JOHNSON & JOHNSON CONSUMER INC.

SUMMARY CLINICAL STUDY REPORT

PROTOCOL TITLE:	Twelve Week Clinical Efficacy of Virtually Supervised Mouth Rinse and Flossing: Effect on Plaque and Gingivitis
PROTOCOL NUMBER:	CCSORC002906 Final Version: Amendment 1, 02 October 2020
SPONSOR:	Johnson & Johnson Consumer Inc. [redacted]
STUDY SITE:	Salus Research, Inc. 1220 Medical Park Drive, Building 4 Fort Wayne, Indiana 46825 [redacted]
PRINCIPAL INVESTIGATOR:	Jeffery Milleman, DDS Address: Refer to Study Site address [redacted]
STUDY DIRECTOR (SD) and DESIGNATED PHYSICIAN REPRESENTATIVE (DPR):	Mary Lynn Bosma, RDH, DDS [redacted]
STUDY INITIATION DATE (First Subject First Visit):	23 October 2020
STUDY COMPLETION DATE (Last Subject Completed):	01 February 2021
SITE AND SPONSOR REVIEW AND APPROVAL:	[redacted]

The principles of the International Council for Harmonisation (ICH) Guidelines for Good Clinical Practice (GCP E6 (R2)) were applied to this study.

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1. STUDY SYNOPSIS

The principles of the International Council for Harmonisation (ICH) Guidelines for Good Clinical Practice (GCP E6 (R2)) were applied to this study.

INTRODUCTION	Bacterial plaque is an important factor in dental diseases such as caries and gingivitis. Plaque control methods include a variety of procedures. Mechanical removal methods include both brushing and flossing. Chemotherapeutic methods of reducing plaque include the use of mouth rinses that contain essential oils. Three controlled studies have been published relating to the relative efficacy of an essential oils containing mouth rinse and dental flossing in the ability to control the accumulation of plaque and subsequently the prevention/reduction of gingivitis.[1,2,3] One of these studies indicated that rinsing twice daily with an essential oils mouth rinse was at least as good as unsupervised daily flossing in reducing interproximal plaque and gingivitis. The second study indicated that the essential oils mouth rinse was as good as floss in controlling interproximal gingivitis. The final study indicated that brushing, flossing and rinsing with an essential oils rinse exhibited statistically and clinically significantly lower mean scores for gingivitis and plaque than brushing, flossing and rinsing with a negative control rinse. This study investigated the effects of mechanical and chemotherapeutic regimens on the prevention and reduction of plaque and gingivitis.
OBJECTIVE	The purpose of this study was to evaluate the efficacy of various regimens in the prevention and reduction of plaque and gingivitis. The regimens were: brushing, flossing, and rinsing with an alcohol containing essential oil mouth rinse or brushing and flossing, versus brushing and rinsing with an alcohol containing essential oil mouth rinse and brushing only.
STUDY DESIGN	A total of 213 generally healthy subjects that met the required inclusion/exclusion criteria were randomized in this 12-week, examiner-blind, single center, randomized, parallel-group controlled clinical trial. The study protocol referenced on page 32 of this report provides the complete study design for the study.
SUBJECT INFORMATION	Adults 18-60 years of age or older in good general and oral health that met the eligibility criteria were enrolled in the study. The complete eligibility criteria for this study were followed as defined in the study protocol referenced on page 32 of this report.

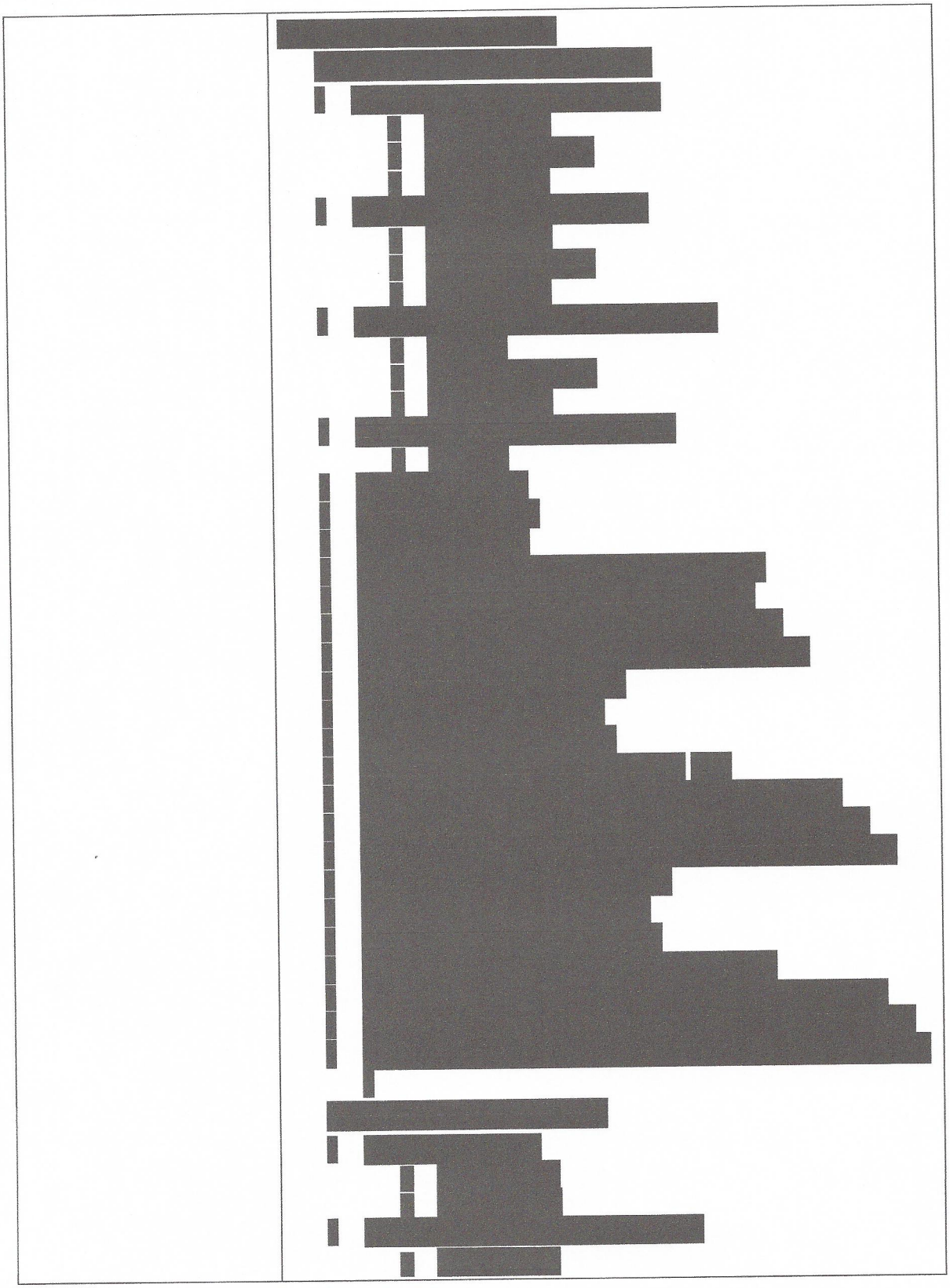
INVESTIGATIONAL STUDY MATERIALS	<table><tr><th>Identification by Group</th><th>Product type</th></tr><tr><td>Brush only</td><td>• Colgate® Cavity Protection Toothpaste</td></tr><tr><td>Brush / Listerine Cool Mint Antiseptic Mouthwash</td><td>• Colgate® Cavity Protection Toothpaste • LISTERINE® Cool Mint® Antiseptic Mouthwash</td></tr><tr><td>Brush / Floss</td><td>• Colgate® Cavity Protection Toothpaste • Reach® Unflavored Waxed Dental Floss</td></tr><tr><td>Brush / Floss / Listerine Cool Mint Antiseptic Mouthwash</td><td>• Colgate® Cavity Protection Toothpaste • Reach® Unflavored Waxed Dental Floss • LISTERINE® Cool Mint® Antiseptic Mouthwash</td></tr></table>
DOSE AND MODE OF APPLICATION	Subjects in all groups: • Used their assigned test product(s) following the label instructions. • Used their assigned test product(s) as directed under virtual supervision once daily during the week. • Used their product(s) for the first time under supervision at the study site. • Received a marketed fluoride-containing dentifrice (Colgate® Cavity Protection) and a soft flat trimmed bristled toothbrush at their Screening/Baseline visit to use throughout the study. **Brush Only (Control) Group** Subjects brushed their teeth under virtual supervision once daily during the week. In the evenings, subjects brushed a second time unsupervised. Over the weekends and on holidays, subjects brushed twice daily unsupervised at home. **Brush/Rinse Group** Subjects performed their regimen (brushing and rinsing) under virtual supervision once daily during the week. In the evenings, subjects brushed/rinsed a second time unsupervised. Over the weekends and on holidays, subjects brushed/rinsed twice daily unsupervised at home. **Brush/Floss Group** Subjects performed their regimen (brushing and flossing) under virtual supervision once daily during the week. In the evenings, subjects brushed (but did not floss) a second time unsupervised. Over the

	weekends and on holidays, subjects brushed/flossed unsupervised at home once daily, and brushed a second time in the evening, unsupervised. **Brush/Floss/Rinse Group** Subjects performed their regimen (brushing, flossing and rinsing) under virtual supervision once daily during the week. In the evenings, subjects brushed and rinsed (but did not floss) a second time unsupervised. Over the weekends and on holidays, subjects brushed/flossed/rinsed unsupervised at home once daily and brushed and rinsed a second time in the evening, unsupervised.
METHODOLOGY	A total of 213 generally healthy subjects that met the required inclusion/exclusion criteria were enrolled in this twelve-week, examiner-blind, single center, randomized, parallel-group controlled clinical trial. Subjects were supervised by dental professionals. For each visit (Visits 1, 2 and 3), subjects were instructed to come to the clinical site having refrained from: oral hygiene (for at least 8 hours, but no more than 18 hours), and eating (for at least 4 hours) prior to the visit. Subjects were permitted to drink water up to 2 hours before their visit. All subjects were scheduled for virtual supervision of product use once daily on weekdays, through a video phone call. For one week between Visits 1 and 2, and during the 11th week of product use before Visit 3, qualified site personnel did the following: • During the daily observation sessions, they observed subjects using their assigned treatment regimens. • They documented technique and time in a Product Use Observation/Comment sheet in subject source documents. These data were evaluated after the conclusion of the trial. Subjects were instructed to use only the products given to them throughout the study. No other oral hygiene products or procedures were permitted while participating in this study, including teeth cleaning, whitening or dental procedures except for an emergency treatment. The decision to withdraw a subject due to emergency dental treatment occurred at the discretion of the investigator.

	Oral tissue tolerance, Modified Gingival Index (MGI), Expanded Bleeding Index (EBI), Turesky Plaque Index (TPI) and Proximal Marginal Plaque Index (PMI) were assessed at all visits.[redacted] <u>Visit 1: Day 0 – Screening/Baseline</u> Subjects provided their informed consent to participate, had their prior and concomitant medications/non-drug therapies, smoking, medical and dental histories and inclusion and exclusion criteria reviewed. Female subjects of childbearing potential were given a urine pregnancy test.[redacted] Subjects were required to fill out the Site's IRB approved Implementation of COVID-19 Prevention Procedures Consent Form. Each subject was given a dexterity test and had baseline examinations, which included an oral hard and soft tissue assessment, MGI, EBI,[redacted] TPI and PMI. After the exams and assessments, subjects received a complete dental prophylaxis. The teeth were checked by another qualified hygienist or dentist for thorough calculus and plaque removal prior to the subject being completed. Qualified subjects were randomly assigned to one of four treatment groups. Subjects received their assigned floss (if applicable), mouth rinse and dose cups (if applicable), a marketed fluoride-containing dentifrice (Colgate® Cavity Protection toothpaste), soft flat trimmed bristled toothbrush, and a subject instructions/diary card to record their evening and weekend/holiday product use times. Subjects assigned to a floss group received individualized flossing instructions. Subjects used their assigned study products following the label instructions for the first time at the site under supervision of study personnel. Adverse events were assessed. Daily observation sessions and the subject's next visit were scheduled.

	Visit 2: Week 4 (Day 28 ± 2 days) Inclusion/exclusion criteria, AE assessment and concomitant medications/non-drug therapies were reviewed to ensure subjects were still eligible to continue participation in the study. Each subject received assessments/examinations that included an oral exam (oral hard and soft tissue assessment), MGI, TPI and EBI and PMI. Daily observation sessions and the subject's next visit were scheduled. Compliance was evaluated by weighing residual volumes of returned mouth rinse and/or floss (if applicable), visually inspecting toothpaste tubes for use and by reviewing the subject diary cards. Visit 3: Week 12 (Day 84 ± 3 days) Inclusion/exclusion criteria, AE assessment and concomitant medications/non-drug therapies were reviewed to ensure subjects were still eligible to continue participation in the study. Female subjects of childbearing potential were given a urine pregnancy test. Assessments/examinations included an oral hard and soft tissue assessment, MGI, EBI, [redacted] TPI and PMI. Compliance was evaluated at Visit 3 by weighing residual volumes of returned mouth rinse and/or floss (if applicable), visually inspecting toothpaste tubes for use and by reviewing the subject diary cards. Tissue tolerance and safety Oral tissue tolerance was monitored through oral exams and the collection of adverse events. Safety was assessed through observation and query of each subject at each visit during the study for any new or continuing symptoms since the previous visit and through the tabulation of adverse events. Details of adverse events including resolution were captured. Any intra-oral adverse events were photographed and sent to the Sponsor.

MEASUREMENT AND EVALUATION SCHEDULE	Investigational products were compared based on a mixed model for repeated measures analysis (MMRM), including terms for treatment and visit, and the corresponding baseline value as a covariate. Treatment-by-visit and baseline-by-visit terms were included to make treatment comparisons and estimate treatment differences at specific visits. Comparisons for Brush/Rinse vs. Brush/Floss and Brush/Floss/Rinse vs. Brush/Floss at 12 weeks followed a fixed sequence testing procedure strongly controlling the family-wise error rate at the 0.0125, one-sided significance level. Therefore, based on the Bonferroni method, the familywise error rate for all comparisons included in this sequential procedure was strongly controlled at the 0.025, one-sided significance level. The number and percentage of subjects experiencing adverse events and treatment-related AEs during the clinical study were presented by MedDRA System Organ Class preferred term and treatment. Oral exam findings were summarized. **Primary Endpoint** The primary efficacy variables were whole mouth mean TPI and whole mouth mean MGI after 12 weeks of product use. **Secondary Endpoints** The secondary efficacy variables were: ***After 4 and 12 weeks of product use:*** • marginal mean TPI • marginal mean MGI • marginal mean EBI • interproximal mean TPI • interproximal mean MGI • whole mouth and interproximal mean EBI • whole mouth and interproximal percent bleeding sites based on the EBI • interproximal of the PMI ***After 4 weeks of product use:*** • whole mouth mean TPI • whole mouth mean MGI [redacted]



	[redacted]
INSTITUTIONAL REVIEW BOARD (IRB)	This study was reviewed and approved by the following IRB/IEC: - Name: IntegReview IRB - Approval date: 30 Sept 2020 Applicable Amendments: - Approval date: 13 Oct 2020
SAFETY AND ADVERSE EVENTS	All Adverse Events (AEs/SAEs) were collected regardless of causal relationship to the subject's participation in the study. The information was collected/reported within the reporting timelines specified in the protocol.
MONITORING, QUALITY CONTROL, AND QUALITY ASSURANCE	The study monitoring was conducted as per the Sponsor's requirements. The Study Site was subject to review by the IRB, to quality assurance audits performed by the Sponsor, and/or to inspection by appropriate regulatory authorities.
CONCLUSIONS	Including twice daily use of an essential oil mouth rinse, Listerine Antiseptic Cool Mint, into a toothbrushing routine provided significantly better oral health outcomes for subjects compared to subjects who only brushed their teeth twice a day. [redacted] The significant benefits in reductions of plaque, gingivitis and bleeding, and increases in percentage of sites that are healthy and plaque-free was seen in the groups that used an essential oil mouth rinse, Listerine Antiseptic Cool Mint, in their oral care regimens. The results of this study may be useful to dental healthcare professionals in recommending the most effective oral care routine for their patients.

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