**PATIENT INFORMATION SHEET**

**Title**

Clinical research study to evaluate the effect on gingival inflammation of a toothpaste containing vitamin D in patients with established dental plaque and gingivitis.

**Principal Investigator:** Professor Sašo Ivanovski

**Chief Investigator:** Dr Ryan Lee

**Associate Investigators:** Dr Valerie Woodford, Dr Pingping Han, Ms Elizabeth Grounds

**Purpose**

You are being considered for participation in this clinical research study. The purpose of this study is to evaluate the effect on gingival inflammation of a toothpaste containing vitamin D (Supplied by Colgate Palmolive Co.) in patients with established dental plaque and gingivitis. Please note that the study is financially sponsored by Colgate Palmolive Co. The purpose of this consent form is to give you information you will need to help you decide whether to be in the study or not. Please read the consent form very carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this consent form that is not clear. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called ‘informed consent.’ We will give you a copy of this form for your records.

**Benefits**

Participation in this study may not benefit you personally. The results of the study may help to characterize this effect of Vitamin D on gum inflammation, leading to the development of a safe and inexpensive prophylactic or therapeutic treatment for periodontal disease. Currently, there are other therapeutic treatments for the control of plaque and gingivitis, such as, professional cleaning, toothpastes and the regular use of dental floss. This clinical trial may help to find alternative methods of controlling plaque and gingivitis

**Test Description**

Approximately Eighty (80) subjects will be enrolled in this study. In order to be selected, you must meet certain inclusion criteria:

1. You must be between 18- 70 years of age;

2. You must be available for the duration of the study;

3. You must have good general health;

4. You must be willing to provide information related to your medical history.

5. You must have minimum of 20 uncrowned permanent natural teeth;

6. You must be diagnosed with a gingivitis index of at least 1.5 as determined by the use of the Loe and Silness Gingival Index and at least 30% of bleeding sites and absence of periodontal disease;

7. You must sign this Informed Consent Form.

8. You must not have oral pathology, chronic disease, or a history of allergy to testing products.

9. You must not be using anticonvulsants, antihistamines, antidepressants, sedatives, tranquilizers, anti-inflammatory medication or daily analgesics within one month prior to the start of the study or scheduled to start such intake during the course of the study.

10. You must not be participating in any other clinical study.

11. You must not have co-habitants participating this current clinical study.

12. You must not be pregnant or breast feeding.

13. You must not be allergic to oral care products, personal care consumer products, or their ingredients.

14. You must not have had extended use of antibiotics or therapeutic mouthwash any time during the three months prior to entry into the study.

15. You must not be taking any vitamin D supplements 3 months prior to the start of the study.

16. You must not be using medications known to affect the gingival (gum) tissues (i.e. calcium channel blockers, phenytoin, cyclosporine).

17. You must not have periodontal pocket depth > 4 mm, determine by the dental examiner;

18. You must not be a current smoker or have a history of alcohol or drug abuse.

19. You must not have an existing medical condition which prohibits you from eating or drinking for periods up to 4 hours.

**Study Procedures**

* **Clinical Examination:**

At the start of the study, you will report to the clinical facility having refrained from any oral hygiene procedures for twelve hours prior to your examination and having refrained from eating, drinking or smoking for four hours prior to your examination. Your teeth and gums will be examined by a trained dental professional to determine if you are eligible for entry into the study. There may be some discomfort associated with the examination procedures. If your teeth and gums are satisfactory, and you meet all the inclusion/exclusion criteria, you will be eligible for entry into the study.

* **Blood Sample Collection**

You will be required to provide **blood samples** at the **start** and at the **end** of the study in order to measure the Vit D blood concentration and inflammatory chemical markers. Blood samples will be collected at the site by trained and qualified onsite registered nurse (RN) practitioners. You will be required to provide gingival fluid and saliva samples at each evaluation.

* **Gum Fluid Collection**

Gum fluid samples will be collected from multiple teeth (front and back teeth – up to 4 teeth) for chemical biomarker testing by using absorbing paper points. Mild-No discomfort is expected from this procedure.

* **Saliva collection**

Collection 3 ml of whole unstimulated saliva will be done without any chewing stimulus and will be based on passive drooling of saliva into a cup.

**Randomisation**

After the initial evaluations, you will be randomly assigned to one of the two study groups. You will be either provided with a commercially available toothpaste (Control Group) or Vit D containing toothpaste (Test Group), and a toothbrush and instructed to brush your teeth at least twice daily (morning and evening) for two (2) minutes with the products provided. All study products are provided to you free of charge.

**Masking**

The examining dentist and his /hers staff will remain blinded to product assignment. Toothpastes will be covered with white over-wrapping in order to conceal the product identity. The products will be distributed in an area separate from the examination room by site personnel not involved in the clinical evaluations. The products will be in a sealed bag to account for any differences in product aesthetics and packaging among study groups. Label information will consist of a study group code, instructions for at-home use and safety information, including emergency contact information.

**Subsequent evaluations**

As part of this study, clinical procedures will be repeated at 20 and 60 days. You are to report to the clinical facility as scheduled. Your teeth and gums will be examined by a trained and calibrated dental clinician (any of investigators listed in this ethics application), using the same procedures employed at baseline. You will be required to provide oral mucosa, dental plaque and saliva samples at each visit. You must only use the toothpaste and toothbrush provided for the duration of the study. These products should not be shared with any other member of your household.

You will be allowed to maintain routine oral hygiene procedures such as flossing or inter-dental stimulators during the study. There will be no restrictions regarding diet habits during the course of the study. You are asked to refrain from routine dental treatment but should not defer any necessary or emergency dental treatment. You are requested to inform the examining dentist immediately if you receive emergency dental treatment, take any antibiotic medication or receive dental treatment that interferes with this study, or if you become pregnant or breast feed.

After the 60 days evaluation, you will have completed the study. After this evaluation, you will discontinue product use and will return to your normal oral hygiene regime. All used and unused products should be returned. In the event that the study is discontinued, you will discontinue product use and will return to your normal oral hygiene regime. All unused products should be returned.

**Potential Risk**

In general, no adverse side effects are anticipated from the use of either of these toothpaste products (Control or Test – Please note that you will be using one of the toothpastes only according to the random allocation process during the study). However, there is a potential for soft tissue/gum irritation and/or temporary tooth hypersensitivity with use of the test products. If either of these conditions occurs, it is expected they will be reversed upon cessation of test article use.

If you experience any problems or any research related injury, you are to contact **Dr Ryan Lee** (**number: (07) 3365 8013**). If you were unable to contact Dr Ryan Lee please call your primary physician. You understand that if any physical injury results from your use of the test products, the sponsoring company will be responsible for medical costs provided you seek medical attention as directed by the sponsoring company or as directed by the Study Investigator.

**Compensation**

You will be monetarily compensated ($50 per visit = $150 in total for the study) for expenses to cover any of your transportation cost and meals during your participation in the study. If you do not complete the study of your own free will, you will not receive the compensation for the missed visit.

**Pregnancy during the course of study**

No pregnant women will intentionally be enrolled in this study. In the event a women enrolled in this clinical research study becomes pregnant during the course of the study, participation in this study will be terminated upon the clinical staff’s notification of the event. The subject’s medical records used in this study will be updated to reflect the pregnancy and there will be follow- up contact (Clinical Coordinator – Ms Elizbeth Grouds) until the end of the pregnancy to record the outcome in the clinical file.

**Confidentiality**

The results of this study may be published and/or submitted to the FDA and/or local regulatory agencies in other countries. Your identity will be kept confidential, only your subject number/ID, gender and/or age may be used in connection with any such publication of the study results. You understand that the study records including any medical records obtained as a result of your participation in the study will be examined by the investigator and may also be examined by local regulatory agencies, Ethics boards (RBWH HREC). No documents that identify you by name (e.g., the signed informed consent form and health questionnaire) will be transferred or submitted to the study sponsor (Colgate Palmolive Co.), but will be maintained in strict confidence by the investigator. However, the investigator must allow auditing by the appropriate national or local authorities and to the sponsor personnel to verify subject enrolment, product safety and study compliance.

If any regulatory inspection, study audit or sponsor monitoring occurs, study documents can be looked at, but no private information will be copied or removed from the clinical site. If any follow up is necessary, the investigator will contact you and ask your permission where applicable to allow the regulatory agencies, ethics board or the sponsor to contact you. Please refer to the privacy notice for more information.

**Maintenance and Confidentiality of Dental/Medical Records**

Your dental/medical records will be kept in accordance with state and federal laws concerning the privacy and confidentiality of medical information. At all times, subjects’ study information will be stored in a secure Research Data Management system, the University of Queensland. Only the delegated study personnel will have access to the identifiable data. De-identified data will be available to the investigator, sponsor and other persons involved in the study. Samples taken will be stored for future analysis and studies (at least for 5 years). For future scientific research projects, the specific details (e.g. specific biomarkers in the body fluids – blood, GCF and Saliva) of which may not be known at present, will used to advance science and public health care or treatment. Appropriate Ethics approval will be sought at that time. As the potential uses for these samples cannot be known at this time, by signing this informed consent, you allow the use of your samples to be analysed in the future. You might leave the study at any time and request the destruction of your collected data.

**New Findings**

You will be informed of any significant new findings related to study products or procedures as soon as they are known. Such information may affect your decision to continue participation in the study.

**What happens if I change my mind? - Right to Leave the Study**

Your consent (Consent Form – separate document) signifies that you understand and agree to the above, and affirms that you have volunteered to participate of your own free will. Further, you assert that you are eighteen (18) years of age but not older than seventy (70) years of age and not nursing a baby or pregnant and that you were given the opportunity to ask questions about the study.

Even after you consent, you have the right to withdraw your consent at any time. Should you choose to withdraw your consent, your investigator (or another member of the Primary Study Team) may ask you to undergo an end of study examination, and will thereafter stop collecting your personal data as part of this study. You should know that if you withdraw your consent, you will not be able to continue taking part in the study. Further, you should understand that data that has already been collected may not be able to be deleted from study records due to regulatory requirements that are designed to safeguard scientific integrity. The investigators may be required to include your personal data in analyses and aggregated study results, but you will not be personally identifiable by name in such reports.

Also, contact information or emergency contacts details which you provided, may be used by the investigators in order to re-establish contact with you, if necessary for subject safety reasons, reporting duties or a vital interest, such as a life status check. Publicly available information such as public registers or social media may be used for these purposes.

To withdraw your consent to the collection, use, and disclosure of your personal data, you need to contact the study Investigators for ***Withdrawal of Consent From*.**

**Privacy Rights**

You have the right to request to review, correct, delete, restrict, object to the use or receive a portable copy of your personal data. Note that such rights may be suspended or restricted under the study, or that exercising them may affect your participation in the study. For example, if you obtain access to your study records during a study where you are not supposed to know whether you are receiving actual medication or a placebo, you may not be able to continue participating in the study. Similarly, there may be legal or regulatory requirements to retain data that have been collected as a part of a study, despite your right to request their deletion. Moreover, if Your De-identified Data has been used in a publication, it may not be possible to delete it.

To submit a request regarding your personal data, please contact your study investigator.

This study is being conducted for the sponsoring company under the direction of **Dr Ryan Lee (telephone number: (07) 3365 8013)**, who can answer any questions related to the study procedure.

**Who has reviewed this study?**

This study has been reviewed and approved by the Royal Brisbane & Women’s Hospital Human Research Ethics Committee (EC00172). Should you wish to discuss the study in relation to your rights as a participant, or should you wish to make an independent complaint, you may contact the Coordinator or Chairperson, Human Research Ethics Committee, Royal Brisbane & Women’s Hospital, Herston, Qld, 4029 or telephone (07) 3647 1007, email: RBWH-Ethics@health.qld.gov.au or the Metro North Research Governance Manager, Phone: 07 3647 9550; Email: MNHHS-RGO@health.qld.gov.au