The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

GSK Medicine: 4-Isopropyl-3-methyl phenol (IPMP) and sodium fluoride (NaF)
Study Number: T3450515
Title: Clinical Efficacy of an Experimental Toothpaste
Rationale: To investigate the ability of an IPMP containing toothpaste to control dental plaque and maintain gingival health following professional dental cleaning.
Phase: I
Study Period: 13th January 2010 to 18th May 2010
Study Design: This was a single centre, examiner blind, two arm, parallel group, randomised study in healthy adult volunteers. Subjects with overnight plaque attended the Pre-Prophylaxis Baseline Visit and underwent baseline oral soft tissue (OST) assessment, plaque sampling (sub-set of subjects only), Modified Gingival Index (MGI) inflammation and Bleeding Index (BI) assessment and then dental plaque assessment. A sub-set of approximately 50 subjects per group had a plaque sample collected for plaque bacteria assessment. A dental prophylaxis was performed on each subject's teeth followed by flossing to ensure complete removal of all plaque. Subjects were provided with oral hygiene instructions on how to brush correctly and provided with a washout toothpaste and toothbrush to use at home for 1 week. Subjects returned to the site after 1 week for an additional oral hygiene instruction visit where they underwent a gross OST assessment and brushed their teeth with the washout toothpaste and toothbrush under supervision in order for study staff to observe their brushing procedure. They then had their plaque disclosed and the study staff highlighted any areas missed during brushing before removing any residual plaque by polishing using the washout toothpaste. Subjects were then reminded of the oral hygiene instruction. The purpose of this visit was to bring the subjects to their optimum achievable gingival health over this period. Subjects returned to site after a further 2 weeks and only those subjects who had demonstrated an improvement in their gingival health (decrease in MGI from pre prophylaxis Baseline Visit) as a result of the dental prophylaxis and oral hygiene instruction were allowed to proceed with the study. Subjects went through the same assessments as were carried out at the Pre Prophylaxis Baseline Visit. They were stratified according to their MGI score from the Pre-Prophylaxis Baseline Visit and randomised into one of two treatment groups. Subjects were instructed to brush their teeth at home with the assigned study treatment twice a day for one timed minute. Study site staff then removed any residual plaque by dental polishing with the subjects' assigned treatment to bring the subject to zero plaque prior to commencing the treatment phase of the study. Subjects returned to the site with overnight plaque after 4, 8 and 12 weeks. At each visit subjects underwent a full OST examination and any adverse events (AEs) were recorded. This was followed by plaque sampling (sub-set of subjects only at 4 and 12 week visits only), MGI inflammation and BI assessment and then dental plaque assessment. An evaluation of the AE profiles from the test and reference treatments were used to monitor the tolerability of the test treatments with a focus on oral related AEs.
Centre: 1, UK
Indication: Dental plaque
Treatments: Test product: Experimental toothpaste containing 0.1w/w IPMP (923 parts per million [ppm] Fluoride [F]), Reference product: Sodium Fluoride Silica toothpaste (923 ppm F) For both, test and reference products, subjects brushed their teeth for one timed minute twice each day (morning and evening) for 12 weeks at home.
Objectives:

Primary objective:

To evaluate and compare gingivitis as measured by MGI and BI following twice daily use of experimental toothpaste compared to reference toothpaste after 12 weeks.

Secondary objectives:

1. To evaluate and compare gingivitis as measured by MGI and BI following twice daily use of experimental toothpaste compared to reference toothpaste after 4 and 8 weeks.
2. To evaluate and compare dental plaque scores (overall and interproximal) following twice daily use of experimental toothpaste compared to reference toothpaste after 4, 8 and 12 weeks.
3. To evaluate and compare changes in cultivable plaque bacterial groups in plaque samples, following twice daily use of experimental toothpaste compared to reference toothpaste after 4 and 12 weeks.

Primary Endpoints:

1. MGI at 12 weeks:
2. BI at 12 weeks:

Secondary Endpoints:

1. MGI at 4 and 8 weeks
2. BI at 4 and 8 weeks
3. Dental plaque scores after 4,8, and 12 weeks
4. Proportion of sites that worsen in MGI,
5. Proportion of sites that worsen in their BI score,
6. Plaque,
7. Gingival MGI,
8. Papillae MGI,
9. Gingival BI,
10. Papillae BI,
11. Interproximal Plaque and
12. Bacterial count data (total anaerobic, total aerobic, S*treptococcus mutans*, total Volatile Sulfur Compounds [VSC]).

Statistical Methods:

All efficacy variables were analysed under a null hypothesis of no difference between experimental and regular toothpaste against an alternate hypothesis of a difference between experimental and regular toothpaste. The MGI and BI were calculated taking the average over all tooth sites for a subject. The MGI was compared between treatments using an analysis of covariance. The Analysis of covariance (ANCOVA) model included factors for treatment group, bacteria sampling and the baseline level (Pre Prophy and Randomisation) of MGI as a covariate. The gingival strata level was not included as the actual baseline level was included as a covariate. The BI was compared between treatments using ANCOVA. The ANCOVA model included treatment group, bacteria sampling and strata level of gingival index as factors and the baseline (Pre Prophy and Randomisation) (BI) as a covariate. Treatment differences and 95% confidence intervals were presented. All tests were two sided and performed at the 5% significance level. The BI and MGI were analysed at 4, 8 and 12 weeks after treatment. The primary timepoint for analysis was 12 weeks. The two primary variables (MGI and BI) were required to show statistical significance between treatments so that no adjustment for multiplicity was required.

The proportion of sites that worsen for MGI and BI was compared between treatments using Analysis of variance (ANOVA) at each visit. The ANOVA model included factors for treatment group, bacteria sampling and strata level of gingival index. The MGI (for gingival and papillae regions separately) was compared between treatments using ANCOVA at each visit. The ANCOVA model included factors for treatment group, bacteria sampling and the baseline level (Pre Prophy and Randomisation) of MGI as a covariate. The gingival strata level will not be included as the actual baseline level is included as a covariate. The BI (for gingival and papillae regions separately), plaque and interproximal plaque were compared between treatments using ANCOVA at each visit. The ANCOVA model included treatment group, bacteria sampling and strata level of gingival index as factors and the baseline(Pre Prophy and Randomisation) (BI or interproximal plaque as appropriate) as a covariate. The bacterial count data was compared between treatments using ANCOVA. The ANCOVA model included treatment group and strata level of gingival index as factors and the baseline (Pre Prophy and Randomisation) bacterial count as a covariate. The bacterial count data (including baselines) was log transformed prior to analysis. For each analysis, treatment differences and 95% confidence intervals were presented. All tests were two sided and performed at the 5% significance level.

Study Population		
Treatment Sequence	0.1% IPMP / 0.5% Sodium Fluoride / Zinc Toothpaste	Sodium Fluoride /Silica Toothpaste
Randomised, N (%)	95	95
Completed, n (%)	88 (92.6)	82 (86.3)
Subjects not completing the study, n (%)	7 (7.4)	13 (13.7)
Due to adverse event	0	1 (1.1)
Protocol violation	5 (5.3)	8 (8.4)
Due to withdrawal of consent	2 (2.1)	4 (4.2)
Intent To Treat (ITT) Population	92(96.8)	90 (94.7)
Demographics (All Randomized Subjects)		
Sex, n (%)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste	Sodium Fluoride /Silica Toothpaste
Males	23 (24.2)	21 (22.1)
Females	72 (75.8)	74 (77.9)
Race, n (%)		
White	95 (100.0)	93 (97.9)
Multiple	0	2 (2.1)
Mean Age, years (Standard Deviation [SD])	41.7 (10.56)	41.5 (12.50)

Primary Efficacy Results				
Table 1 Modified Gingival Index Score				
Baseline	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
	Prophy	Randomization	Prophy	Randomization
N	92	92	90	90
Mean (SD)	1.97 (0.199)	1.61 (0.226)	1.96 (0.197)	1.58 (0.218)
Treatments (Week 12)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
n	88		82	
Mean (SD)	1.80 (0.236)		1.84 (0.205)	
Adjusted means [1]	1.80		1.84	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2] 95% CI	-0.04 (-0.09, 0.01)			
% Difference[3]	-2.24			
p-Value [1]	0.0927			

[1] From ANCOVA with factors for treatment group and bacteria sampling (yes/no) with pre prophy and randomization baseline as covariates.
[2] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[3] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100%].*

Table 2 Analysis of Bleeding Score				
Baseline	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
	Prophy	Randomization	Prophy	Randomization
n	92	92	90	90
Mean (SD)	0.48 (0.190)	0.25 (0.113)	0.47 (0.191)	0.24 (0.113)
Treatments (Week 12)	0.1% IPMP / 0.5% Sodium		Sodium Fluoride /Silica	

	Fluoride /Zinc Toothpaste	Toothpaste
n	88	82
Mean (SD)	0.14(0.084)	0.15 (0.090)
Adjusted means [1]	0.35	0.37
Back Transformed Mean [2]	0.13	0.14
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.01	
Difference [3] 95% CI	-0.02 (-0.05, 0.01)	
% Difference[4]	-10.64	
p-Value [1]	0.1502	

[1] From ANCOVA (square root transformation) with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high) with pre prophy and randomisation baseline as covariates.
[2] Based on back transformed values (value squared).
[3] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[4] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100%] using back transformed values.*

Secondary Efficacy Results

Table 3 Analysis of Modified Gingival Index Score – Week 4 and 8

	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
Baseline	Prophy	Randomization	Prophy	Randomization
N	92	92	90	90
Mean (SD)	1.97 (0.199)	1.61 (0.226)	1.96 (0.197)	1.58 (0.218)
Treatments (Week 4)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
n	92		90	
Mean (SD)	1.68 (0.191)		1.71 (0.164)	
Adjusted means [1]	1.67		1.71	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2] 95% CI	-0.05 (-0.08, -0.01)			
% Difference[3]	-2.64			
p-Value [1]	0.0242			

Treatments (Week 8)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste	Sodium Fluoride /Silica Toothpaste
n	88	85
Mean (SD)	1.73 (0.200)	1.75 (0.184)
Adjusted means [1]	1.72	1.75
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2] 95% CI	-0.03 (-0.07, 0.01)	
% Difference[3]	-1.71	
p-Value [1]	0.1421	

[1] From ANCOVA with factors for treatment group and bacteria sampling (yes/no) with pre prophy and randomization baseline as covariates.
[2] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[3] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100%].*

Table 4 Analysis of Bleeding Score – Week 4 and 8

	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
Baseline	Prophy	Randomization	Prophy	Randomization

N	92	92	90	90
Mean (SD)	0.48 (0.190)	0.25 (0.113)	0.47 (0.191)	0.24 (0.113)
Treatments (Week 4)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
n	92		90	
Mean (SD)	0.21 (0.121)		0.23 (0.119)	
Adjusted means [1]	0.44		0.47	
Back Transformed Mean [2]	0.19		0.22	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2]	-0.03			
Difference [3] 95% CI	-0.03 (-0.06, 0.00)			
% Difference[4]	-11.96			
p-Value [1]	0.0513			

Treatments (Week 8)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste	Sodium Fluoride /Silica Toothpaste
n	88	85
Mean (SD)	0.16 (0.101)	0.16 (0.087)
Adjusted means [1]	0.38	0.39
Back Transformed Mean [2]	0.15	0.16
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.01	
Difference [3] 95% CI	-0.01 (-0.04, 0.02)	
% Difference[4]	-6.25	
p-Value [1]	0.4029	

[1] From ANCOVA (square root transformation) with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high) with pre prophy and randomisation baseline as covariates.
[2] Based on back transformed values (value squared).
[3] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[4] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100%] using back transformed values.*

Table 5 Analysis of Plaque Score – Week 4, 8, and 12 (ITT Population)

	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
Baseline	Prophy	Randomization	Prophy	Randomization
N	92	92	90	90
Mean (SD)	2.78 (0.465)	2.42 (0.315)	2.71 (0.522)	2.43 (0.347)

Treatments (Week 4)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste	Sodium Fluoride /Silica Toothpaste
n	92	90
Mean (SD)	2.30 (0.352)	2.31(0.393)
Adjusted mean [1]	2.28	2.30
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2] 95% CI	-0.02 (-0.10, 0.06)	
% Difference[3]	-1.00	
p-Value [1]	0.5761	

Treatments (Week 8)	0.1% IPMP / 0.5%	Sodium Fluoride /Silica

	Sodium Fluoride /Zinc Toothpaste	Toothpaste
n	88	85
Mean (SD)	2.34 (0.363)	2.42 (0.426)
Adjusted mean [1]	2.33	2.43
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2] 95% CI	-0.10 (-0.18, -0.01)	
% Difference[3]	-4.04	
p-Value [1]	0.0242	
Treatments (Week 12)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste	Sodium Fluoride /Silica Toothpaste
n	87	82
Mean (SD)	2.15 (0.433)	2.31 (0.505)
Adjusted mean [1]	2.15	2.30
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2] 95% CI	-0.15 (-0.26, -0.05)	
% Difference[3]	-6.59	
p-Value [1]	0.0047	

[1] From ANCOVA with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high) with pre prophy and randomisation baseline as covariates.
[2] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[3] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100%].*

Table 6 Analysis of Interproximal Plaque Score– Week 4, 8, and 12 (ITT Population)

	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
Baseline	Prophy	Randomization	Prophy	Randomization
N	92	92	90	90
Mean (SD)	2.94 (0.532)	2.51 (0.353)	2.85 (0.599)	2.51 (0.392)
Treatments (Week 4)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
n	92		90	
Mean (SD)	2.39 (0.374)		2.41 (0.436)	
Adjusted mean [1]	2.37		2.41	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2] 95% CI	-0.04 (-0.13, 0.05)			
% Difference[3]	-1.70			
p-Value [1]	0.3522			
Treatments (Week 8)	0.1% IPMP / 0.5% Sodium Fluoride /Zinc Toothpaste		Sodium Fluoride /Silica Toothpaste	
n	88		85	
Mean (SD)	2.43 (0.397)		2.51 (0.469)	
Adjusted mean [1]	2.42		2.53	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2] 95% CI	-0.11 (-0.20, -0.02)			
% Difference[3]	-4.37			
p-Value [1]	0.0200			
Treatments (Week 12)	0.1% IPMP / 0.5% Sodium		Sodium Fluoride /Silica	

	Fluoride /Zinc Toothpaste	Toothpaste
n	87	82
Mean (SD)	2.24 (0.458)	2.41 (0.538)
Adjusted mean [1]	2.23	2.39
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2] 95% CI	-0.16 (-0.27, -0.06)	
% Difference[3]	-6.89	
p-Value [1]	0.0034	
[1] From ANCOVA with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high) with pre prophy and randomization baseline as covariates. *[2] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.* *[3] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100].*		
Table 7 Analysis of Proportion of Sites With Increase in MGI Score Compared to Pre Prophy Visit (ITT Population)		
Baseline	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
N	92	90
Mean (SD)	0.05 (0.039)	0.05 (0.041)
Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	92	90
Mean (SD)	0.05 (0.043)	0.07 (0.056)
Adjusted mean [1]	0.19	0.22
Back Transformed Mean[2]	0.04	0.05
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.01	
Difference [3] 95% CI	-0.03 (-0.06, 0.00)	
% Difference[4]	-26.89	
p-Value [1]	0.0211	
Treatments (Week 8)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	85
Mean (SD)	0.07 (0.056)	0.08 (0.061)
Adjusted mean [1]	0.23	0.24
Back Transformed Mean[2]	0.05	0.06
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	0.00	
Difference [3] 95% CI	-0.01 (-0.04, 0.02)	
% Difference[4]	-6.05	
p-Value [1]	0.6164	
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	82
Mean (SD)	0.09 (0.074)	0.10 (0.067)
Adjusted mean [1]	0.27	0.29
Back Transformed Mean[2]	0.07	0.09
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		

Difference [2]	-0.01	
Difference [3] 95% CI	-0.03 (-0.06, 0.01)	
% Difference[4]	-17.31	
p-Value [1]	0.1402	
[1] From ANOVA (square root transformation) with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high). *[2] Based on back transformed values (value squared).* *[3] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.* *[4] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100] using back transformed values.*		
Table 8 Analysis of Proportion of Sites With Increase in MGI Score Compared to Baseline		
Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
N	92	90
Mean (SD)	0.19 (0.113)	0.22 (0.115)
Adjusted mean [1]	0.41	0.45
Back Transformed Mean[2]	0.16	0.20
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.04	
Difference [3] 95% CI	-0.04 (-0.08, -0.01)	
% Difference[4]	-18.82	
p-Value [1]	0.0150	
Treatments (Week 8)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	85
Mean (SD)	0.23 (0.112)	0.25 (0.108)
Adjusted mean [1]	0.46	0.48
Back Transformed Mean[2]	0.21	0.23
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.03	
Difference [3] 95% CI	-0.03 (-0.06, 0.01)	
% Difference[4]	-11.03	
p-Value [1]	0.0993	
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	82
Mean (SD)	0.28 (0.134)	0.31 (0.126)
Adjusted mean [1]	0.51	0.54
Back Transformed Mean[2]	0.26	0.29
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.03	
Difference [3] 95% CI	-0.03 (-0.07, 0.00)	
% Difference[4]	-11.28	
p-Value [1]	0.0845	
Table 9 Analysis of Proportion of Sites With Increase in Bleeding Index Score Compared to Pre Prophy Visit		
Baseline	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
N	92	90

Mean (SD)	0.10 (0.045)	0.09 (0.040)
Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	92	90
Mean (SD)	0.08 (0.047)	0.09 (0.043)
Adjusted mean [1]	0.27	0.28
Back Transformed Mean[2]	0.07	0.08
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.01	
Difference [3] 95% CI	-0.01 (-0.04, 0.01)	
% Difference[4]	-8.71	
p-Value [1]	0.2831	
Treatments (Week 8)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	85
Mean (SD)	0.06 (0.038)	0.06 (0.032)
Adjusted mean [1]	0.23	0.23
Back Transformed Mean[2]	0.05	0.05
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	0.00	
Difference [3] 95% CI	0.00 (-0.02, 0.02)	
% Difference[4]	-1.11	
P-Value [1]	0.9151	
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	82
Mean (SD)	0.05 (0.027)	0.05 (0.035)
Adjusted mean [1]	0.22	0.22
Back Transformed Mean[2]	0.05	0.05
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	0.00	
Difference [3] 95% CI	0.00 (-0.02, 0.02)	
% Difference[4]	-1.26	
p-Value [1]	0.9020	

[1] From ANOVA (square root transformation) with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high).
[2] Based on back transformed values (value squared).
[3] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[4] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100] using back transformed values*

Table 10 Analysis of Proportion of Sites With Increase in Bleeding Index Score Compared to Baseline

Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
N	92	90
Mean (SD)	0.10 (0.050)	0.11 (0.055)
Adjusted mean [1]	0.30	0.32
Back Transformed Mean[2]	0.09	0.10
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.01	

Difference [3] 95% CI	-0.02 (-0.04, 0.01)			
% Difference[4]	-10.46			
p-Value [1]	0.1542			
Treatments (Week 8)	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
n	88		85	
Mean (SD)	0.07 (0.042)		0.08 (0.043)	
Adjusted mean [1]	0.26		0.27	
Back Transformed Mean[2]	0.07		0.07	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2]	-0.01			
Difference [3] 95% CI	-0.01 (-0.04, 0.01)			
% Difference[4]	-9.73			
p-Value [1]	0.2615			
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
n	88		82	
Mean (SD)	0.06 (0.036)		0.07 (0.040)	
Adjusted mean [1]	0.24		0.26	
Back Transformed Mean[2]	0.06		0.07	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2]	-0.01			
Difference [3] 95% CI	-0.02 (-0.04, 0.00)			
% Difference[4]	-13.81			
p-Value [1]	0.0972			

[1] From ANOVA (square root transformation) with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high).
[2] Based on back transformed values (value squared).
[3] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[4] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100] using back transformed values.*

Table 11 Analysis of Modified Gingival Index - Margin Score (ITT Population)

	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
Baseline	Prophy	Randomisation	Prophy	Randomisation
N	92	92	90	90
Mean (SD)	1.87 (0.205)	1.47 (0.217)	1.85 (0.197)	1.44 (0.209)
Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
n	92		90	
Mean (SD)	1.52 (0.216)		1.55 (0.196)	
Adjusted mean [1]	1.51		1.56	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2] 95% CI	-0.05 (-0.10, 0.00)			
% Difference[3]	-3.13			
p-Value [1]	0.0401			

Treatments (Week 8)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	85
Mean (SD)	1.56 (0.218)	1.59 (0.205)
Adjusted mean [1]	1.55	1.59
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2] 95% CI	-0.04 (-0.09, 0.00)	
% Difference[3]	-2.65	
p-Value [1]	0.0738	
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	82
Mean (SD)	1.63 (0.237)	1.68 (0.225)
Adjusted mean [1]	1.63	1.68
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2] 95% CI	-0.05 (-0.10, 0.00)	
% Difference[3]	-3.00	
p-Value [1]	0.0601	

[1] From ANCOVA with factors for treatment group and bacteria sampling (yes/no) with pre prophy and randomisation baseline as covariates.
[2] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[3] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100].*

Table 12 Analysis of Modified Gingival Index - Papillae Score

	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
Baseline	Prophy	Randomisation	Prophy	Randomisation
N	92	92	90	90
Mean (SD)	2.09 (0.215)	1.77 (0.255)	2.08 (0.225)	1.73 (0.252)
Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
n	92		90	
Mean (SD)	1.85 (0.182)		1.87 (0.155)	
Adjusted mean [1]	1.84		1.88	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2] 95% CI	-0.04 (-0.08, 0.00)			
% Difference[3]	-2.17			
p-Value [1]	0.0296			
Treatments (Week 8)	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
n	88		85	
Mean (SD)	1.91 (0.199)		1.92 (0.183)	
Adjusted mean [1]	1.90		1.92	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2] 95% CI	-0.02 (-0.06, 0.02)			
% Difference[3]	-0.83			

p-Value [1]	0.4300	
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	82
Mean (SD)	1.98 (0.248)	2.01 (0.199)
Adjusted mean [1]	1.98	2.01
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2] 95% CI	-0.03 (-0.08, 0.02)	
% Difference[3]	-1.53	
p-Value [1]	0.2123	

[1] From ANCOVA with factors for treatment group and bacteria sampling (yes/no) with pre prophy and randomisation baseline as covariates.
[2] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[3] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100].*

Table 13 Analysis of Bleeding Index - Margin Score

	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
Baseline	Prophy	Randomisation	Prophy	Randomisation
N	92	92	90	90
Mean (SD)	0.57 (0.266)	0.27 (0.143)	0.57 (0.269)	0.25 (0.158)

Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	92	90
Mean (SD)	0.21 (0.127)	0.26 (0.163)
Adjusted mean [1]	0.43	0.48
Back Transformed Mean[2]	0.19	0.23
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.04	
Difference [3] 95% CI	-0.05 (-0.09, -0.01)	
% Difference[4]	-19.18	
p-Value [1]	0.0156	
Treatments (Week 8)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	85
Mean (SD)	0.17 (0.132)	0.18(0.124)
Adjusted mean [1]	0.38	0.40
Back Transformed Mean[2]	0.14	0.16
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.01	
Difference [3] 95% CI	-0.02 (-0.06, 0.03)	
% Difference[4]	-8.96	
p-Value [1]	0.4106	
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste	Sodium Fluoride / Silica Toothpaste
n	88	82

Mean (SD)	0.13 (0.091)		0.15 (0.114)	
Adjusted mean [1]	0.34		0.36	
Back Transformed Mean[2]	0.11		0.13	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2]	-0.02			
Difference [3] 95% CI	-0.02 (-0.06, 0.01)			
% Difference[4]	-13.19			
p-Value [1]	0.1757			
[1] From ANCOVA (square root transformation) with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high) with pre prophy and randomisation baseline as covariates. *[2] Based on back transformed values (value squared).* *[3] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.* *[4] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100] using back transformed values.*				
Table 14 Analysis of Bleeding Index - Papillae Score				
	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
Baseline	Prophy	Randomisation	Prophy	Randomisation
N	92	92	90	90
Mean (SD)	0.40 (0.189)	0.24 (0.141)	0.36 (0.188)	0.22 (0.123)
Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
n	92		90	
Mean (SD)	0.22 (0.196)		0.20 (0.146)	
Adjusted mean [1]	0.42		0.42	
Back Transformed Mean[2]	0.17		0.18	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2]	0.00			
Difference [3] 95% CI	0.00 (-0.05, 0.04)			
% Difference[4]	-1.17			
p-Value [1]	0.9117			
Treatments (Week 8)	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
n	88		85	
Mean (SD)	0.15 (0.130)		0.14 (0.106)	
Adjusted mean [1]	0.35		0.36	
Back Transformed Mean[2]	0.12		0.13	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [2]	-0.01			
Difference [3] 95% CI	-0.01 (-0.05, 0.03)			
% Difference[4]	-7.00			
p-Value [1]	0.5371			
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste		Sodium Fluoride / Silica Toothpaste	
n	88		82	
Mean (SD)	0.15 (0.119)		0.15 (0.125)	
Adjusted mean [1]	0.35		0.36	

Back Transformed Mean[2]	0.12	0.13
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [2]	-0.01	
Difference [3] 95% CI	-0.01 (-0.06, 0.03)	
% Difference[4]	-7.75	
p-Value [1]	0.5134	

[1] From ANCOVA (square root transformation) with factors for treatment group, bacteria sampling (yes/no) and gingival strata (low, high) with pre prophy and randomisation baseline as covariates.
[2] Based on back transformed values (value squared).
[3] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[4] Second named treatment is taken as reference for calculation of % difference [(Difference/Reference)*100] using back transformed values.*

Table 15 Analysis of Plaque Bacteria Count Data - Total Anaerobic

	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]		Sodium Fluoride / Silica Toothpaste Log[1]	
Baseline	Prophy	Randomisation	Prophy	Randomisation
N	34	34	33	33
Mean (SD)	7.30 (0.368)	7.34 (0.298)	7.34 (0.349)	7.25 (0.292)

Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]	Sodium Fluoride / Silica Toothpaste Log[1]
n	34	33
Mean (SD)	7.30 (0.464)	7.45 (0.304)
Adjusted mean [2]	7.29	7.46
Treatment comparison (IPMP toothpaste vs NaF toothpaste)		
Difference [3] 95% CI	-0.18 (-0.34, -0.01)	
Ratio[4]	0.67	
p-Value [2]	0.0397	

Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]	Sodium Fluoride / Silica Toothpaste Log[1]
n	33	32
Mean (SD)	7.15 (0.443)	7.19 (0.528)
Adjusted mean [2]	7.14	7.21
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [3] 95% CI	-0.07 (-0.29, 0.16)	
Ratio[4]	0.85	
p-Value [2]	0.5447	

[1] Log values are to the base 10.
[2] From ANCOVA with factors for treatment group and gingival strata with pre prophy and randomization baseline bacterial counts as covariates.
[3] Difference in adjusted mean based on log-values of first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[4] Second named treatment is taken as reference for calculation of ratio 10**Difference. (ie Anti log of difference)*

Table 16 Analysis of Plaque Bacteria Count Data - Total Aerobic

	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]		Sodium Fluoride / Silica Toothpaste Log[1]	
Baseline	Prophy	Randomisation	Prophy	Randomisation
N	34	34	33	33
Mean (SD)	7.10	7.11	7.00	6.93

	(0.325)	(0.324)	(0.369)	(0.376)
Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]		Sodium Fluoride / Silica Toothpaste Log[1]	
n	34		33	
Mean (SD)	7.28 (0.352)		7.31 (0.375)	
Adjusted mean [2]	7.27		7.32	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [3] 95% CI	-0.05 (-0.22, 0.13)			
Ratio[4]	0.90			
p-Value [2]	0.5890			
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]		Sodium Fluoride / Silica Toothpaste Log[1]	
n	33		32	
Mean (SD)	6.86 (0.519)		6.93 (0.608)	
Adjusted mean [2]	6.81		6.98	
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)				
Difference [3] 95% CI	-0.17 (-0.42, 0.07)			
Ratio[4]	0.67			
p-Value [2]	0.1644			

[1] Log values are to the base 10.
[2] From ANCOVA with factors for treatment group and gingival strata with pre prophy and randomization baseline bacterial counts as covariates.
[3] Difference in adjusted mean based on log-values of first named treatment minus second named treatment such that a negative differencefavours the first named treatment.
*[4] Second named treatment is taken as reference for calculation of ratio 10**Difference. (ie Anti log of difference).*

Table 17 Analysis of Plaque Bacteria Count Data - Streptococcus Mutans

	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]		Sodium Fluoride / Silica Toothpaste Log[1]	
Baseline	Prophy	Randomisation	Prophy	Randomisation
N	34	34	33	33
Mean (SD)	1.71 (0.052)	1.70 (0.000)	1.70 (0.000)	1.70 (0.000)
Treatments (Week 4)	0.1% IPMP toothpaste Log[1]		NaF toothpaste Log[1]	
n	34		33	
Mean (SD)	1.70 (0.000)		1.70 (0.000)	
Treatments (Week 12)	0.1% IPMP toothpaste Log[1]		NaF toothpaste Log[1]	
n	33		32	
Mean (SD)	1.70 (0.000)		1.70 (0.000)	

[1] Log values are to the base 10.
An analysis was not carried out on this variable as nearly all values were < 50.

Table 18 Analysis of Plaque Bacteria Count Data - Total VSC

	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]		Sodium Fluoride / Silica Toothpaste Log[1]	
Baseline	Prophy	Randomisation	Prophy	Randomisation
N	22	34	23	33
Mean (SD)	6.80 (0.788)	6.72 (0.619)	6.61 (0.871)	6.59 (0.559)

Treatments (Week 4)	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]	Sodium Fluoride / Silica Toothpaste Log[1]
n	34	33
Mean (SD)	6.87 (0.531)	6.82 (0.533)
Adjusted mean [2]	6.78	6.90
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [3] 95% CI	-0.12 (-0.41, 0.18)	
Ratio[4]	0.77	
p-Value [2]	0.4287	
Treatments (Week 12)	0.1% IPMP / 0.5% Zinc Toothpaste Log[1]	Sodium Fluoride / Silica Toothpaste Log[1]
n	33	32
Mean (SD)	6.56 (0.645)	6.71 (0.692)
Adjusted mean [2]	6.56	6.95
Treatment comparison (IPMP/zinc toothpaste vs. Sodium fluoride/silica toothpaste)		
Difference [3] 95% CI	-0.39 (-0.71, -0.06)	
Ratio[4]	0.41	
p-Value [2]	0.0208	

[1] Log values are to the base 10.
[2] From ANCOVA with factors for treatment group and gingival strata with pre prophy and randomization baseline bacterial counts as covariates.
[3] Difference in adjusted mean based on log-values of first named treatment minus second named treatment such that a negative difference favours the first named treatment.
*[4] Second named treatment is taken as reference for calculation of ratio 10**Difference. (ie Anti log of difference)*

Safety Results (Safety population)

Table 19 Treatment Emergent Adverse Events

Treatments	0.1% IPMP/0.5% Zinc Toothpaste	Sodium Fluoride/Silica Toothpaste
N	95	95
Number of Subjects With at Least one AE, n (%)	70 (73.7)	63 (66.3)
Oral		
Aphthous stomatitis	4 (4.2)	3 (3.2)
Gingival injury	6 (6.3)	7 (7.4)
Oropharyngeal pain	9 (9.5)	3 (3.2)
Oral herpes	6 (6.3)	3 (3.2)
Gingival bleeding	5 (5.3)	4 (4.2)
Mouth ulceration	3 (3.2)	3 (3.2)
Gingival pain	6 (6.3)	2 (2.1)
Thermal burn	2 (2.1)	5 (5.3)
Mouth injury	6 (6.3)	1 (1.1)
Sensitivity of teeth	3 (3.2)	3 (3.2)
Tooth fracture	3 (3.2)	2 (2.1)
Toothache	2 (2.1)	3 (3.2)
Oral mucosal exfoliation	0	3 (3.2)
Tongue ulceration	1 (1.1)	2 (2.1)
Tooth disorder	2 (2.1)	1 (1.1)
Breath odour	1 (1.1)	1 (1.1)
Chapped lips	1 (1.1)	1 (1.1)
Cheilitis	2 (2.1)	0

Dry mouth	2 (2.1)	0
Glossitis	2 (2.1)	0
Oropharyngeal plaque	0	1 (1.1)
Tonsillitis	2 (2.1)	0
Gingival abscess	1 (1.1)	0
Gingival ulceration	1 (1.1)	0
Glossodynia	1 (1.1)	0
Lichen planus	0	1(1.1)
Lip ulceration	0	1(1.1)
Mouth cyst	1 (1.1)	0
Oral mucosal erythema	0	1 (1.1)
Oral pain	0	1 (1.1)
Oropharyngeal blistering	1 (1.1)	0
Paraesthesia oral	1 (1.1)	0
Tongue haematoma	0	1 (1.1)
Tooth abscess	0	1 (1.1)
Non Oral		
Headache	29 (30.5)	26 (27.4)
Upper Respiratory Tract Infection	10 (10.5)	15 (15.8)
Nasopharyngitis	5 (5.3)	7 (7.4)
Migraine	3 (3.2)	3 (3.2)
Back pain	3 (3.2)	1 (1.1)
Dysmenorrhoea	1 (1.1)	1 (1.1)
Dyspepsia	4 (4.2)	0
Lower respiratory tract infection	1 (1.1)	3 (3.2)
Myalgia	2 (2.1)	2 (2.1)
Arthralgia	3 (3.2)	0
Ear infection	2 (2.1)	1 (1.1)
Influenza	1 (1.1)	2 (2.1)
Rhinitis seasonal	2 (2.1)	1 (1.1)
Malaise	2 (2.1)	0
Musculoskeletal pain	1 (1.1)	1 (1.1)
Neck pain	1 (1.1)	1 (1.1)
Skin laceration	1 (1.1)	1 (1.1)
Urinary tract infection	1 (1.1)	1 (1.1)
Abdominal pain	1 (1.1)	0
Abdominal pain upper	1 (1.1)	0
Abortion spontaneous	1 (1.1)	0
Acne	1 (1.1)	0
Cough	1 (1.1)	0
Dizziness	1 (1.1)	0
Fatigue	1 (1.1)	0
Hand fracture	0	1 (1.1)
Herpes virus infection	1 (1.1)	0
Hypothyroidism	0	1 (1.1)
Joint sprain	1 (1.1)	0
Kidney infection	0	1 (1.1)
Labyrinthitis	0	1 (1.1)
Limb injury	0	1 (1.1)
Muscle injury	0	1 (1.1)
Muscle strain	1 (1.1)	0
Pain	1 (1.1)	0
Procedural pain	1 (1.1)	0

Rash	1 (1.1)	0
Sinus congestion	0	1(1.1)
Skin infection	0	1(1.1)
Transient ischaemic attack	0	1(1.1)
Vomiting	0	1(1.1)
Serious Adverse Events (SAEs) - On-Therapy		
No serious adverse events were reported		