Confidential

Tufts UNIVERSITY | School of Dental Medicine

Exploratory Study on Effect of Whitening Agent with Emulsion Gel in Xerostomic Population

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Study Location: Tufts University School of Dental Medicine
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Sponsor: Procter & Gamble

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I) Introduction

A) Aim/Hypothesis/Objective

Objectives:

- Primary aim: To see a reduction in the self-reported subjective perception of dryness in the oral cavity.
- Secondary aims: To measure self-reported sensitivity of the teeth, self-reported perception of teeth whiteness, and objective measurement of improvement of saliva production.

II) Background and Rationale

Xerostomia, is a subjective sensation of dryness of the mouth, which may have a significant effect in a persons quality of life. The sensation of dryness of the mouth may be caused by autoimmune diseases which attack the saliva producing glands irreversibly e.g., salivary glands, or the sensation of dryness could be caused by therapeutic radiation, which can destroy the salivary glands at the genetic level and impede their functions. Additionally, there are more than 700 medications including antihypertensives, anti-anxiety agents, psychiatric remedies, and antihistamines that can effect neural transmission. Neural transmission is when the neuro transmission is hindered reversibly leading to the salivary hypofunction that results in dry mouth. It is estimated that 12-47% of the elderly and 10-19.3% in their early 30's suffer from dry mouth (6)(7). In a study, it was found that the prevalence of xerostomia was 10.0% (with no apparent gender difference) among 32-year-olds and was significantly higher among those taking antidepressants (odds ratio =4.7) (5). At risk groups may present much higher (60+%) rates of xerostomia. A systemic literature review suggests a prevalence of 27 –32% of the medicated population suffer from xerostomia as a side effect (7).

Saliva, the bulk fluid of the oral cavity is very important in maintaining the functions and balance in the oral cavity including candidiasis and enamel erosion prevention. In past studies, residual mucosal fluid levels were seen to vary in different oral cavity sites from an average of 70–100 μm (2)(3). In addition, the vault of the hard palate has much less mucosal fluid thickness than the floor of the mouth. Over the moisture layer is the lipid layer and reduction or loss of this

moisture layer can contribute to the subjective perception of the dryness in the mouth. An addition of the lipid layer will also increase lubrication in the oral cavity.

Unstimulated salivary flow in dry mouth patients has shown an increased clinical oral dryness score and mucosal wetness is at a significantly reduced rate ($p<0.05$) when compared with healthy subjects (4).

Historically, various products containing methylcellulose, water, oily emulsions etc., have been used to alleviate the subjective sensation of dryness in the oral cavity in the forms of rinse, gel, ointment and paste. However, the alleviation of the dry mouth symptoms has been varied.

This study will investigate a semi solid cohesive gel (referred to as Whitening Gel) that has the primary marketed purpose of teeth whitening. We theorize that the whitening gel's retention in the oral cavity is longer than rinse forms and this is likely to promote the flow of saliva by stimulating taste buds which could alleviate the sensation of dryness in the oral cavity.

The study product contains an inert hydrophobic phase in an amount from 30% to 98%, preferably from 40% to 90% by weight of the composition. It also contains an emulsifying system in an amount from 1% to 10%, preferably from 3% to 7% by weight of the composition.

P&G's whitening gel emulsifying system is comprised of at least one surfactant having an hydrophilic-lipophilic balance (HLB) <10, preferably comprised between 3 and 7, and at least one surfactant with HLB>10, preferably comprised between 12 and 16.

The optimal duration and frequency of application for whitening is up to 4 times a day. For the purpose of this study, the whitening gel will set on the subject's teeth for 5 minutes during each use.

The product being used is a commercially available product, known as "Crest Whitening Emulsions", will be used as the investigative product. There will be no active control group. This is not the first time P&G whitening gel will be used in humans. We do believe this is the first study investigating dry mouth sensation from using a whitening gel.

III) Research Plan

A) Experimental Design

This will be a single center, two visit study investigating the effectiveness of dryness in the oral cavity, whiteness of teeth, and teeth sensitivity after one week's use of whitening agent.

B) Sample Size and Statistical Analysis

Sample size

This is a single site study. All study-related procedures will take place at TUSDM. Based on our preliminary data from a previous study, we anticipate 25 subjects will be needed to achieve the necessary statistical power required to observe expected differences in relief of dryness in the oral cavity. Because we anticipate the potential of many screen failures due to the VAS scale and saliva production requirements outlined in the exclusion/inclusion criteria section, we will screen/enroll a total of 100 subjects to conservatively account for potential dropouts or screening failures.

Statistical analysis

The subjects will be asked to complete one questionnaire each visit. Completing the first part before the application of the study product, and completing the second part after the application of the study product, as directed on the questionnaire. The self-reported scores from the visual analogue scales (VAS) will be considered on the first and final visit. The salivary flow before and after the application of the product, Pre & Post-Product Use Dry Mouth & Sensitivity Questionnaire before and after the product application will be compared using a student -t test method. The same method will be used to make comparisons of these gathered data points between the first and final visits.

Randomization

This will be an open label study; thus no randomization plan is necessary.

Blinding

There will be no blinding for this study.

C) Products

The investigational product to be used in this study is manufactured by P&G and called, "Crest Whitening Emulsions". The amount of each dose should be enough to cover the entire tip of the whitening wand, approximately ½ a tsp. The use of the study product in this study will be for what they are approved for. Per the manufacturer's instructions, study subjects will be asked to apply the study product up to 4 times a day.

Procter and Gamble will be supplying the study product gel to the study team. IDS will not be involved in this study.

The investigative product to be used in this study is a hydrophobic emulsion containing agent (a teeth whitening gel with emulsification gel). It contains:
Petrolatum, Water, Hydrogen Peroxide, Flavor, Sucralose, Sorbitan Palmitate

D) Subject Characteristics
   1) Inclusion Criteria
      - At least 18 years of age.
      - The inability to produce more than < 0.18mL/min of unstimulated saliva.
      - Score of 5 or more on question 1 of the VAS dry mouth scale (How severe is your dryness right now?), evaluated in the Pre-Product Use Dry Mouth & Sensitivity Questionnaire .
      - Evidence of currently taking Xerostomia-inducing medication such as, antihypertensives, anti-anxiety agents, psychiatric remedies, antihistamines.
      - Subject not currently using any teeth whitening or desensitizing products that contain potassium nitrate such as Sensodyne or Pronamel.
      - Subject willing to comply with the study regimen and products.

   2) Exclusion Criteria
      - Subjects who are currently pregnant *(self-reported).*
      - Subjects able to produce more than 0.18mL/min of unstimulated saliva

- Subjects that have ever received therapeutic radiation in the head and neck area.
- Subjects with a diagnosis of conditions that would affect salivary flow such as Sjogren's Syndrome.
- Subjects with a condition the investigator believes not suitable for the study such as autoimmune diseases that impact salivary flow.
- Subjects that currently use whitening toothpaste, desensitizing toothpaste, or any other products causing similar results.
- Subjects currently participating in any other research studies.
- Subject unable to provide consent (ex. Cognitively impaired adults).
- Non-English speaking

3) Subject Withdrawal/Termination Criteria
   - Subjects who do not comply with the study procedures, such as use of teeth whitening products, may be withdrawn from the study.
   - The study team may terminate subjects if they no longer fulfill inclusion criteria, if an exclusion criterion is met, or if they do not show up for scheduled study visits.
   - Subjects who experience an unanticipated adverse drug effect will be withdrawn from the study.
   - Subjects unable to complete the study procedures due to a medical condition such as dry mouth and sensitivity conditions that result in the inability to capture meaningful data during the study procedures.
   - Subjects may choose to withdraw from the study at any time.

   Subjects may remain patients of TUSDM if they decide to withdraw from the study or are withdrawn by the study team.

   If during the course of their participation in the study, a subject chooses to withdraw or is withdrawn by the research team, any data that has been

collected will not be included in the analysis and the subject will be asked to return any leftover whitening gel and the diary. The subject is able to keep the toothpaste and toothbrush.

Subjects will not be able to partially withdrawal from study intervention and just be involved with continued data collection.

The Principal Investigator will determine whether subjects (either withdrawn subjects or subjects completing the study) are in need of additional treatment and/or follow-up observation as a result of participation in this trial and will refer them to their primary care provider for further care. Subjects and/or their insurance will be responsible for the cost of any standard of care follow-up visits or additional treatment that is not part of this study.

4) Vulnerable Populations

Transgender subjects will be recruited as part of this study. All subjects will be asked on the Medical/Dental History Form to identify their sex, to which they will answer however they choose. They will not be sought out or targeted for participation and will not be discriminated against as a result of their sexual orientation/gender identity. The subjects will not be asked to disclose if they are transgender or not on the Medical/Dental History Form.

Cognitively impaired adults and pregnant adults will not be enrolled in this study. There would be no direct benefits to these specific vulnerable populations by enrolling them. Pregnancy will be determined through self-reporting.

Non-English speakers will be excluded from the study because the study team does not have validated questionnaires developed in multiple languages. The study team also does not have the resources to translate the take home diary or manufacturer's

instructions. In addition, the visual demonstration of the application of the study product will not be able to be effectively translated using the Interpreter Machine available at TUSDM. There are no physical translators available at TUSDM to assist in translating the visual demonstration. There are no direct benefits to this population by participating in this study.

E) Assessment

1) Risk

The standard risk associated with teeth whitening products include causing gum irritation, gum or teeth bleaching, teeth sensitivity, and irritation of the oral mucosa (cheeks, lips, tongue). In addition, there is a risk of irritation or whitening from contact with skin from using this study product. Subjects may also feel discomfort when they abstain eating or drinking before the study visit.

There is the risk of loss of confidentiality to the subject by participating in this study. This risk will be kept to a minimum by following procedures listed under confidentiality section.

2) Benefits

There is no direct medical benefit to the subject for participation in this study. However, the results of the study will help better understand whether the application of hydrophobic emulsion containing agents have a beneficial effect in alleviating subjective sensation of mouth dryness along with teeth whitening in a Xerostomic population. The results of this study will help in understanding the contributing factors that alleviate dry mouth and increase esthetics through whitening of teeth.

3) Alternatives

Patients may choose not to participate in the study and to receive the standard of care treatment for dry mouth at TUSDM at normal clinic fees.

F) Study Procedures

Visit 1 (*1-1.5 hours)* **Screening/ Baseline (Day 0)**

1. Subject will be called 1-2 days before their appointment to confirm that in order to participate, they must:
    a. Not consume alcohol for 24 hours prior to their visit.
    b. Not brush their teeth for 1.5 hours prior to their visit.
    c. Not have had anything to eat or drink (including chewing gum or eating candy) for 1.5 hours prior to their visit). Water is acceptable to drink up to 1 hour prior to the study visit.
    d. Not smoke 1.5 hours prior to their visit.
2. The subjects will be asked to read the informed consent form (ICF). Subjects will be given ample time to have any questions answered. If a subject decides to participate, he or she will be asked to sign the ICF. A copy of the ICF will be given to the subject.
3. Subject will be asked to complete demographic information and a medical history.
4. An oral exam, including evaluation of oral cavity, soft and hard tissues, will be completed following standard of care procedures in US dentistry using a mouth mirror and dental explorer.
5. Subject medications with potential side effects being dry mouth will be verified using the Physician's Reference Desk.
6. Saliva Collection 1 (pre-product application): Saliva will be collected by asking subjects to do nothing but drool into a pre-weighed vial for 5 minutes (referred to as the Drooling Method). The post collection weight will be subtracted from the pre-weight to determine the flow rate. The saliva samples will be discarded after they are weighed.
7. A paper questionnaire will be given to subject to complete before application of study product and after application of study product. Questionnaire includes Visual Analogue Scale (VAS) questionnaire on dry mouth, quantity of saliva, and perceived sensitivity of teeth.

8. Inclusion/exclusion criteria will be evaluated and eligibility for the study will be determined.
9. Demonstration and application of study product:
    a. A visual and oral demonstration of application of the whitening gel will be performed by a study team member. The script for the demonstration will be the one provided in the information packet in each study product box so the subject can bring the instructions home. The study team member will mimic the necessary steps to properly apply the gel, without using the product. The study team member will then have the subject complete the steps while applying the gel to their own teeth. Subjects will then be asked to sit for 5 minutes to let the gel set on their teeth.
10. Saliva Collection 2 (post-product application): Saliva will be collected using the same Drooling Method as Saliva Collection 1. The saliva samples will be discarded after they are weighed.
11. Photographs of subject teeth will be taken by a standard dental camera. The photos will only contain subject teeth and oral cavity with no subject identifiers visible. In addition to the ICF, the subjects will be asked to sign a photo release form. If the subject does not wish to sign this form, their photographs will not be taken. Those who do not consent to having their photos taken will be tracked in the enrollment log. Photographs will be taken pre-application of the study product at visit 1.
12. Distribution of study product and diary: One box of study whitening gel product, (0.88Oz) toothpaste, and a toothbrush will be dispensed by study team members. This is to ensure all participants are using the exact same dental products during the trial period. The subjects will be asked to not use any other oral tools or products during the trial period aside from the ones distributed by the study team at Visit 1. A diary will also be dispensed for the record keeping of the application of the products. A study team member will again verbally tell the participant the instructions that are provided with the study product and that per the

instructions, they can apply the product up to 4 times per day until their next study visit. The same script from step 9.a. will be used.

13. Gift card will be distributed upon successful completion of visit.

Visit 2 *(1-1.5 hours)* ***Final Visit - 7 ∓ 2 days after visit 1***

1. Subject will be called 1-2 days before their appointment to confirm that in order to participate, they must:
    a. Not consume alcohol for 24 hours prior to their visit.
    b. Not brush their teeth for 1.5 hours prior to their visit.
    c. Not have had anything to eat or drink (including chewing gum or eating candy) for 1.5 hours prior to their visit). Water is acceptable to drink up to 1 hour prior to the study visit.
    d. Not smoke 1.5 hours prior to their visit.
2. Medical history will be reviewed, and any changes will be noted. Any changes to medications will also be reviewed and noted.
3. Eligibility and subject withdrawal criteria will be reviewed to ensure the subject still qualifies for the study.
4. Subject medications with potential side effects being dry mouth will be verified using the Physician's Reference Desk. Subjects will be asked to confirm that they have taken their medications as prescribed since Visit 1.
5. An oral exam, including evaluation of oral cavity, soft and hard tissues, will be completed following standard of care procedures in US dentistry using a mouth mirror and dental explorer.
6. Saliva Collection 1 (pre-product application): Saliva will be collected using the drooling method for 5 minutes into a pre-weighed vial. The post collection weight will be subtracted from the pre-weight to determine the flow rate. The saliva samples will be discarded after they are weighed.

7. The paper questionnaire will be given to subject to complete before application of study product and after application of study product. The questionnaire

includes the Visual Analogue Scale (VAS) questionnaire on dry mouth, quantity of saliva, and perceived sensitivity of teeth.

8. Application of study product: A study team member will ask the subjects to apply the gel to their teeth. Subjects will then be asked to sit for 5 minutes to allow the gel to set on their teeth.
9. Saliva Collection 2 (post-product application): Saliva will be collected using the same drooling method as Saliva Collection 1. The saliva samples will be discarded after they are weighed.
10. Photographs of subject teeth will be taken by a standard dental camera. The photos will only contain subject teeth and oral cavity with no subject identifiers visible. Photographs will be taken post-application of the study product at visit 2.
11. The study diary and any leftover whitening gel product will be collected.
12. Gift card will be distributed upon successful completion of visit.

	Screening/ Baseline Visit Day 0	Visit 2 Day 7 (±2 days)
Informed Consent Form	x	
Demographics	x	
Collect and/or Review Medical History	x	x
Review eligibility and withdrawal criteria		x
Confirmation of Xerogenic Medications	x	
Pre-Product Use Dry Mouth & Sensitivity Questionnaire	x	x
Post-Product Use Dry Mouth & Sensitivity Questionnaire	x	x
Unstimulated Salivary Test	x	x
Oral Exam	x	x
Evaluate eligibility criteria	x	
Oral Photographs	X (Pre-Application)	X (Post-Application)
Demonstration of Product Use	x	
Product Usage	x	x

Post Product Use Unstimulated Salivary Test	x	x
Product Distribution or Collection	x	x
Adverse Event Reporting (if applicable)	x	x
Stipend	x	x

G) Subject Safety

1) Adverse Event Reporting

Adverse Events

An adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal physical exam or laboratory finding, symptom, or disease, temporally associated with a subject's participation in the research.

Adverse events will be recorded in source documents and on case report forms. All adverse events and non-serious situations will be recorded, monitored, and reported to the IRB at time of continuing review or at the study's termination if this occurs before the study's next continuing review.

Serious Adverse Events

A serious adverse event is one that results in death, or is life-threatening, or results in hospitalization or prolongation of existing hospitalization, or results in a persistent or significant disability/incapacitation, or results in a congenital anomaly/birth defect, or may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed above.

Serious adverse events will be recorded in source documents and on case report forms. Serious Adverse Events that meet the criteria of an unanticipated problem will be reported to the IRB within 5 business days following the Reportable New Information Policy. Serious Adverse Events not meeting the criteria for an unanticipated problem will be reported to the IRB at time of continuing review or at the study's termination if this occurs before the study's next continuing review.

Unanticipated Problems

An unanticipated problem is an incident, experience, or outcome that meets all of the following criteria: 1) The nature, severity, or frequency is unexpected for the subject population or research activities as described in the current IRB approved protocol, supporting documents, and the ICF(s); 2) it is related or possibly related to participation in the research; 3) it suggests the research may place the subject or others at a greater risk of harm then was previously recognized.

Unanticipated problems will be recorded in source documents and on case report forms. Unanticipated problems will be reported to the IRB within 5 business days after the PI/study team becomes aware of the problem. A Reportable New Information Form will be submitted to the IRB no later than 5 business days after the PI/study team becomes aware of the problem.

Unanticipated Adverse Device Effects (UADEs)

Unanticipated adverse device effect means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

UADEs will be documented in source documents and on case report forms as to onset, severity, duration, management, outcome and relatedness to the test device. UADEs will be reported to the IRB within 5 business days after learning of the effect.

H) Subject Participation

1) Screening

The PI/CO-I (Dr. Mabi Singh and Dr. Athena Papas) will conduct screening examinations to identify subjects who meet the inclusion / exclusion criteria for enrollment into the study.

2) Informed Consent

The PI or his representative will introduce the study. Consenting will take place in a private clinic room at on the 14th floor of Tufts University School of Dental Medicine (TUSDM) and the patient will be given as much time as they need to consider participation or have any questions answered by the PI. The participant will be invited to include or exclude any associates (e.g., loved ones) in the consent process.

Patients will be asked to read the consent form and be given ample opportunity to have their questions answered. To avoid coercion, the consenting investigator will read through the copy of the consent form with the participant section by section, making sure the participant understands each section and has an opportunity to ask questions. If at any time the participant indicates they are not interested in participation, the meeting will end.

If after going through the consent form, the participant indicates they would like to discuss the study with associates or think about participating, then the meeting will be ended, and the participant will be asked to contact the study when they make their decision. If the participant contacts the study in the future for participation, they will be invited back to the clinic, and if informed consent is given at that time, study activities will begin then.

If the participant indicates they may be interested in participating after going through the consent form with the investigator, and the investigator determines the participant has the capacity to provide informed consent, the participant will be asked to provide informed consent at that time. Written consent will be obtained following

"SOP: Written Documentation of Consent (HRP-091)" and we will follow the "SOP: Informed Consent Process for Research (HRP-090)." Patients will certify their willingness to participate in the study by signing and dating the IRB approved informed consent document. The subject will be given a copy of the consent form.

If any new finding requires any change to the informed consent form, the subject will be reconsented.

Study Location:
Tufts University School of Dental Medicine

3) Personnel

All study personnel will be GCP and CITI certified and trained on all their roles, responsibilities, and study procedures.

I. **Ongoing communication with the IRB and sponsor**– The PI
II. **Subject Recruitment** – The PI or his representative
III. **Obtaining Informed Consent** – The PI, Co-I, or a study coordinator, who is CITI and GCP trained, will obtain informed consent.
    a. The PI or CO-I will be available to answer any medical questions the subject may have.
IV. **Conducting inclusion/exclusion evaluation** – the PI or CO-I
V. **Saliva collection, questionnaire dissemination, product use demonstration and dissemination** – The PI or his representative
VI. **Maintaining participant's research records** – The PI
VII. **Monitoring and reporting of adverse events** – The PI

4) Payment for Participation

(a) Compensation

Subjects will be given a $75 Target gift card upon successful completion of each study visit. In total, subjects will receive $150 for their full participation in the study, as long as they attend both visits and are not withdrawn. Subjects that withdraw before either study visit is completed will not be provided a parking voucher. Subjects who fail to meet the inclusion criteria of the study will receive a $25 Target gift card.

(b) Transportation

- *Travel reimbursement and transportation costs.*

Subjects will be provided a parking voucher to accommodate their parking needs at TUSDM at the successful completion of each study visit.

(c) Costs and Insurance

Neither the subject, nor their insurance company, will be billed for any study procedures.

5) Study Results

Subjects will not receive information regarding the results of the study.

A final report and results will be transferred to the sponsor when requested. Individual data will not be transferred. The study team will consult with Tufts University Technology Transfer to determine whether an agreement is needed to permit the transfer of data/specimens, and an agreement (e.g., contract, Clinical Trial Agreement, Collaboration Agreement, Data Use Agreement (DUA), or Material Transfer Agreement (MTA)) has been or will be established that will cover any transfer of data/specimens, and the agreement will be executed ***prior*** *to any transfer.*

Study records will be retained for the timeframe described in the record retention policy of the "SOP – Records Retention Timeframe – Investigators". The study team will follow the "Confidentiality and Data Security Guidelines for Electronic Research Data" for electronic data.

6) Confidentiality

To ensure confidentiality of subject information, each subject enrolled in the study will be assigned a unique alphanumeric code. Subjects' paper files will be kept in a secure, locked cabinet in a secure room (TUSDM 742 or 1418) when the files are not being reviewed. Coded items will be kept in a separate locked drawer in 742 or 1418 from those with identifiers. The information will only be shared between the researchers on this study team. All HIPAA requirements will be followed. All electronic files will be kept on a password protected Tufts-encrypted computer in a secure, locked office.

No information or samples collected as part of this study will be used or distributed for future research studies.

(a) Coding

Each subject will be assigned a subject identification number. Alphanumeric identification numbers will be assigned sequentially. This will be accessible by study personnel only.

The study team will maintain a confidential list of the subjects separate from the consent forms, which will serve as a means of linking the subject ID number to the study records. This key between subject ID number and identifiable information will be kept in password protected document in Tufts BOX. The gift card receipt documents and parking vouchers, which have both subject ID and identifiers on them, will also be kept in a password protected Tufts Box Folder and/or in a locked cabinet in 742 or 1418 separate from coded subject files. All data used in analysis and reports will be used without identifiable reference to the subjects; only Subject ID will be used. Only the research team will have access to the key code for the subject ID numbers, study files, and data. No *identifiable* photographs will be recorded as part of this study. Genetic information will not be collected from the subjects for the purpose of this study. The study data entry and study management systems used by Tufts University School of Dental Medicine research

staff will be secured and password protected. At the end of the study, all study databases will be archived at the Tufts University School of Dental Medicine.

(b) Access

Only study personnel will have access to data. Investigators will permit monitoring, audits, and regulatory inspections and will provide direct access to study related documentation. The study sponsor will not have access to any identifiable data.

8) Data Safety Monitoring Plan:

Study personnel will monitor this trial for all safety related issues to determine whether an unreasonable risk to subjects develops. Quality control measures include routine inspection of case report forms, source documents, data tabulations, and tracking of adverse events.

9) New Findings:

The subject will be informed of any significant new findings discovered during the course of this study that might influence the subject's continuation and participation in the study. Subjects will be told at a study appointment or via telephone of new findings during the study. If new findings require revisions to the ICF, the subject will be re-consented.

I) Record Retention

1) Study Records

The Principal Investigator will maintain all study records and documents during the study period. All paper files and documents will be kept in a locked file cabinet, within a locked room, 742. For electronic records, the study team will use Tufts BOX, which is HIPAA compliant, and data would only be accessible to study team members.

2) Long Term Retention

All study records will be kept for a minimum of 7 years after the study has ended as described in the record retention policy of the "SOP – Records Retention Timeframe

– Investigators". All research records will be kept at Tufts University School of Dental Medicine, de-identified, and in a locked cabinet in office 742 for a minimum of two years after the study close. At the end of the two years, the research material can be sent to Iron Mountain for the remainder of the seven years. The study team will follow the "Confidentiality and Data Security Guidelines for Electronic Research Data" for electronic data.

K) Reporting

Unanticipated problems, adverse events, and RNI will be reported per the Tufts MC/TUHS IRB Reportable New Information Policy.

The IRB will be notified of any deviations from the protocol in cases of medical emergencies when the change is necessary to eliminate an apparent immediate hazard to the subject.

Progress reports on the investigation shall be submitted to the IRB at regular intervals, but in no event less often than yearly, e.g., at continuing review.

L) Protocol Deviations

No protocol changes or deviations will be made without prior agreement by the IRB and study sponsor unless implemented to prevent an immediate hazard to subjects. All other protocol changes or deviations will be made by a formal amendment subject to IRB approval. All such changes or deviations will be reported to the IRB and sponsor as they occur and included in the final study report.

M) Study Termination

This study may be terminated for the following reasons:

Discovery of unforeseen risk that could jeopardize the dental/physical well-being of subjects.

Enrollment or recall rates that are not likely to produce sufficient data for evaluation of safety and efficacy.

Non-compliance with the clinical investigational plan, the Investigator

Agreement, applicable FDA regulations or conditions of approval imposed by the reviewing IRB.

Withdrawal of IRB approval.

In the event of study termination, the Principal Investigator will determine whether subjects are in need of additional treatment and/or follow-up observation as a result of participation in this trial.

N) Subject Recruitment/Advertising

Paper flyers will be posted throughout TUSDM and Oral Medicine Clinic. Permission is not required for these posting locations. Flyers will remain posted until enrollment goals are met. Subjects will be recruited through responding to posted study advertisements. These posted advertisements will be visible to faculty, staff, students, and patients.

Investigators may also inform clinic patients about the study.

All of the forms of recruitment will be submitted for IRB approval prior to use.

A phone screening script and voicemail script will be used for recruitment. When an interested subject responds to the recruitment material, they will be informed of the general purpose of the study, procedures that will take place, and study time commitment. The study coordinator will conduct a brief screening via phone to determine eligibility. During this screening call, the coordinator will collect subject name, telephone number, email address, and mailing address for future correspondence.

Patients coming into the Oral Medicine Clinic for regularly scheduled visits will also be recruited. AxiUm maintains a computerized database of patient information of the Tufts Dental School. Potential subjects will be identified and prescreened from the Oral Medicine Clinic patient list containing the ICD 10 code number # code R68.2, which is the diagnosis code for xerostomia. These patients will be recruited using the same phone script outlined above. In the event the subject does not answer the phone, a voicemail script will be used. Up to 3 attempts will be made to contact potential subjects.

Screen failure data will be retained by PI in a screening log using Subject ID #. Identifiable information will not be recorded in the screening log and study sponsor will not have access to it.

O) References/Bibliography

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