Independent Scientific Clinical Study of Safety and Efficacy: POPWHITE® Toothpaste

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CLAIMS TESTED:
1. Whitens teeth __ shades in 14 days simply by brushing 2x/day
2. Safe to use
3. Doesn't cause irritation of gums or tooth pain/sensitivity
4. Whitens as well as a leading whitening toothpaste that contains peroxide (Colgate Optic White)
5. Whitens better than the market leading "whitening" toothpaste that doesn't contain peroxide (Crest Vivid White)
6. This whitens _____% better than the market leading "whitening" toothpaste.
7. This whitens ___% better than the "whitening" toothpastes that actually DO contain whitening ingredients, like peroxide.

SUBJECTIVE CLAIMS: **The following claims will be verified using subjective survey**
1. Taste wasn't offensive/tasted pleasant
2. Believe to be convenient, easy, fast to use
3. Would recommend to friend
4. Prefer this method of whitening to using strips/trays
5. Pleasant experience
6. Would use again

MAJOR OBJECTIVES: The major objective of the study was to test the safety and effectiveness of the newly developed POPWHITE® Toothpaste, which contains POP Technology that delivers a whitening enhancement formulation to the teeth while brushing. The recommended protocol is brushing twice daily for 2 minutes, yielding a 4-minute daily total exposure.

The study was conducted in accordance with the Guidelines for Good Clinical Practice and ADA Guidelines for Testing of Toothpaste and Home Whitening Products.

STUDY METHODS: 60 subjects in three (3) groups as shown in Table 1 below.

Table 1

Manufacturer	Brand	Active Ingredient
POPWHITE **EXPERIMENTAL; N=20**	Truly White	POP Technology
Colgate-Palmolive **CONTROL OW; N=20**	Optic White	1% Hydrogen Peroxide
Procter and Gamble **CONTROL VW; N=20**	Crest Vivid White	Hydrated Silica, sodium hexametaphosphate, and detergents

Twenty subjects were assigned to each group. The same toothbrushes (Oral-B Pro-Health Soft Full Head Toothbrush) were given to all 60 subjects to brush their teeth. Before starting the study, oral hygiene instruction was given to subjects, including tooth brushing times and technique. Subjects were instructed to brush their teeth twice a day, in the morning after breakfast and in the evening before sleeping. Subjects were not given any instructions about drinking and eating, and were allowed to follow their previous patterns for these activities.

As per the protocol established by the American Dental Association, two experienced, trained examiners, who have achieved a 90% agreement during a pre-study calibration, performed the oral soft tissue examinations and shade assessments at baseline. Shade assessments were made by comparing the shade tabs from a Vita shade guide, with the facial aspects of the upper and lower central incisor teeth and selecting the closest matching shade.

Teeth shades of subjects were evaluated, near one window, between 10:00 am and 12:00 am in natural light, so as to simulate real life perceptions of teeth lightness. The examinations took place at the following time intervals: Baseline, Day 1, Day 2, Day 3, Day 4, Day 5, Day 6, Day 7 and Day 14. All subjects were asked to sign consent forms and were asked to complete a brief baseline consumer perception survey.

Subject Demographics
Subjects were chosen from a pool of candidate living in the South Florida area (Palm Beach and Broward Counties). Each Experimental and control group will contain at least 7 persons who have identified themselves as cigarette smokers (at least 1/2 pack per day). All subjects will range between 18 – 85 years in age.

Product Use Protocols
Procedure for the Experimental and Control Toothpastes were as follows:
1. Baseline tooth shade was recorded using Vita-Shade Guide and Spectrophotometer
2. Participants were provided with a toothbrush and 3.5 oz. test or control toothpaste with written instructions
3. Participants were given a short pre-use survey
4. Participants dispensed a bead of test toothpaste on the toothbrush and were timed as they brush for 2 minutes, then rinse.
5. Participants were instructed to follow tis procedure and use product twice daily for 4 minutes total exposure time each day. The product was to be used for 2 weeks.

Statistical analysis
Data from the study were entered into statistical software (SSPS for Mac, Version 15.0; SPSS Inc, Chicago, USA). The Student's T-test, Fisher's exact chi-square test, and ANOVA analysis was used to compare the quantitative data from the study. Results were tested for significance at the ($P<0.05$) level.

Ethics
An Expedited IRB Study Approval application was submitted due to the non-invasive nature of the proposed study. The study was conducted in accordance with the Guidelines for Good Clinical Practice and ADA Guidelines for Testing Home Use Whitening Products. All procedures were reviewed by PSC Research Institute Principal Investigator (Dr. Giniger) and followed manufacturer's published or proposed directions for treatment application. Study subjects were required to sign an informed consent form and met all entrance requirements.

Randomization
Randomization will be handled as follows: All of the Experimental and Control products will be placed into identical, numbered white paper bags to assist with the blind randomization process. Each subject will receive a computer generated random number between 1 and 80, and each subject will receive a random white box that contains one of the 3 Control or Experimental product.

Inclusion Criteria:
1. Male and female Subjects in good general health and between the age 18 to 85 years at the time of enrollment with a tooth shade greater than or equal to A3 for all six non-restored maxillary anterior teeth prior to treatment.
2. Subjects have to be willing to not use any other dental whitening product, with the exception of toothpaste, during the course of the study
3. Preference will be given to person who smoke at least ½ pack of cigarettes per day (at least 7 participants who smoke in each group)
4. Preference will be given to study participants over the age of 50 (at least 7 participants over age 50 in each group)
5. Participants will be asked to refrain from consumer dark foods / beverages that tend to stain teeth for ½ hour after the application of their assigned product during the course of the study.

Exclusion Criteria:
1. Subjects with fewer than 6 gradable anterior maxillary teeth or subjects whose anterior maxillary teeth have had restorations, dentures or dental implants.
2. Subjects who have had a dental cleaning procedure within the last 6 months.
3. Subjects who reported current sensitivity on maxillary anterior teeth.
4. Subjects with a history of sensitivity to peroxides or glycols and a documented history of untreated caries, dentin exposure, recession, abfractions, cracks or chips on the teeth to be treated or severely malposed anterior teeth.
5. Subjects with a history of diabetes or any other systemic disease, which in the Investigator's opinion could have interfered with the assessment of the oral soft/hard tissue
6. Subjects taking any photo-reactive medications
7. Subjects who had previously used teeth whitening gels or peroxide-based teeth bleaching products within the last 6 months.

Assessment of Tooth Color Change
Two examiners were available to assess Vita Shade Score. The primary examiner was a well experienced and calibrated dentist. The second examiner is Dr. Giniger, who also served as a project director and is a published and well known, experienced authority in the measurement of teeth color. For consistency's sake, and to ensure maximum impartiality, the primary examiner determined all Vita Shade Scores. The second examiner (Dr. Giniger; project director) was used when the primary examiner felt that he had become un-blinded (with regard to which product is being used) , or when he felt that he could not decide on a definitive shade match. When the second examiner was called into action, the decisions of the second examiner was used as the final determination of Vita Shade Score.

Shade change was calculated by determining the change in the number of shade guide units that occurred toward the lighter end of the value-oriented list of shade tabs. Although the scale is not in the truest sense linear, the changes were treated as representing a continuous and approximately linear ranking for the purpose of analysis as is standard practice in the dental literature.

As detailed below, the Vita Shade Score was used to determine the general efficacy of teeth whitening caused by the Experimental and Control products. In order to measure the efficacy of deep set stain removal, we utilized a specially calibrated spectrophotometer (Minolta CR-321Chromameter) in accordance with ADA guidelines for acceptance of teeth whitening products (reference: Tavares et al. Light augments tooth whitening with peroxide. J Am Dent Assoc 2003;134;167-175) with the meter set at a depth of 1.5mm. We intend to report here both measures of teeth whiteness (Superficial and 1.5 mm Deep).

Vita Shade Assessment For Measurement of Surface Tooth Color
The principal investigator assessd tooth color change of each subject's teeth in a room with color corrected lighting (5500K light bulbs). A blue bib was placed over clothing and the dental light turned off. Subjects were instructed not to wear lipstick and to sit in a position where the teeth in the maxillary arch were parallel to the floor during the evaluation. Anterior maxillary teeth #6 through #11 will be used for assessment. Gradations within the value-oriented Vita® Shade Guide (Vita Zahnfabrick GmbH, Sackingen, Germany) were utilized. The shade guide was arranged in the chromatic rank order [1 = lightest shade; 16 = darkest shade] as recommended by the manufacturer and described in the literature. Shade change was calculated by determining the change in the number of shade guide units that occurred toward the lighter end of the value oriented list of shade tabs. Although the scale is not in the truest sense linear, the changes will be treated as representing a continuous and approximately linear ranking for the purpose of analysis as is standard practice in the dental literature.

Spectrophotometer Assessment of Tooth Lightness
To measure the ability of the Experimental and Control Products to affect deep set stains, we used a Minolta CR-321 spectrophotometer to record triplicate L* measurements of the baseline and maxillary central incisor teeth at each examination interval. The meter was calibrated according to manufacturer's instructions and set at a depth of 1.5 mm for the measurement of deep set stains. For each measurement, the spectrophotometer tip was carefully placed in the center of each tooth, assuring that it was parallel and flush against enamel surface. After each reading obtained, the meter tip was repositioned carefully in a similar manner. The mean of the three-recorded L* values for each tooth was entered into a spreadsheet for each examination interval. The group means, standard deviation calculations and T-test statistical analyses were derived from these values. We used L* as the objective measurement of tooth lightness because it is derived from the CIE LAB perceptual color space, the most commonly used color space in studies of human tooth color. We also believe that using L* would yields most accurate and objective assessment of whitening efficacy because L* vector is the only one that is visually uniform. Furthermore, small movements in L* value are more clinically visible than a* or b*, and hence likely to be the most clinically relevant. Finally, we believe that L* to be a good choice since the overall objective of tooth bleaching is to visibly "lighten" the color of teeth.

RESULTS AND SUMMARY OF FINDINGS:

DEMOGRAPHICS: All subjects were residents of South Florida and all major races were represented in the study groups. All subjects were healthy and had healthy, natural maxillary teeth that were judged to have a Vita shade of A3 or darker.

1. There were 20 subjects in each group and each group was balanced for mean age and gender.
2. At least 7 persons in each group identified themselves as cigarette smokers (at least 1/2 pack per day).

A summary of the demographics is found in Table 1 below:

TABLE 1				
DEMOGRAPHICS OF STUDY SUBJECTS				
STUDY GROUP	**MEAN AGE**	**S.D.**	**NUMBER OF SMOKERS**	**M:F RATIO**
CONTROL VW (n=20)	45.2	± 16.3	7	10:10
CONTROL OW (n=20)	46.9	± 18.4	7	10:10
POPWHITE TEST (n=20)	44.2	± 17.6	7	10:10
NOTES: All Groups balanced for age, gender and number of smokers Each Group contained 7 subjects who were over 55 years of age				

WHITENING EFFICACY RESULTS: We judged the whitening efficacy of the Control and Test products using Vita Shade Score analysis and confirming the results with a Minolta CR-321 Spectrophotometer according to ADA Guidelines and industry standards.

Table 2 below shows the "Mean Vita Shade Score" for all the subjects groups at the nine (9) measurement intervals. It shows that only POPWHITE caused a significant improvement ($p < 0.05$) after just one use. It also shows that it works 57% better than Colgate Optic White and 97% better than Crest Vivid White after 14 days of use.

TABLE 2									
MEAN VITA SHADE SCORES AT EACH EXAMINATION INTERVAL - ALL SUBJECTS CONTROL VW = Crest Vivid White CONTROL OW = Colgate Optic White EXPERIMENTAL = POPWHITE Whitening Toothpaste									
STUDY GROUP	**BASE**	**DAY 1**	**DAY 2**	**Day 3**	**DAY 4**	**DAY 5**	**DAY 7**	**DAY 10**	**DAY 14**
CONTROL VW (n=20)	9.85	9.75	9.65	9.50	9.25	8.95	8.40	8.40	8.00
CONTROL OW (n=20)	9.85	9.70	9.40	9.00	8.65	8.05	7.45	7.10	6.60
EXPERIMENTAL (n=20)	9.85	8.35	8.00	7.60	7.25	6.65	5.90	4.95	4.20
NOTES: Experimental Toothpaste works 90% better than Control VW (significant; $p < 0.001$) Experimental Toothpaste works 57% better than Control OW (significant; $p < 0.001$) Experimental Toothpaste was the only toothpaste to statistical improvement after one use ($p = 0.034$)									

Furthermore, as reported in the **Table 2**, the Experimental toothpaste works statistically significantly better than all the control toothpastes at <u>ALL</u> measurement intervals. All groups started with the same mean baseline tooth shade, but as early as Day 1, the Experimental Group (POPWHITE Toothpaste) performed statistically better than all the control toothpastes tested, including those containing peroxide as an active ingredient.

Table 3 shows the shade improvement for each product on each examination day. Only the Experimental Group showed real statistical improvement after just 1 day. At day 14, the Experimental group improved 5.65 shades and this was high statistically better than all the other toothpaste control groups. Crest Vivid White (whitening toothpaste without peroxide) achieved only 1.85 shades after 14 days; the Experimental Group achieved this same level of whitening 7 times faster (Day 2). Optic White (whitening toothpaste with 1% hydrogen peroxide) achieved only 3.25 shades after 14 days; the Experimental Group achieved this same level of whitening 2 times faster (before Day 7).

TABLE 3							
MEAN VITA SHADE CHANGE AT EACH EXAMINATION INTERVAL CONTROL VW = Crest Vivid White CONTROL OW = Colgate Optic White EXPERIMENTAL = POPWHITE Whitening Toothpaste							
STUDY GROUP	**DAY 1**	**DAY 2**	**Day 3**	**DAY 4**	**DAY 5**	**DAY 7**	**DAY 10**	**DAY 14**
CONTROL VW (n=20)	0.10	0.20	0.35	0.60	0.90	1.45	1.45	1.85
CONTROL OW (n=20)	0.15	0.45	0.85	1.20	1.80	2.40	2.75	3.25
EXPERIMENTAL (n=20)	1.50	1.85	2.25	2.60	3.20	3.95	4.90	5.65
NOTES: Experimental Toothpaste Works 7x Faster than Control VW Toothpaste Experimental Toothpaste Works more than 2x Faster than Control OW Toothpaste							

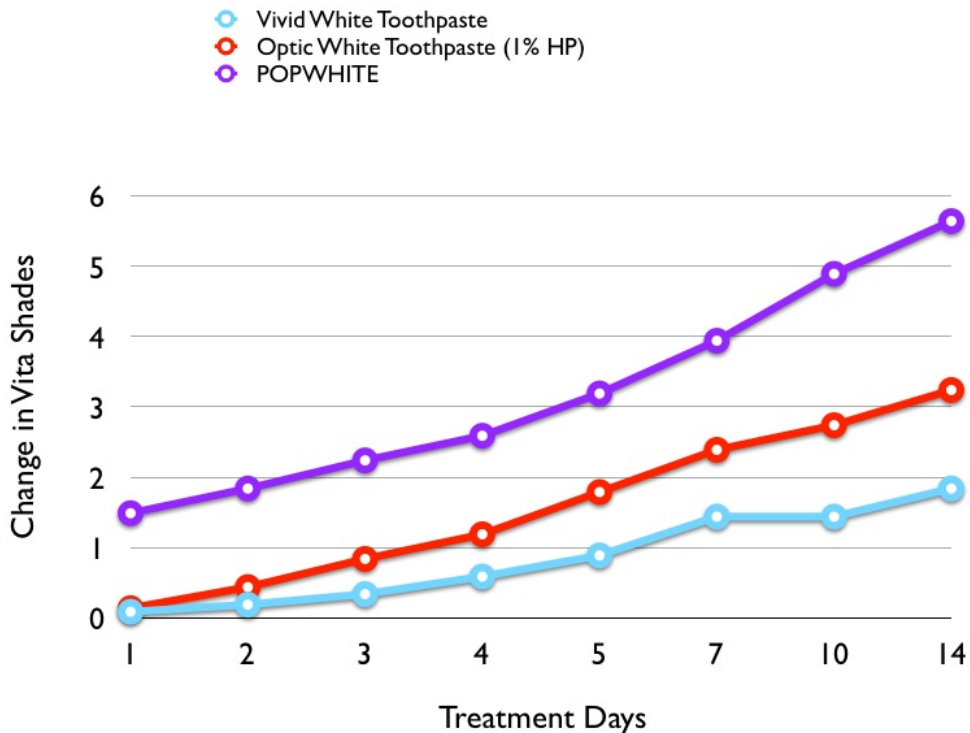

VITA SHADE SCORE IMPROVEMENT OVER TIME

Table 4 below shows the "Mean Spectrophotometer L* Score" for all the subjects groups after the first measurement interval. It shows that only POPWHITE caused a significant improvement (p < 0.05) in brightening after just one use. It also shows that it works 5x better than Colgate Optic White and 37x better than Crest Vivid White.

TABLE 4			
SPECTROPHOTOMETER L* (BRIGHTNESS) Minolta CR321 Spectrophotometer Reading @ 1.5 mm Beneath Enamel Surface (Larger L* Score is Brighter Tooth)			
STUDY GROUP	**L* BASELINE**	**L* END OF TX**	**CHANGE (Δ L*)**
CONTROL VW (n=20)	64.49	64.57	0.08
CONTROL OW (n=20)	65.45	66.10	0.65
EXPERIMENTAL (n=20)	66.73	69.74	3.01
NOTES: VW & OW Toothpastes did not improve teeth brightness (N.S.; p<0.05) Truly Whitening showed significant brightness improvement (significant; p>0.05)			

BRIGHTENING ABILITY OF TOOTHPASTES AFTER ONE USE
(Change in L* Spectrophotometer Scores)
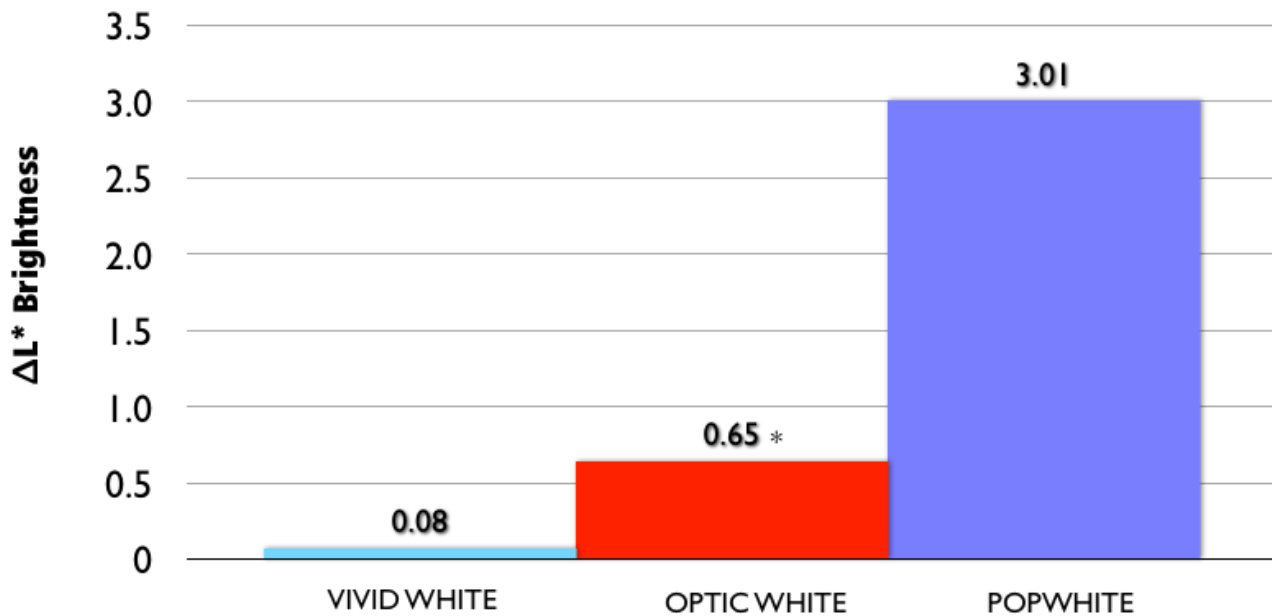
SAFETY: We judged safety of the Control and Test products based on the results of Loe and Silness Ginigival Index scoring, VAS Sensitivity Index scoring and through thorough monitoring the hard tissue / soft tissue oral health of the 60 subjects entered in the study.

Overall Safety

We found that there were no ill effects caused by the use of any of the products in all subjects tested. There were no adverse reactions found and there were no tissue changes found.

Gum Irritation

We found that the Control Toothpastes and the Experimental Toothpastes were all very gentle to the gingival tissue and did not cause any significant gum irritation as shown in **Table 5.**

TABLE 5

MEAN GINGIVAL INDEX SCORE CHANGE
CONTROL VW = Crest Vivid White
CONTROL OW = Colgate Optic White
EXPERIMENTAL = POPWHITE Whitening Toothpaste

STUDY GROUP	BASE	DAY 1	DAY 3	DAY 5	DAY 7	DAY 14
CONTROL VW (n=20)	-	0.02	0.11	0.12	0.13	0.17
CONTROL OW (n=20)	-	0.03	0.03	0.07	0.07	0.08
EXPERIMENTAL (n=20)	-	0.01	0.01	0.02	0.03	0.03

NOTES:
No significant difference in gum irritation seen in any "toothpaste" group ($p > 0.05$)

Teeth Sensitivity

We found that the Control Toothpastes and the Experimental Toothpastes were all very gentle to the dental pulp and did not cause any significant teeth sensitivity as shown in **Table 6.**

TABLE 6

MEAN VAS SENSITIVITY SCORE CHANGE
CONTROL VW = Crest Vivid White
CONTROL OW = Colgate Optic White
EXPERIMENTAL = POPWHITE Whitening Toothpaste

STUDY GROUP	BASE	DAY 1	DAY 3	DAY 5	DAY 7	DAY 14
CONTROL VW (n=20)	-	0.10	0.15	0.20	0.10	0.30
CONTROL OW (n=20)	-	0.10	0.05	0.05	0.05	0.10
EXPERIMENTAL (n=20)	-	0.10	0.05	0.15	0.10	0.05

NOTES:
No significant difference in Teeth Sensitivity seen in any "toothpaste" group
($p > 0.05$)

CONSUMER PERCEPTIONS: We were asked to administer pre-use and post-use consumer surveys to all subjects. Below is a summary of some of the most important post-use responses given by the 20 subjects in the POPWHITE Toothpaste test group:

1. POPWHITE has a pleasant taste: ***100% Agreed***
2. POPWHITE is convenient, easy and fast to use: ***100% Agreed***
3. I saw visible results after a single application: ***100% Agreed***
4. I saw visible results after two weeks of use: ***100% agreed***
5. I prefer using POPWHITE over strips / trays for whitening my teeth: ***100% agreed***
6. Freshens my breath: ***100% Agreed***
7. I would recommend to family and friends: ***90% Agreed***
8. I would purchase: ***90% Agreed***

We conclude that consumers unanimously found that the POPWHITE Toothpaste:

1. Tastes pleasant
2. Is convenient, easy, fast to use
3. More preferred than whitening to using strips/trays to whiten teeth
4. Gives clearly visible results seen after 1 use
5. Gives even greater clearly visible results after 14 days of use
6. Freshens breath

CLAIMS VERIFIED: **FOR SUJECTS OF ALL AGES – POPWHITE Toothpaste System:**

1. Whitens teeth 4 shades in 7 days simply by brushing 2x/day
2. Whitens teeth 5 shades in 10 days simply by brushing 2x/day
3. Whitens teeth 5.5 shades in 14 days simply by brushing 2x/day
4. Safe to use
5. Doesn't cause irritation of gums or tooth pain/sensitivity
6. Whitens better than the leading "whitening" toothpaste that doesn't contain peroxide (Crest Vivid White)
7. Whitens better than the leading whitening toothpaste that contains peroxide (Colgate Optic White)
8. Possible to see visible results within in just one day (Achieves a mean of 1.5 shades)
9. System whitens "intrinsic" as well as "extrinsic" stains such as tobacco
10. This system has no harsher abrasives than any other whitening toothpaste
11. This whitens 97% better than your typical "whitening" toothpaste.
12. This whitens 57% better than the "whitening" toothpastes that actually DO contain whitening ingredients, like peroxide.

TESTIMONIAL:	All of the claims that were requested to be tested by POPWHITE Inc. was "verified to be true" by our clinical scientists and we stand behind these findings under the testing conditions described above.

VERIFIED:	X _____	Date: October 19, 2014

Martin Giniger, DMD, MsD, PhD, FICD
Principal Investigator