Indiana University Informed Consent Statement for Research

Effect of an active compound containing gum on dental plaque formation on a 4-day accumulation model IRB# 25945

You are being asked to participate in a research study. This consent form will give you information about this study to help you decide whether you want to participate. It is your choice whether or not you want to be in this research study. Please read this form, and ask any questions you have, before agreeing to be in this study.

Why is This Study Being Done?

The purpose of this study is to test the effectiveness in lowering plaque formation on your teeth with an experimental active compound chewing gum containing a natural protein (protein MIIP-E2) which is a purified form of Lactoferrin (milk protein present in cow's milk). The MIIP-E2 treatment will be compared to two other treatments, an inactive compound chewing gum (no MIIP-E2) and a no chewing gum treatment. If you decide to participate you will participate in each of the three treatment periods during which you will be randomly assigned to a gum/no gum group, one per treatment period. You will not be able to brush your teeth or use any other oral hygiene products during the 96 hours treatment periods.
We are asking you if you want to be in this study because you have been in other plaque studies at the Oral Health Research Institute (OHRI) or have expressed an interest in being in studies at OHRI.

The study is being conducted by Dr. Ana Gossweiler of the Indiana University School of Dentistry, Oral Health Research Institute. It is funded by Lactea Therapeutics.

What is in the Experimental Study Gum?

The experimental chewing gum contains a protein called MIIP-E2 which is an ultrapure form of Lactoferrin. Lactoferrin is a natural protein which is purified and extracted directly from raw cow's milk. It is normally found on infants' formula and more recently, it has been used on dental products due to its antibacterial effects.

Lactoferrin has been designated as GRAS (generally recognized as safe) by the FDA in infant formula. The amount of Lactoferrin (MIIP-E2) used in the experimental gum is less than that recognized as GRAS by the FDA.

What Will Happen During the Study?

Before today's visit you were asked to not use any dental hygiene products or chew gum for 12 hours (+/-two hours) before your visit. You were also asked to not eat or drink anything for two hours before today's visit. If you did not follow these instructions, your visit will need to be rescheduled.

Following the consenting procedure, visit 1 will include the following (estimated to take about an hour to 1 hour and 45 minutes to complete, including consenting):

1. Complete an interview about your medical history and the medications you take.
2. Complete a demographic form.
3. Answer eligibility questions (like age, appointment availability, etc.)
4. Complete an oral exam by the study dentist who will look at the general condition of your mouth and gums.
5. Swish with a red disclosing solution (temporary dye) that will show where plaque is on your teeth. This will be followed by a plaque examination where the dentist scores the amount of plaque on each tooth. You will need to score a 2 or greater to participate.
6. If you qualify to this point, complete a dental cleaning by a licensed dental hygienist.
7. If you do not qualify, you will brush and floss your teeth to remove the disclosing solution.
8. Regardless of qualification, you will receive payment for the screening visit. If you qualified, you will be scheduled your next visit.

<u>Treatment Start Visits 2, 4 and 6 (estimated to take 1 hour and 30 minutes to complete)</u>
You cannot eat or drink anything (except water for two hours before each visit. You will need to rinse with water approximately 30 minutes before the visit.
At each of these visits, you will complete the following:

1. Answer continuance questions to be sure you remain eligible to be in the study.
2. Complete an oral exam by the study dentist.
3. Provide saliva samples as per instructed by a team member.
4. Complete a polish and flossing of your teeth by a licensed hygienist. If needed, the hygienist may use a dental instrument to remove calculus (scaling)
5. Disclosing solution (temporary dye) will be applied with a cotton swab to show where plaque is on your teeth. If plaque is present the hygienist will remove it, as needed.
   Disclosing solution will again be applied followed by a plaque exam by the dentist.
6. Complete the taking of photos of your teeth, including the front and both sides.
7. Be randomized to which gum/no gum group you will be assigned to. You will be assigned to one of the three groups, one at each of the three period start visits.
8. Receive your study product and home use diary with instructions on their use. You will use the first piece of gum (or no gum) under supervision of a study team member and complete your first diary entry at this visit. You may not brush or use any oral hygiene products from this point onward until your next visit, even if when you are assigned to the no gum group.
9. Receive payment for the visit and schedule next visit.

<u>End of Treatment Visits 3, 5 and 7 (estimated to take 1 hour to 1 hour and 10 minutes to complete)</u>
This visit must occur 96 hours (+/- 3 hours) from your last visit. You will be asked to rinse your mouth with water approximately 30 minutes before the visit.

The last time you will chew your study gum (if assigned) will be after dinner the night before this visit. You may not eat or drink (except water) for two hours before the appointment. You will need to rinse your mouth with water approximately 30 minutes before this visit.

1) Answer continuance questions to be sure you remain(ed) eligible to be in the study.
2) Receive a review of your home use diary and your returned, unchewed gum (or no gum)
3) Receive an oral exam.
4) Provide saliva samples as per instructed by a team member.
5) Swish with disclosing solution.

6) Complete the taking of photos of your teeth.
7) Receive a plaque exam by the study dentist.
8) Brush and floss the disclosing solution from your teeth.
9) Receive payment for the visit and schedule your next visit in approximately 10 days except at visit 7. During this period, you will go back to your normal brushing and oral hygiene procedures.

Study Restrictions

- No brushing or oral hygiene products/methods may be used for during each 96-hour treatment period, even when you are in the no gum treatment period.
- You will follow your normal oral hygiene/brushing procedures during each break period between each treatment group.
- When in the treatment periods where you are assigned the gum, you must use the chewing gum provided after each meal (three times a day—breakfast, lunch, and dinner). Chewing on one side of your mouth for one minute, then switch to the other side and chew for another minute. After that, you can continue chewing the remaining time in any way you want.
- You will be required to maintain a diary of your daily gum use, when in the gum groups.
- You should not have any elective dental procedures during the study, such as a dental cleaning. Emergency dental procedures may occur, if required.
- Please do not comment about the study on social media or electronic platforms. Do not discuss the study outside of family members/guardians/caretakes, medical professionals, or study staff.

What Are the Risks of Taking Part in the Study?

Below is the list of possible risks for this study along with a counter action to reduce each risk:

1. Use of Lactoferrin: The use of Lactoferrin in supplements is generally considered safe, with the U.S. Food and Drug Administration (FDA) recognizing Lactoferrin as GRAS (Generally Recognized As Safe). However, potential side effects can exist when Lactoferrin is taken in excessive amounts. Common side effects may include stomach pain, reduced appetite, and constipation. These risks are reduced in this study since the Lactoferrin amount used in the gum product is less than that recognized as GRAS. Should you experience any side effects from the use of the gum products, contact the research group immediately.
2. Cross contamination (germ spreading) is possible. To reduce this risk, the examiner will be a trained and licensed dentist and the entire team will follow strict infection control procedures outlined by the IU School of Dentistry.
3. Use of Disclosing Solution: The disclosing solution (red dye) you will rinse with prior to the plaque exams will temporarily stain the plaque on your teeth red. The soft tissues of the mouth (gums. tongue etc.) will also stain red. You will brush your teeth before leaving the visit to remove stain from the teeth and lessen the intensity of the red dye on the soft tissues. The remaining soft tissue stain will gradually wear away throughout the day.
4. During the dental exams or photographs irritation or accidental injury to the oral soft tissues (gums, cheek linings, etc.) is a possibility. These risks will be reduced by trained and experience personal performing the procedures.

5. There is the potential risk of loss of confidentiality of study records. To reduce this risk, all study documents, will be identified with an assigned study number instead of your name. All electronic records will be stored in an encrypted, password-protected computer file that only study personnel can access. All paper records will be stored in a locked area that only study personnel can access. Paper records that contain your name (like the signed consent form) will be stored in a separate locked area from other paper study documents.

Who Will Pay for my Treatment if I am Injured?

If you have an injury or illness due to participating in the study, necessary medical treatment will be provided to you. Lactea Therapeutics has agreed to pay for the reasonable costs of the diagnosis and treatment of any injury or illness which directly results from the use of MIIP-E2. Lactea Therapeutics will not pay any other costs, such as costs related to any pre-existing abnormal medical condition or underlying disease, or loss of dental fillings, crowns, or other pre-existing tooth repair as a result of chewing, unless the pre-existing condition, repair, or underlying disease is made worse by use of MIIP-E2. However, signing this form won't take away any of your legal rights if you are injured.

What Are the Benefits of Taking Part in the Study?

You will receive a dental cleaning at the screening visit if you qualify to participate in the study. If you do not receive dental cleanings on a regular basis, you might benefit from this cleaning. This cleaning should not replace your regular dental cleanings with your dentist as we will not be taking X-rays or providing fluoride treatment like your dentist would do.
We don't think you will have any other personal benefits from taking part in this study, but we hope to learn things that will help other people in the future.

Will I be Paid for Participating?

You will receive $30 on a payment card if you complete the screening visit, regardless of whether you qualify to be in the study. You will receive $50 for completing each treatment start visit that will be added to your card following the visit and $100 for completing each end of treatment visit, added to your card following the completion of the visit. Your total payment for completing all visits will be $480.

To pay you, we will need your Social Security number (SSN) or tax identification number (TIN). If you are paid $600 or more from IU in one year, you will receive a 1099 tax form from IU in January of the next year, and you will need to report this.

How Will My Information be Protected?

We will do our best to keep your personal information private, but we cannot promise complete confidentiality. We won't share any information that we think could be used to identify you in publications about this study. However, your personal information may be shared outside the research study as described above and/or if required by law.

Your personal information may be shared outside the research study if required by law. We also may need to share your research records with other groups for quality assurance or data analysis. These groups include the Indiana University Institutional Review Board, its designees, the sponsor, and other state or federal agencies who may need to access the research records (as allowed by law).

Information collected for this study may be used for other research studies or shared with other researchers who are conducting their own research studies. This may include sharing with researchers outside Indiana University and sharing with private companies. It may also include making the information available in public and private databases of research data so that other researchers can use the information to answer research questions.

If we share your information in this way, we will remove information that could identify you, such as your name and contact information before any information is shared. Since identifying information will be removed, we will not ask for your additional consent for this sharing.

Who Should I Call with Questions or Problems?

For questions about the study contact the Principal Investigator, Dr. Ana Gossweiler, at (317) 274-8822. If you are experiencing a study related injury after business hours, please call 317-278-5035. The paging service will contact one of the researchers who will get back with you as soon as possible.
For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Research Protection Program office at 800-696-2949 or at irb@iu.edu.

What if I Do Not Want to Participate or Change my Mind?

After reviewing this form and having your questions answered, you may decide to participate in the study. You may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your relationship with Indiana University School of Dentistry or the Oral Health Research Institute.
If you change your mind and decide to leave the study in the future, please contact the study team. The study team may wish to do an exam of your mouth and collect your study products.

The researchers may stop your participation in the study even if you do not want to stop if they feel it is not safe for you to continue or they do not feel you are properly following study instructions.

Agreement to be Contacted by Email

We may want to communicate with you about this study by email. We might use email to send you reminders about upcoming visits, check on how you are doing, or tell you about the progress of the research.
Email messages are not a secure method of communication. The information sent over email, which may include sensitive or personal information, such as protected health information, could be accessed or read by someone other than you. If you would like us to communicate with you by email, please initial the lines below and provide your email address(es) you would like us to use.

_____ I authorize the researchers to send me emails related to this research study.

Email address for this communication: _____

You can still participate in this study even if you do not want us to contact you by text or email.

Participant's Consent

I agree to participate in this research study.

Participant's Printed Name:_____

Participant's Signature:_____**Date:**_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent: _____**Date:**_____