

reduction in gingivitis in the stannous fluoride group and a statistically not significant 6.6-percent increase in the bleeding index. There was a 17.8-percent reduction in a Turesky modified Quigley-Hein Plaque Index and a 1.1-percent reduction using the Silness & Loe Plaque Index system. Two graders were used in this study, and they obtained large numerical differences in their assessments at the 3-month assessment period and the final 7-month assessment. No significant shifts in the microbial flora were reported after 3 and 6 months of product use.

Three supportive double-blind and independent studies (CC-174, CC-178, and CC-205) have been reported (Ref. 91). Two studies (CC-174 and CC-178) continued for 6 months and the third study (CC-205) for 2 months. Study CC-174 demonstrated statistically significant differences in the indices from the stannous fluoride group compared with the negative control at the 1.5- and 3-month grading periods. However, all indices were not significant at the 7-month grading period.

Study CC-178 (Ref. 91) revealed no significant differences in the gingival, bleeding, and plaque indices after 2 months use in the stannous fluoride group, compared with the control. After 6 months use, there was a statistically significant difference in the gingivitis index (9.3 percent) in the stannous fluoride group. Significant differences were not detected in the bleeding and plaque indices among the two groups.

Study CC-205 (Ref. 91), which was conducted for 2 months only, revealed a significant difference (15.4 percent) in the gingivitis index of the stannous fluoride group compared with the control. There was a reported 23.9 percent difference in the bleeding index. However, the scores for both groups were exceptionally low compared with all of the study groups. Statistically significant differences in plaque scores among the groups were not detected.

In five of the six studies reported, no significant differences in plaque scores were observed at the end of the evaluation period in subjects using stannous fluoride dentifrices compared with those using a control dentifrice. In 7 of 12 exams in two of the six studies, there was a reported statistically significant reduction in bleeding scores, and in five of the six studies there was a reduction in gingivitis scores associated with the use of stannous fluoride dentifrices.

The Subcommittee evaluated additional information on the effectiveness of a 0.454 percent stannous fluoride dentifrice, including

additional analyses it requested. The results of these analyses helped to establish that the study populations were appropriate for the OTC gingivitis indication recommended by the Subcommittee. Disease levels in the populations used in clinical studies supporting the stannous fluoride dentifrice were only slightly higher than disease levels established in published epidemiological studies and in surveys of oral health status conducted by the National Institute of Dental Research.

Additional data were presented concerning the clinical relevance of the observed beneficial effects of the dentifrice on gingivitis. These data included site-specific analyses demonstrating that a 0.454 percent stannous fluoride dentifrice provided uniform efficacy in reducing gingivitis across the dentition and, in particular, in regions of significant disease. This site-based analysis was further expanded to compare treatment effects (e.g., causing a bleeding site to become a nonbleeding site) with benefits in preventing new disease (e.g., preventing a nonbleeding site from becoming a new bleeding site) during clinical studies. These analyses revealed that, compared to placebo, the stannous fluoride dentifrice was beneficial in preventing and reducing gingivitis and gingival bleeding.

An analysis of the clinical benefits of stannous fluoride in reducing gingivitis compared to increased brushing, flossing, and frequent visits to a dentist indicated that a stannous fluoride dentifrice provides benefits comparable to the improvements observed from these established dental hygiene procedures.

Finally, odds ratio analyses were used to determine the likelihood of an individual deriving a benefit from the use of a stannous fluoride dentifrice. Based on the benefits achieved from dental hygiene and benefits seen in studies CC-191 and CC-238 (Ref. 89), a meaningful benefit for a subject was defined as at least a 33-percent reduction in bleeding. Using this definition, the results of five long-term studies (Refs. 89 and 91) were pooled to estimate an overall odds ratio for improvement relative to a sodium fluoride control. After 3 months of use, the odds ratio was 1.57 with a 95-percent confidence interval of 1.29 to 1.85.

A review of the cited literature indicates that a number of studies examined the effects of stannous fluoride in gels, mouthrinses, and dentifrices. Many of these studies were of short duration, used few subjects, or used special groups of subjects. Thus,

the quality and relevance of the data are, in some instances, questionable. The results are far from uniform in showing benefits from the use of stannous fluoride.

With the exception of the studies submitted by the sponsor, there appear to be few studies involving the use of dentifrices containing stannous fluoride. Ogaard *et al.* (Ref. 92) studied the effect of a stannous fluoride dentifrice on plaque regrowth in 15 subjects for 24 hours and 21 subjects for 3 weeks using a crossover design. Stannous fluoride was compared to a sodium monofluorophosphate dentifrice and a dentifrice without fluoride. Stannous fluoride gave significantly lower regrowth values than monofluorophosphate or placebo.

In the 3-week crossover study (Ref. 92), 21 orthodontic subjects brushed twice daily for 1 minute with a stannous fluoride dentifrice or placebo paste. Less plaque was observed in the stannous fluoride group when the orthodontic brackets were 1 to 5 millimeters (mm) from the gingiva; if the brackets were closer, there was no difference in the effects of the stannous fluoride and the placebo dentifrice. No significant improvement was observed in gingival health regardless of treatment group.

Bay and Rolla (Ref. 93) conducted a double-blind, crossover study in 40 pupils aged 15 years to compare the effects of a stannous fluoride dentifrice and a placebo dentifrice without stannous fluoride. The number of times the dentifrice was used was not stated, and the gender of the pupils was not disclosed. The study continued for 4 weeks. There was reduced plaque formation in the stannous fluoride group and a small reduction in gingival index.

Svatun (Ref. 94) compared the effect of dentifrices containing: (1) 0.4 percent stannous fluoride, (2) a similar dentifrice without stannous fluoride, (3) 0.4 percent stannous fluoride plus stannous pyrophosphate, and (4) 0.8 percent chlorhexidine gel. Twelve female dental students were included and tests lasted for 4 days. The test products were placed in cap splints that covered the teeth only and held in place for 2 minutes twice daily. Subjects rinsed with sucrose (15 percent) for 1 minute every other hour to enhance plaque formation. No mechanical oral hygiene was allowed during the study. The dentifrice containing 0.4 percent stannous fluoride plus stannous pyrophosphate gave significantly lower plaque scores than the dentifrice containing 0.4 percent stannous fluoride alone, or a similar dentifrice without stannous fluoride. There was a wide