submission including carton labels, package inserts, instructional manuals, articles, promotional literature and graphics that accompany the device or could otherwise be construed as labeling, sufficient to describe the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury, its intended use, and the directions for use as detailed in Part 3 of this guidance.

2.4 ADDITIONAL SPECIAL CONTROL: STANDARDS

Encapsulated Amalgam, Amalgam Alloy and Dental Mercury devices should meet the current edition of the relevant recognized voluntary consensus standards discussed below:

- ANSI/ADA Specification No. 6 (Revised American National Standard/American Dental Association Specification No. 6 for Dental Mercury) (This standard is applicable to the encapsulated amalgam and the dental mercury)

- International Standard ISO 1559;1995 Dental Materials Alloys for Dental Amalgam [Note: This standard is applicable to the encapsulated amalgam and the amalgam alloy. The following exception applies: Section 7.2.1 (f) of the ISO standard suggests that elements present in the alloy in concentrations greater than 0.1%(m/m) be listed. The Agency recommends that all ingredients be included in the product labeling.]

Under the provisions of the Food and Drug Modernization Act (FDAMA), a sponsor may submit a declaration of conformity to a recognized standard as part of an abbreviated 510(k) submission or a statement regarding conformity (see http://www.fda.gov/cdrh/ode/guidance/1131.html). Conformance to industry standards should be noted on the package label.

3: CONTENT AND FORMAT OF LABELING

3.1 IMMEDIATE CONTAINER LABELS

The information displayed on the outer package label of the primary vial or package from which the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury is dispensed should include the information listed below. If the package is too small to display all of the information on the immediate container label, then the below-listed information may appear elsewhere on the labeling, such as in an outer package label and/or in a package insert:

If the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury has an established trade name, its label should bear, to the exclusion of any other nonproprietary name

(except the applicable systematic chemical name or the chemical formula), that established brand or trade name, prominently and clearly displayed.

- CHEMICAL NAME ESTABLISHED BY COMMON NOMENCLATURE

- LISTING OF INGREDIENTS

The label should contain a list of each ingredient based upon the descending order of the weight percentage. It is not necessary to disclose the exact percentages of each ingredient. If a statement of the percentage of an ingredient of the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury is included, the term "percent" should mean percent by weight. The declaration should contain only such fractions as are generally used in expressing the quantity of the ingredients. A common fraction should be reduced to its lowest terms, and a decimal fraction should not be carried out to more than three places. The label should list all component elements in the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury. [Note: This is an exception to the ISO standard recommendations: Section 7.2.1 (f) of ISO 1559 suggests that elements present in the alloy in concentrations greater than 0.1%(m/m) be listed. The Agency recommends that all ingredients be included in the product labeling.]

The ingredient information should be conspicuously placed in the labeling so that it can be read and understood under customary conditions of use. Ingredients should be listed without any intervening written, printed, or graphic matter.

The labeling may be misleading under section 502(a) of the act if the use of a fanciful trade name or chemical name implies that the ingredient has a unique effectiveness or composition when, in fact, it is a common ingredient, the limitations of which are readily recognized when Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury ingredients are listed by an established name.

The labeling may be misleading under section 502(a) of the act if an ingredient is presented in a manner that creates an impression of value greater than its true functional role in the formulation.

The labeling may be misleading under section 502(a) of the act, if an ingredient is designated by a trade name that, because of similarity in spelling or pronunciation, may be confused with the trade name or the established name of a different Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury device or their ingredients.

If the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury is packaged in a vial or package too small to display the quantitative ingredient information, then the information can appear elsewhere on the labeling, such as in an outer package label and/or in a package insert.

- IDENTIFYING LOT, BATCH, OR CONTROL NUMBER REFERENCE

Encapsulated Amalgam, Amalgam Alloy, and Dental Mercury devices can be considered misbranded if labeled with an incorrect lot number. Section 502(a) of the act provides that a device is misbranded if its labeling is false or misleading in any particular. The lot number on Encapsulated Amalgam, Amalgam Alloy, and Dental Mercury labels should provide the complete manufacturing history of the material. For dental mercury, and encapsulated amalgam also refer to section 5.2.1 of ANSI/ADA Spec. #6.

- NAME AND ADDRESS OF THE MANUFACTURER OR DISTRIBUTOR, INCLUDING STREET ADDRESS, CITY, STATE AND ZIP CODE OF THE MANUFACTURER, PACKAGER OR DISTRIBUTOR
  Reference ANSI/ADA Spec #6 sec. 5.2.2

- STATEMENT OF APPROPRIATE WARNINGS OR PRECAUTIONS AS DESCRIBED BELOW

- DECLARATION OF CONTENTS, INCLUDING THE NET QUANTITY OF MASS AND NUMBER OF PREDOSED VIALS OR DISPENSING PACKAGES
  Reference ISO 1559 sec. 7.2.1

The statement of quantity of Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury in its immediate container should be expressed in terms of the weight of the component in terms avoirdupois pound and ounce or grams (or fractions thereof).

- APPROPRIATE STORAGE INSTRUCTIONS

- EXPIRATION DATE

If an expiration date is used, it should appear on the immediate container and also on the outer package, unless it is easily visible through the outer package. However, if single-dose containers are packed in individual cartons, the expiration date may properly appear on the individual carton instead of the immediate product container.

3.2 PACKAGING DISPLAY PANELS/PACKAGE INSERTS

The side or back panel placement should be arranged and printed to provide size and prominence of display in proportion to the size and prominence of the front panel display.

All the information that should be on the immediate container label should also appear on the carton or other package inserts.

3.2.1. INSTRUCTIONS FOR USE

Instructions for use for Amalgam Alloy and Dental Mercury products should include the optimal ratio of alloy to mercury to produce a mix that is suitable for an operator who works at a standard pace. An optimal ratio should also be provided for an accelerated set. Additional instructions for Encapsulated and component products should describe the mixing specifications (speed, time) for each brand and model of amalgamator. These settings should be listed for 1, 2, and 3 spill sizes.

Alloys that contain zinc should caution the operator about corrosion and expansion that may result from moisture contamination. Reference ISO 1559 7.3.1, 7.3.2 and 7.3.3 for amalgam alloy and encapsulated amalgam devices as stated in 3.2.4.

3.2.2. HANDLING AND STORAGE INSTRUCTIONS

Directions for the handling and storage of Encapsulated Amalgam, Amalgam Alloy, and Dental Mercury should be described in detail. For example, the outer package label information should bear a recommendation to store Encapsulated Amalgam, Amalgam Alloy, and Dental Mercury at temperatures no higher than 25 °C. Unused amalgam material should be discarded in accordance with federal regulations and local policies. Reference ANSI/ADA Spec #6 sec 5.2.4 for dental mercury and encapsulated amalgam.

3.2.3 CONTRAINDICATIONS

Contraindication statements should describe situations in which the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury should not be used because the risk of use outweighs any possible benefit. These situations include use in a patient known to have a

hypersensitivity to these products; use in patients, who, because of their particular age, gender, concomitant therapy, disease state, or other condition have a substantial risk of being harmed by the device; or use in a patient who is likely to experience an unacceptably hazardous adverse reaction. Only known hazards should be listed. The practitioner should be instructed to discontinue use of that product if sensitivity reactions do occur. If no contraindications are known, this section of the labeling should state "None known."

3.2.4. WARNINGS

Warning statements should describe serious adverse reactions and potential safety hazards, limitations in use, and steps that should be taken if adverse reactions occur. A warning should be added to the labeling as soon as there is reasonable evidence of association of a serious hazard with an Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury product. The frequency of serious adverse reactions should be stated in an "Adverse Reactions" section of the labeling. All warnings that are included in ISO 1559 for amalgam alloy and encapsulated amalgam and ANSI/ADA Specification No. 6 for dental mercury and encapsulated amalgam should be present in the device labeling. FDA is not recommending any additional warnings that would apply to these products.

If the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury device contains a material which may cause a sensitivity reaction (e.g., beryllium or nickel), a warning statement should be displayed identifying the component(s) and the potential adverse reaction(s). If the product contains zinc, the following warning should be provided (in bold type):

"THIS PRODUCT CONTAINS ZINC; THE AMALGAM MADE FROM ZINC MAY SHOW EXCESSIVE EXPANSION IF MOISTURE IS INTRODUCED DURING MIXING OR COMPACTING"

3.2.5. PRECAUTIONS

Precautions should state information about the need for special care to ensure safe and effective use of the Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury device. Labeling should include advice to clinicians about the use, when possible, of barrier techniques to reduce inhalation and ingestion of restorative materials during placement and removal.

4: ADDITIONAL INFORMATION

4.1 FOR MORE LABELING INFORMATION

For questions concerning the labeling of Encapsulated Amalgam, Amalgam Alloy, or Dental Mercury products, contact the Dental Branch, Division of Dental, Infection Control, and General Hospital Devices, Office of Device Evaluation, Center for Devices and Radiological Health (HFZ-480), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301-443-8879.

4.2 GENERAL QUESTIONS REGARDING 510(k)s

For general information about the preparation of a 510(k) submission, contact the Division of Small Manufacturers Assistance, Office of Health Industry Programs, Center for Devices and Radiological Health, Food and Drug Administration, at 800-638-2041 or 301-443-6597.