



**Study DPIARM 2002-01****Study Classification: Class A****Title: Effects of Stannous Fluoride Dentifrice on Diurnal Plaque Levels – A DPIARM Study****Introduction**

Stannous fluoride dentifrices have been proven effective for the control of gingivitis, though antiplaque effects are variable. In general, almost all short term antiplaque studies of stannous fluoride gels and dentifrices show reproducible antiplaque activity, while longer term clinical observations show less clear effects. Researchers have theorized that artifacts in clinical designs including the lack of control of timing of hygiene (vs. plaque evaluations), tooth stains mimicking ‘plaque coverage’ and lack of sensitivity for categorical plaque indices in brushing populations may contribute to variability in antiplaque effects observed for stannous fluoride in long term large base size clinical studies.

The cost, variability and reduced sensitivity of large base size clinical studies preclude their utility for routine antiplaque assessments of new or improved stannous fluoride dentifrices. Research has shown that Digital Plaque Image Analysis Repeated Measures (DPIARM) presents a unique and sensitive methodology for the assessment of dentifrice benefits for the inhibition of plaque regrowth and plaque removal *in vivo*. This model is now recognized as an excellent test platform toward the assessment of plaque cleaning attributes of dentifrices and toothbrushes.

This study was undertaken to examine antiplaque effects for a stannous fluoride dentifrice containing 0.454 % stannous fluoride. Plaque effects were compared to standard Crest Cavity Protection control.

The study was a repeated measures intervention design with treatment legs each lasting two weeks.

**Methods and Materials**

In test period A — panelists brushed with Crest Cavity Protection (regular flavor). A stick-on label was applied reminding panelists to use only this paste during treatment. In test period B, subjects intervened with brushing instructions for 0.0454% stannous fluoride dentifrice.

This study was a dual treatment intervention design, where a baseline period of two weeks Crest Cavity Protection (hereafter Crest WB) utilization (period A) was followed by two week brushing with test dentifrice containing 0.0454% stannous fluoride (period B):

RH    2 Weeks Crest WB     $\longrightarrow$     RH    2 Week Stannous Fluoride Dentifrice

**Period A**

RH = Rigorous Hygiene

**Period B****Period A-B – Subject Selection**

Subjects entering the protocol were part of a pre-qualified subject panel. These panelists exhibit reproducible ‘off treatment’ plaque levels on teeth both before and after hygiene applications and are

trained/interested in new protocols and oral hygiene techniques. The study objective was to enter and complete 15-20 subjects through periods A-B.

#### Period A

Subjects entered the dental clinic to participate in a 'rigorous hygiene clean up' (see attachment I) which rendered them essentially plaque free at the start of the study treatments. Subjects were provided with Crest WB dentifrice and Oral B 40 toothbrushes. Following rigorous oral hygiene – subjects were instructed to brush as they normally do twice per day throughout the weekend and Monday a.m. During the week subjects were graded on three separate occasions (Tuesday – Friday) permitting an off day. On the evening prior to a grading day, subjects carried out their standard p.m. hygiene immediately prior to retiring in the evening. Subjects were instructed not to eat or drink after this hygiene. Subjects reported to the imaging laboratory in the grading morning prior to any food/beverages and without oral hygiene. Subjects disclosed dental plaque and subjected themselves to 'pre brush a.m.' plaque imaging, after which subjects carried out a timed brushing for 40 seconds with assigned Crest WB dentifrice provided in metered 1.5 gram doses using an Anchor brush. Following brushing, subjects re-disclosed dental plaque and subjected themselves to a second plaque imaging, a so-called "a.m. post brushing plaque imaging". Following rinsing of dentition of disclosing solution, subjects were free to have breakfast and lunch, as well as snacks etc. throughout the grading day. In the afternoon from 2-3:30 p.m. subjects again reported to the dental imaging lab for a third plaque disclosure and measurement, the so-called 'p.m. plaque regrowth measurement'. Subjects were instructed to avoid food and drink for at least ½ hour prior to this evaluation. Subjects left the clinic and followed either their normal hygiene (if following day is not graded) or panel directed hygiene (herein for grading days) with assigned Crest WB dentifrice.

Period A treatments occurred over *two weeks* providing 6 repeat measures of plaque formation and removal. Instructions to subjects for period A are included in Attachment II.

#### Period B

After completing 6 repeat measures during period A, subjects were resupplied as needed with new Oral B 40 toothbrushes and each received assigned 0.454% stannous fluoride dentifrice, blind labeled. No rigorous hygiene preceded continuing on to period B. Following product assignment and supply, subjects were instructed to brush as they normally do twice per day throughout the weekend and Monday a.m. During the week subjects were graded on three separate occasions (Tuesday – Friday) permitting an off day. On the evening prior to a grading day, subjects carried out their standard p.m. hygiene immediately prior to retiring in the evening. Subjects were instructed not to eat or drink after this hygiene. Subjects reported to the imaging laboratory in the grading morning prior to any food/beverages and without oral hygiene. Subjects disclosed dental plaque and subjected themselves to 'pre brush a.m.' plaque imaging, after which subjects carried out a timed brushing for 40 seconds with assigned SnF<sub>2</sub> dentifrice provided in metered 1.5 gram doses using an Anchor brush. Following brushing, subjects re-disclosed dental plaque and subjected themselves to a second plaque imaging, a so-called "a.m. post brushing plaque imaging". Following rinsing of dentition of disclosing solution, subjects were free to have breakfast and lunch, as well as snacks etc. throughout the grading day. In the afternoon from 2-3:30 p.m. subjects again reported to the dental imaging lab for a third plaque disclosure and measurement, the so-called 'p.m. plaque regrowth measurement'. Subjects were instructed to avoid food and drink for at least ½ hour prior to this evaluation. Subjects left the clinic and followed either their normal hygiene (if following day is not graded) or panel directed hygiene (herein for grading days) with assigned SnF<sub>2</sub> dentifrice.

Period B treatments occurred over *two weeks* providing 6 repeat measures of plaque formation and removal. Instructions to subjects for period B are included in Attachment III.

Crest WB and 0.454% stannous fluoride dentifrices were supplied in 4.6 oz tubes with a label to remind them to follow study usage instructions, provide safety contact numbers and report fluoride composition in the product. Oral B toothbrushes were provided for home use - laboratory (Anchor) toothbrushes (fresh/sterile) were used for 'in-laboratory' brushing.

Group coding for products was carried out by the study monitors and was validated by a witness. Coding was recorded in the study record and notebook. Similarly, product distribution was carried out with a duplicate witness to ensure proper distribution of assigned product, signed off by both the study monitor and the subjects.

Crest WB Label:

**Fluoride Toothpaste**  
**Contains 0.15 % (w/v) Fluoride Ion**  
**FOR PANELIST USE ONLY- USE AS DIRECTED**  
**KEEP OUT OF THE REACH OF CHILDREN. Do Not Swallow**  
 In the Unlikely Event of Medical Emergency, Call  
 The Product Safety Line on 1-800-XXX-XXXX.  
 Made by Procter&Gamble Mason Ohio 45040  
 Net Weight 4.6 oz. Lot #2190GF

Stannous Fluoride Label:

**Stannous Fluoride Toothpaste**  
**Contains 0.15 % (w/v) Fluoride Ion**  
**FOR PANELIST USE ONLY- USE AS DIRECTED**  
**KEEP OUT OF THE REACH OF CHILDREN. Do Not Swallow**  
 In the Unlikely Event of Medical Emergency, Call  
 The Product Safety Line on 1-800-XXX-XXXX  
 Made by Procter&Gamble Mason Ohio 45040  
 Net Weight 4.6 oz. Lot #HCS3538-112

#### Evaluation Parameters

Dental plaque levels were evaluated using standardized Digital Plaque Image Analysis. Fluorescein disclosed plaque images were taken under standardized UV lighting with Fuji 2000 imaging camera system. Utilizing standardized RedGreenBlue decision rules, the total area of tooth (in pixels) was assayed which includes plaque free tooth portions as well as plaque covered portions. Plaque covered tooth pixel portions were numerically divided by total tooth area pixels to provide a % of tooth coverage for each image. The % tooth coverage was the assayed parameter in comparative assessments. In separate analyses, plaque pixel coverage was directly compared for efficacy.

Plaque disclosure for imaging utilized a fluorescein buffer solution containing 1800 ppm fluorescein. Prior to photographing, subject plaque was disclosed by fluorescein with the following instructions:

- Rinse for 10 seconds with 25 ml of phosphate buffer;
- Rinse for 1 minute with 5.0 ml of 1800 ppm fluorescein in phosphate buffer;
- Rinse 3 x 10 seconds with 25 ml of phosphate buffer.

Phosphate buffer was comprised of 3.62 grams of monosodium phosphate and 0.349 grams of disodium phosphate diluted to 2 liters with ultrapure water. The final pH of this mixture is 5.5. Solution was prepared fresh - in a GMP approved process laboratory each day.

### Statistical Analysis

Analysis of variance for repeated measures was carried out for comparison of plaque levels for period B stannous fluoride as compared to period A Crest WB dentifrice use.

Panel Subject Inclusion/Exclusion/Continuance Criteria Included the following:

Subjects will be initially screened to ensure:

- No use of other oral hygiene products: use of any other oral hygiene products, mouthrinses, toothpastes, etc. while on the study is prohibited. For daily floss users, flossing is permitted between the back teeth only throughout the study. Chewing gum should be avoided unless it is a daily habit to be maintained consistently throughout the study – NO “whitening” or “dental” gums allowed.
- No dental visits are planned for duration of panel participation;
- No recent (2 week) use of antibiotics;
- No special dietary and diet adjustment expected during the trial;
- Subjects are able to meet all scheduled visits in image analysis clinical and comply with protocol;
- Subjects agree to not participate on other panels, and further agree not to use other oral products than those assigned;
- Subjects are in good general health and good overall dental health (as self assessed and confirmed by subject disclosure that they have routine dental visits);
- Panel subjects report no significant general allergy problems or specific allergies to dyes;
- Panel subjects demonstrate sufficient plaque levels in pilot pre-screening to warrant participation.
- Not pregnant or nursing.
- No prior experience of adverse reactions to currently marketed **oral care** products.

Subjects will sign an informed consent related to these questions.

A copy of the informed consent is shown in attachment IV.

### Safety

Subjects were pre-screened on the reporting of no adverse reactions to conventional products and the absence of allergies to dyes. Subjects were instructed to stop product use and call the number listed on labeling instructions if any important health or safety issues come into question. Reports of any adverse reactions to the study monitors were forwarded to the study safety toxicologist. Note: soft tissues were not evaluated during the study.

## Results

A total of 15 subjects completed both periods A and B of the study protocol during the 4 weeks duration. There were no reports of side effects or adverse events during the course of product use. Table 1 shows results for average plaque levels of subjects during the trial, combining treatments. As shown, panelists varied significantly in their propensity to form dental plaque.

**Table I**  
**Panelist Variation in Plaque Accumulation - Aggregate Averages**  
**Across Treatments**

<b>Subject</b>	<b>Plaque Coverage Fraction %</b>
5	8.84
6	11.04
7	6.66
11	14.43
16	10.91
18	14.28
19	11.26
20	6.37
21	11.73
22	7.05
23	7.68
24	11.45
25	9.30
26	13.45
27	10.88

**$p < 0.0001$  for group, significant differences between individuals**

Additional analyses revealed no visit effects or regression to mean effects in repeated measurements including both the Period A and Period B treatments indicating a valid intervention study where post treatment effects could be ascribed to product only.

Separate assessments of pre brushing a.m. plaque, post brushing a.m. plaque and afternoon plaque regrowth p.m. plaque are highlighted in Tables 2-4.

**Table 2**  
**Plaque On Teeth - A.M. Regrowth - PreBrushing n = 15**

Treatment	Plaque Coverage Fraction %	% Reduction vs. White Box Crest	p value vs. WB (ANOVA)
Stannous Fluoride Dentifrice	11.81	30.3	< 0.05
WB Control	16.95	-----	-----

**Table 3**  
**Plaque on Teeth - Post Brushing A.M. n = 15**

Treatment	Plaque Coverage Fraction %	% Reduction vs. White Box Crest	p value vs. WB (ANOVA)
Stannous Fluoride Dentifrice	6.84	14.4	< 0.05
WB Control	7.99	-----	-----

**Table 4**  
**Plaque On Teeth - P.M. Regrowth n=15**

Treatment	Plaque Coverage Fraction %	% Reduction vs. White Box Crest	p value vs. WB (Anova)
Stannous Fluoride Dentifrice	8.16	34.9	<0.05
WB Control	12.53	-----	-----

Stannous fluoride dentifrice effected significant reductions in dental plaque coverage at each sample measuring point including a.m. pre brushing (overnight growth), post brushing and in the afternoon following plaque growth from the morning brushing (p.m. regrowth). The average effectiveness of stannous fluoride dentifrice averaged 14-35 % relative to the negative control – Crest WB.

### **Discussion**

Stannous fluoride dentifrices have been proven effective for the control of gingivitis, though antiplaque effects are variable. This study was undertaken to examine antiplaque effects for a stannous fluoride dentifrice containing 0.454 % stannous fluoride. Plaque effects were compared to standard Crest Cavity Protection control.

Stannous fluoride dentifrice was observed to produce significant inhibition of dental plaque in three discrete measurements points in this repeated measurement protocol. Thus, stannous fluoride was proven effective in:

- Inhibiting plaque development following overnight brushing until the morning, as compared with Crest WB control dentifrice;
- Removing plaque to a significantly lower level of coverage following brushing, as compared with Crest WB control dentifrice;
- Inhibiting plaque development following morning brushing until mid afternoon, as compared with Crest WB control dentifrice.

These results strongly support the significant and clinically meaningful reductions in dental plaque formation provided by 0.454% stannous fluoride dentifrice.

# Attachment I

## Clean Up (Rigorous Oral Hygiene) Protocol for DPIARM 2002-02 Period A

The purpose of this protocol is to provide a rigorous oral hygiene intervention of subjects participating in plaque growth and removal evaluations in the Digital Plaque Imaging Analysis Repeated Measures protocol – rendering subjects essentially plaque free via visible grading of facial surfaces.

Upon entry into DPIARM protocol subjects are provided with a personal hygiene kit including Oral B 40 toothbrushes, dental picks, toothpicks, dental floss. These are personally used in Rigorous Self Oral Hygiene procedures.

Subjects will present to the dental clinic during scheduled visits. They will be provided with a fresh Oral B 40 toothbrush. Subjects will be instructed to a premeasured dose (1.5gm) of Ultrabrite Whitening Dentifrice (high abrasive content for enhanced cleaning) and to brush their teeth for 2 full minutes – timing this with the laboratory timer. Following brushing subjects will be instructed to rinse their mouths with tap water. At this point subjects will disclose their remaining plaque with DPIARM fluorescein dye using a fluorescein buffer solution containing 1800 ppm fluorescein. Disclosure will be carried out as follows:

- Rinse for 10 seconds with 25 ml of phosphate buffer;
- Rinse for 1 minute with 5.0 ml of 1800 ppm fluorescein in phosphate buffer;
- Rinse 3 x 10 seconds with 25 ml of phosphate buffer.

Phosphate buffer is comprised of 3.62 grams of monosodium phosphate and 0.349 grams of disodium phosphate diluted to 2 liters with ultrapure water. The final pH of this mixture is 5.5. Solution is prepared fresh - in a GMP approved process laboratory each day.

Following plaque disclosure, subjects will self examine remaining plaque coverage to their teeth employing a UV blacklight available in the clinic. Subjects will be asked to clean areas of residual plaque with a wet brush, tooth picks, interdental cleaners (all provided fresh in sterile packaging) until plaque is visibly removed to their examination. Subjects will then be asked to floss their entire dentition with Oral B waxed dental floss available to each subject. Lastly subjects are asked to brush a final time with Ultrabrite dentifrice for 1 minute and rinse with water.

Subjects will place their floss and picks etc. into their hygiene kit and begin using their assigned toothpaste or other products during at home brushing.

## Attachment II

### DPIARM2002-02 Period A SUBJECT INSTRUCTIONS

In Period A we will establish baseline levels of dental plaque formation and removal within your normal hygiene regimen

You will begin with an initial rigorous self applied oral hygiene program where toothbrushing, flossing and interdental cleaners will be used to obtain a virtually plaque free dentition, verified by fluorescein disclosure. (See Rigorous Hygiene Instructions). You will be provided with regular Crest Dentifrice in blank labeled tubes. Following three days product use to obtain a rough equilibrium of hygiene - you will begin reporting to the Imaging Laboratory before morning toothbrushing (before you have food or drink). Three days a week, plaque will be disclosed and graded. Following two weeks of product use (6 plaque assessments over the two weeks) you will again be asked to perform rigorous oral hygiene and will be re-supplied with a new toothpaste.

While using your assigned product, your oral hygiene, brushing regimen and dietary habit allowances will be dependent upon whether you are planned for a plaque evaluation the next day. While on this test you should not carry out additional hygiene measures. Flossing is permitted within the directions of the study monitor – e.g. only on molar teeth not graded by imaging.

#### Non-Graded Days:

If you are NOT scheduled for a plaque evaluation on the next day, you should follow your normal hygiene practices, using your assigned toothpaste with brushing performed in the morning and evening prior to bed. This latter habit is particularly important to maintain. This will include the weekends. Use only your assigned Crest Regular toothpaste during this period. Flossing is permitted within the directions of the study monitor – e.g. only on molar teeth not graded by imaging.

#### Graded Days:

Graded plaque days are defined by the period ranging from the EVENING BEFORE a scheduled plaque evaluation to the AFTERNOON FOLLOWING a scheduled plaque evaluation. To be clear, graded days may occur on sequential days – on which this protocol must similarly be followed.

**Evening Brushing:** For scheduled graded days you will carry out an evening toothbrushing with assigned Crest Regular dentifrice prior to bed. Note, in this protocol your evening brushing will be a NORMAL TOOTHBRUSHING including all tooth surfaces front and back as you normally carry out. You can then spit out your toothpaste and rinse with water if this is your normal regimen, following brushing. After your toothbrushing please refrain from food or drink before bed, water drinking is allowed at any time.

**Morning:** In the morning of a grading day DO NOT CARRY OUT HYGIENE, EAT OR DRINK AT BREAKFAST PRIOR TO YOUR PLAQUE GRADE. Please come in to the clinic for plaque grading in the a.m. You will disclose and have plaque graded. Following which, you will carry out a brushing with your assigned dentifrice using a metered amount of paste with blind timing. Follow the monitors directions. You will brush all surfaces, brushing as you normally do. Following this you will have another plaque grade. After

plaque grading you can rinse your mouth out and have breakfast and lunch and snacks at your leisure. No other oral hygiene is permitted during the grading day.

**Mid Afternoon:** Return to dental clinic for a final plaque grading after 2 p.m. Please refrain from eating and drinking for ½ hour prior to your plaque grade.

**Evening Hygiene:** Follow routine prescribed for either graded day or non-graded day depending upon schedule

## SUBJECT INSTRUCTIONS Period A

### Period A Schedule

Friday p.m.	Subject reports to lab for rigorous Oral Hygiene to 'Plaque Free': Brush + Floss + Interdental Cleaners  Subject receives test product
Saturday	Subject brush ad - lib 2X per day
Sunday	Subject brush ad - lib 2X per day
Monday	Subject brush ad - lib 2X per day – possible p.m. 'grading day' regimen if scheduled for plaque grade next day
Tuesday - Friday	Follow regimen for 'grading day' or 'non-grading day as appropriate
Saturday - Sunday	Subject brush ad - lib 2X per day
Monday	Subjecty brush ad - lib 2X per day – possible p.m. 'grading day' regimen if scheduled for plaque grade next day
Tuesday - Friday (week 2)	Follow regimen for 'grading day' or 'non-grading day as appropriate
Friday p.m. week 2	Subject members receive New Test Product

**SUBJECT INSTRUCTIONS Period A****I DO NOT HAVE PLAQUE GRADED TOMORROW**

- **BRUSH AS NORMAL IN MORNING**
- **BRUSH AS NORMAL IN EVENING**
- **NO OTHER ORAL PRODUCTS PLEASE**

**I DO HAVE PLAQUE GRADED TOMORROW – EVENING AND GRADED DAY SCHEDULE**

- **BRUSH IN EVENING AS NORMAL – ALL SURFACES OF TEETH – NO FOOD OR DRINK BEFORE BED WATER OK**
- **REPORT TO CLINIC IN A.M. – NO HYGIENE OR BREAKFAST --- NO BEVERAGES EXCEPT WATER**
- **FOLLOW CLINIC INSTRUCTIONS FOR BRUSHING AND PLAQUE GRADING**
- **LEAVE CLINIC – EAT BREAKFAST AND LUNCH AS NORMAL NO OTHER HYGIENE**
- **IN P.M. – RETURN TO CLINIC FOR FINAL PLAQUE GRADE – MAKE SURE NOT TO EAT OF DRINK FOR ½ HOUR PRIOR TO PLAQUE GRADE**

## **DPIARM2002-02 Period B SUBJECT INSTRUCTIONS**

In Period B we will establish the effects of baseline or test dentifrice on dental plaque formation and removal within your normal hygiene regimen.

No rigorous hygiene procedure will be done prior to beginning this phase of the study. You will be provided with regular Crest Dentifrice or a test dentifrice in blank labeled tubes. You will use paste as directed each and every day. Following three days product use to obtain a rough equilibrium of hygiene - you will begin reporting to the Imaging Laboratory before morning toothbrushing (before you have food or drink). Three days a week, plaque will be disclosed and graded. Following two weeks of product use (6 plaque assessments over the two weeks) you will again be asked to perform rigorous oral hygiene and will be re-supplied with a new or baseline toothpaste product.

While using your assigned product, your oral hygiene, brushing regimen and dietary habit allowances will be dependent upon whether you are planned for a plaque evaluation the next day. While on this test you should not carry out additional hygiene measures. Flossing is permitted within the directions of the study monitor – e.g. only on molar teeth not graded by imaging.

### **Non-Graded Days:**

If you are NOT scheduled for a plaque evaluation on the next day, you should follow your normal hygiene practices, using your assigned toothpaste with brushing performed in the morning and evening prior to bed. This latter habit is particularly important to maintain. This will include the weekends. Use only your assigned toothpaste during this period. Flossing is permitted within the directions of the study monitor – e.g. only on molar teeth not graded by imaging.

### **Graded Days:**

Graded plaque days are defined by the period ranging from the EVENING BEFORE a scheduled plaque evaluation to the AFTERNOON FOLLOWING a scheduled plaque evaluation. To be clear, graded days may occur on sequential days – on which this protocol must similarly be followed.

**Evening Brushing:** For scheduled graded days you will carry out an evening toothbrushing with assigned dentifrice prior to bed. Note, in this protocol your evening brushing will be a NORMAL TOOTHBRUSHING including all tooth surfaces front and back as you normally carry out. You can then spit out your toothpaste and rinse with water if this is your normal regimen, following brushing. After your toothbrushing please refrain from food or drink before bed, water drinking is allowed at any time.

**Morning:** In the morning of a grading day DO NOT CARRY OUT HYGIENE, EAT OR DRINK AT BREAKFAST PRIOR TO YOUR PLAQUE GRADE. Please come in to the clinic for plaque grading in the a.m. You will disclose and have plaque graded. Following which, you will carry out a brushing with your assigned dentifrice using a metered amount of paste with blind timing. Follow the monitors directions. You will brush all surfaces, brushing as you normally do. Following this you will have another plaque grade. After plaque grading you can rinse your mouth out and have breakfast and lunch and snacks at your leisure. No other oral hygiene is permitted during the grading day.

**Mid Afternoon:** Return to dental clinic for a final plaque grading after 2 p.m.. Please refrain from eating and drinking for ½ hour prior to your plaque grade.

**Evening Hygiene:** Follow routine prescribed for either graded day or non-graded day depending upon schedule

## SUBJECT INSTRUCTIONS Period B

### Period B Schedule

Friday p.m.	Subject reports to lab for rigorous Oral Hygiene to 'Plaque Free': Brush + Floss + Interdental Cleaners  Subject panel receives test products
Saturday	Subject brush ad - lib 2X per day
Sunday	Subject brush ad - lib 2X per day
Monday	Subject brush ad - lib 2X per day – possible p.m. 'grading day' regimen if scheduled for plaque grade next day
Tuesday - Friday	Follow regimen for 'grading day' or 'non-grading day as appropriate
Saturday - Sunday	Subject brush ad - lib 2X per day
Monday	Subject brush ad - lib 2X per day – possible p.m. 'grading day' regimen if scheduled for plaque grade next day
Tuesday - Friday (week 2)	Follow regimen for 'grading day' or 'non-grading day as appropriate
Friday p.m. week 2	p.m. Members report again to lab for Rigorous Oral Hygiene to 'Plaque Free': Brush + Floss + Interdental Cleaners

**SUBJECT INSTRUCTIONS Period B****I DO NOT HAVE PLAQUE GRADED TOMORROW**

- **BRUSH AS NORMAL IN MORNING**
- **BRUSH AS NORMAL IN EVENING**
- **NO OTHER ORAL PRODUCTS PLEASE**

**I DO HAVE PLAQUE GRADED TOMORROW – EVENING AND GRADED DAY SCHEDULE**

- **BRUSH IN EVENING AS NORMAL – ALL SURFACES OF TEETH –**
- **NO MORE FOOD OR DRINK BEFORE BED - WATER OK**
- **REPORT TO CLINIC IN A.M. – NO HYGIENE OR BREAKFAST --- NO BEVERAGES EXCEPT WATER**
- **FOLLOW CLINIC INSTRUCTIONS FOR BRUSHING AND PLAQUE GRADING**
- **LEAVE CLINIC – EAT BREAKFAST AND LUNCH AS NORMAL NO OTHER HYGIENE**
- **IN P.M. – RETURN TO CLINIC FOR FINAL PLAQUE GRADE – MAKE SURE NOT TO EAT OR DRINK FOR ½ HOUR PRIOR TO PLAQUE GRADE**

**Attachment IV**  
**DPIARM 2002-02 Plaque Imaging Study**  
**Study/Imaging Team Consent Form**

**Study Type:** **DPIARM2002-02 Period A and B**  
**Digital Plaque Image Analysis Repeated Measures Study**

**Nature and Purpose of the Study:** You are being asked to participate in a plaque imaging study to evaluate the ability of a test dentifrice to both remove and prevent plaque accumulation on the surfaces of the teeth. The study will involve brushing your teeth with standard Crest Regular fluoridated dentifrice. The test will comprise two periods:

- Period A – where you will brush for two weeks with standard dentifrice to establish a baseline.
- Period B – where you will brush for two weeks with baseline or test dentifrice.

During the test, you will be asked to return to the imaging room for scheduled brushings and imaging on 2-4 (Tues-Fri) days per week for a total of 6 days of imaging for each testing period. During the study you will be required to only use the test products assigned, and set aside all other oral hygiene practices (i.e. floss, mouthwash, dental picks, etc.).

**Ingredients and Formulations:**

**Crest WB Dentifrice:** Crest WB dentifrice will be used during period A by all panelists. This is a non-tartar control standard fluoridated paste known commercially as Crest Cavity Protection Regular Paste. This toothpaste contains standard amounts of fluoride and cleaning abrasives.

**Test Dentifrice:** Half of the panelists will use a test dentifrice containing 0.454% stannous fluoride. This test formulation is approved for use through toxicology.

**Plaque Disclosure – Dye:** During the study you will be rinsing with sodium fluorescein solution, which temporarily dyes the dental plaque permitting us to photograph it and determine the area of tooth coverage. This dye is safely used in various medical procedures, however like all food dyes has the potential to produce allergic response in susceptible individuals. If you have had a previous reaction to food dyes or to fluorescein dye please notify the study monitor.

**Study Requirements: *To participate, you must confirm/agree to the following:***

- No use of other oral hygiene products: - you are required not to use any other oral hygiene products, mouthrinses, toothpastes, etc. while on the study. For daily floss users, you may floss between the back teeth only throughout the study. Avoid chewing gum unless it is a daily habit you will maintain consistently throughout the study – **NO “whitening” or “dental” gums allowed.**
- No dental visits are planned for duration of panel participation;
- No recent (2 week) use of antibiotics;
- No special dietary and diet adjustment expected during the trial;
- Presence of ‘color matched’ restorations (filling) work on facial (front) surfaces of the front teeth.
- Subjects are able to meet all scheduled visits in image analysis clinical and comply with protocol;
- Subjects agree to not participate on other panels, and further agree not to use other oral products than those assigned;
- Subjects are in good general health and good overall dental health (as self assessed and confirmed by subject disclosure that they have routine dental visits);
- Subjects report no significant general allergy problems or specific allergies to dyes;
- Subjects demonstrate sufficient plaque levels in pilot pre-screening to warrant participation.
- Do not participate in this study if you pregnant or nursing.
- You do not experience adverse reactions to currently marketed **oral care** products.

**Study Procedures:**

Please see specific instructions.

**Reasonably Foreseeable Risks Or Discomforts:**

- **Formulations:** The formulations for home-use are approved by safety/toxicology for use in this study. The ingredients in these products are currently used in oral care products and/or are commonly used in foods. However there is a very small chance that some ingredients in these products may have potential for increased irritation and / or sensitivity. These types of effects may include slight tingling, burning, redness, swelling or other mouthfeel changes. In the unlikely event that you should experience any such sensations in the mouth after use of the products, you should notify the contact telephone number on the product label. Depending upon the complaint, you may be instructed to end study participation and be evaluated by a dentist.
- **Plaque Disclosure:** During the plaque evaluation periods, you will rinse with fluorescent dye solution to disclose plaque. Sodium fluorescein applied topically for plaque disclosure has not produced allergy symptoms to our knowledge. On the other hand, fluorescein - when ingested orally at doses 30-70 times those used in plaque disclosure has produced minor allergic reactions in the

form of itching or hives. You should immediately report any unusual symptoms, e.g. itching or hives, following fluorescent dye use to study monitor, the project toxicologist or seek treatment at Health Services.

- **Study Protocol - Hygiene variations:** The brushing protocols and hygiene variations are not expected to produce substantial changes in oral health while participating in the study. If you experience changes in oral condition that you think may be related to the brushing protocol, please report this to the study monitor. Depending upon the complaint, you may be instructed to end study participation and be evaluated by a dentist.

**Benefits To Be Expected:** Other than payment for participating, you may or may not experience any personal benefits from using products in this study. You will receive compensation as described by the study monitor for your full participation.

**Study Participation/Withdrawal:** Your participation in this study is voluntary. You may withdraw your consent and discontinue participation at any time. Should you fail to comply with study procedures, your participation in this study may be terminated. If you withdraw, or your participation is terminated, your compensation may be prorated based on your participation.

**Confidentiality:** The results obtained from this study, excluding personal information which would identify you, will be reviewed by the examiners of this study.

I have read and understand the information contained in this informed consent and agree to take part in this study. I further understand that my participation is voluntary, and that I am free to withdraw this consent and discontinue my participation at any time without prejudice, I have received a copy of this informed consent.

**Subject:**

\_\_\_\_\_  
Printed Name

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

**Witness:**

\_\_\_\_\_  
Printed Name

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date