

DEPARTMENT OF HEALTH AND HUMAN SERVICES**Food and Drug Administration****21 CFR Part 356****[Docket No. 81N-033P]****RIN 0910-AA01****Oral Health Care Drug Products for Over-the-Counter Human Use; Antigingivitis/Antiplaque Drug Products; Establishment of a Monograph****AGENCY:** Food and Drug Administration, HHS.**ACTION:** Advance notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing an advance notice of proposed rulemaking that would establish conditions under which over-the-counter (OTC) drug products for the reduction or prevention of dental plaque and gingivitis are generally recognized as safe and effective and not misbranded. This notice is based on the recommendations of the Dental Plaque Subcommittee of the Nonprescription Drugs Advisory Committee (NDAC) and is part of FDA's ongoing review of OTC drug products.

DATES: Submit written or electronic comments by August 27, 2003. Submit reply comments by October 27, 2003.

ADDRESSES: Submit written and reply comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

FOR FURTHER INFORMATION CONTACT: Robert L. Sherman, Center for Drug Evaluation and Research (HFD-560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-2222.

SUPPLEMENTARY INFORMATION: In accordance with part 330 (21 CFR part 330), FDA received on December 3, 1998, a report on OTC antigingivitis/antiplaque drug products from the Dental Plaque Subcommittee (the Subcommittee). FDA regulations (§ 330.10(a)(6)) provide that the agency issue in the **Federal Register** a proposed rule containing: (1) The monograph recommended by the Subcommittee, which establishes conditions under which OTC antigingivitis/antiplaque drug products are generally recognized as safe and effective and not misbranded; (2) a statement of the conditions excluded from the

monograph because the Subcommittee determined that they would result in the drugs not being generally recognized as safe and effective or would result in misbranding; (3) a statement of the conditions excluded from the monograph because the Subcommittee determined that the available data are insufficient to classify these conditions under either (1) or (2) of this paragraph; and (4) the conclusions and recommendations of the Subcommittee.

The unaltered conclusions and recommendations of the Subcommittee are issued to stimulate discussion, evaluation, and comment on the full sweep of the Subcommittee's deliberations. The report has been prepared independently of FDA, and the agency has not yet fully evaluated the report. The Subcommittee's findings appear in this document to obtain public comment before the agency reaches any decision on the Subcommittee's recommendations. This document represents the best scientific judgment of the Subcommittee, but does not necessarily reflect the agency's position on any particular matter contained in it.

The Subcommittee was asked for its general recommendations on combination products in which antigingivitis/antiplaque ingredients are combined with other oral health care ingredients. The Subcommittee recommended the following as rational oral health care combination products: (1) An antigingivitis/antiplaque active ingredient combined with an anticaries active ingredient, (2) an antigingivitis/antiplaque active ingredient combined with a tooth desensitizer active ingredient, and (3) an antigingivitis/antiplaque active ingredient combined with an anticaries active ingredient and a tooth desensitizer active ingredient.

However, the agency is not aware of any marketing history of such combination products eligible for the OTC drug review, nor were such combinations submitted to the Subcommittee. Therefore, the agency is dissenting from these recommendations at this time. Data are needed to establish the safety and effectiveness of these combination products. Accordingly, none of the combination products described above may be marketed OTC at this time under this advance notice of proposed rulemaking. The agency invites supporting data and information demonstrating that these combination products can be generally recognized as safe and effective for OTC use.

Based on proposals from industry, the Subcommittee also made general recommendations on testing requirements for final product

formulations to be considered effective. The agency is seeking specific information from interested parties on testing protocols, effectiveness criteria, and statistical methods employed to analyze the data from these tests.

The agency notes that the Subcommittee concluded that an active ingredient could be either an antigingivitis agent or an antigingivitis/antiplaque agent. While an ingredient may also be effective in reducing plaque, the Subcommittee stated that the therapeutic endpoint for both antigingivitis and antigingivitis/antiplaque active ingredients is a significant reduction in gingivitis, which can be measured using gingival index scores (see section II.C of this document).

The Subcommittee concluded that there is an association between plaque and gingivitis. The Subcommittee agreed, however, that the exact relationship between plaque and gingivitis cannot be quantified. Because the data submitted to support the effectiveness of stannous fluoride in reducing plaque were inconclusive, the Subcommittee proposed an "antigingivitis" statement of identity for this ingredient. However, the Subcommittee's proposed indication for this ingredient includes a reference to plaque reduction.

Although it did not require that antigingivitis ingredients also be effective in reducing plaque, the Subcommittee agreed that ingredients that work primarily by means other than plaque reduction would be inappropriate for use in OTC antigingivitis drug products because these products may mask the symptoms of a more serious condition and cause consumers to delay seeking the advice of a dentist. Because the Subcommittee believed that none of the submitted active ingredients acted other than by reducing plaque, this issue was not further discussed.

Therefore, the agency is seeking comment on the basis for allowing an antigingivitis active ingredient that has not demonstrated effectiveness in reducing plaque to bear labeling statements relating to plaque reduction. More importantly, because of the safety concern that antigingivitis ingredients that work by a mechanism other than plaque reduction (e.g., anti-inflammatory) may give consumers a false sense of security by masking symptoms of a more serious disease, the agency is also seeking comment on whether products that are solely antigingivitis agents, i.e., products that do not significantly reduce plaque,