

wild-type organisms obtained from saliva sampling. Representative organisms include, but are not limited to, typed stains of: *Actinomyces viscosus*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Bacteroides forsythus*, *Candida* species, *Streptococcus mutans*, and gram negative enteric rods. Kill-time testing should be conducted using an exposure time of 30 seconds in the presence of exogenous protein. An initial inoculum of 1 percent transmission should be used.

(2) Demonstrate the in vivo activity of the product in a short-term experimental gingivitis study of at least 2 weeks duration. Formulation comparability in this test is established if the new mouthrinse formulation satisfies the "at least as good as" statistical criteria for both plaque and gingivitis with respect to the clinically tested standard, or another generally accepted statistical test of clinical comparability. The criterion for study

validation is statistically significant differences in plaque and gingivitis between the clinically tested standard and the negative control.

(c) *Stannous fluoride dentifrice*.

(1) In addition to tests required by § 355.70 of this chapter, testing should include an in vitro determination of the antimicrobial activity against representative plaque organisms commonly associated with gingivitis. Representative organisms include, but are not limited to, typed stains of: *Actinomyces viscosus*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Bacteroides forsythus*, *Candida* species, *Streptococcus mutans*, and gram negative enteric rods. Testing to determine a product's in vitro antimicrobial activity should include MIC assays, 30-second kill-time studies, or plaque biofilm assays, as appropriate.

(2) Demonstrate the biological activity of the product ex vivo using PGRM.

(d) *Test modifications*. The formulation or mode of administration of certain products may require modification of the testing procedures in this section. In addition, alternative assay methods (including automated procedures) employing the same basic chemistry or microbiology as the methods described in this section may be used. Any proposed modification or alternative assay method shall be submitted as a petition in accordance with § 10.30 of this chapter. The petition should contain data to support the modification or data demonstrating that an alternative assay method provides results of equivalent accuracy. All information submitted will be subject to the disclosure rules in part 20 of this chapter.

Dated: May 12, 2003.

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[FR Doc. 03-12783 Filed 5-28-03; 8:45 am]

BILLING CODE 4160-01-S