Consent Form

Title of Research Study: **Effect of Non-Surgical Periodontal Therapy With and Without Minocycline HCl Microspheres, 1 mg on Bacterial Load and Systemic Markers of Inflammation**

Investigator Team Contact Information: **Michelle Arnett, RDH, BS, MS**

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

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Key Information About This Research Study

The purpose of this study is to investigate scaling and root planning (SRP) with and without minocycline HCl microspheres, 1 mg for the management of periodontal disease (gum disease) and the impact on bacteria in the saliva and inflammatory markers in the blood.

SRP is known as a "deep cleaning" to treat gum disease. Minocycline HCl microspheres, 1 mg is an antibiotic. The antibiotic is in a powder form and is placed in a pocket of the gums. The antibiotic (minocycline HCl microspheres, 1 mg) is approved by the Food and Drug Administration (FDA) as an adjunctive therapy to treat gum disease.

Participants in this study will be randomized to one of two groups. The group participants are placed by chance, like flipping a coin. Neither the participant nor the study members will choose what group participants are in. One group will have deep cleaning and the other will have a deep cleaning with the powder antibiotic placed in the pockets of their gums.

Both groups will have saliva, fluid samples around teeth, blood collected, and their gums measured at four different times. For saliva collection, you will rinse with a solution and spit in a tube. The fluid around your teeth will be collected by a paper strip that is placed between your gums and your teeth. Neither of the methods of fluid collection are painful. Blood will be collected just like a regular blood draw at a doctor's appointment. The measurement of your gums is the same as a dental exam.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you either need SRP or localized SRP.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The research is being done to compare the changes of bacteria in saliva, bacteria in the fluid around teeth, and inflammatory markers in the blood with the treatment of SRP with and without minocycline HCl microspheres, 1 mg.

In this study, we want to know if SRP with and without minocycline HCl microspheres, 1 mg will decrease bacteria levels in the saliva and in the fluid around the teeth. Collecting saliva and fluid around the teeth is a non-invasive way to determine the effectiveness of SRP with and without minocycline HCl microspheres, 1 mg. We also want to know if SRP with and without minocycline HCl microspheres, 1 mg decreases inflammatory markers in the blood. Minocycline HCl microspheres, 1 mg is Food and Drug Administration (FDA) approved to use with SRP and is commonly practiced at a regular dental visit.

Oral health impacts general health. There is evidence that inflammation in the mouth increases inflammation in the body. This study may benefit others by providing information on how to manage gum disease. In addition, determine early onset and management of chronic inflammatory diseases.

How long will the research last?

We expect that you will be in this research study for six months. There are four visits total. Visits will range from 1-3 hours in time.

What will I need to do to participate?

You will be asked to participate in four research visits. You will have SRP completed one time with or without minocycline HCl microspheres, 1 mg. You will be asked for four saliva and blood samples. The fluid around your teeth will be collected and measurements of your gums will be recorded four times as well. During two of the four visits, you will also have your teeth cleaned.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

There are no known risks for SRP with or without minocycline HCl microspheres, 1 mg different than having this procedure completed at your regular dental visit.

The collection of saliva, fluid around your teeth, or measurements of your gums is non-invasive and similar to a regular dental visit. In addition, having your blood drawn poses no more risk than having your blood drawn at a regular medical visit.

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include treatment of your gum disease with SRP (with or without minocycline HCl microspheres, 1 mg) and two periodontal maintenances (teeth cleanings) over a six month period at no cost. After participation of this study, treatment for your gum disease is your responsibility.

Doctors, researchers, and the public may benefit from this study by having information to manage gum disease. In addition, this study may provide information on the identification, onset, and management of oral and systemic chronic diseases.

What happens if I do not want to be in this research?

Research is completely voluntary and you do not have to participate if you do not want to. Instead of being in this research study, your choices may include having your gum disease treated at the University of Minnesota (UMN) School of Dentistry (SoD) or your dental home at your own cost.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect about 60 people will be in this research study.

Who can take part in this study?

To participate in this study, you must:

- Be at least 21 years of age
- Have gum disease and need a deep cleaning
- Have eight sites with pockets ≥5mm with bleeding on probing (any quadrant)

You cannot participate in this study, if you:

- Are unable to comply with study protocol
- Had a deep cleaning within the last 6 months
- Have smoked cigarettes within the last year
- Have taken antibiotics ≥2 weeks or taken antibiotics in the last six weeks.
- Are pregnant, planning to become pregnant, or unsure of pregnancy status (self- reported) and mothers who are breastfeeding.
- Have cardiac (heart) conditions
- Have any uncontrolled medical condition or immunocompromised that may impact the study (uncontrolled diabetes HbA1c > 7, HIV, etc.)
- Have a tetracycline allergy
- Are taking any medications that may impact periodontal conditions (Phenytoin, calcium antagonists, cyclosporin, warfarin, or NSAIDS)

What happens if I say "*Yes, I want to be in this research*"?

If you decide to take part in the study, you will be randomized to one of two groups. The group you will be in is by chance, like flipping a coin. Neither you nor the study members will choose what group you are in. One group will have SRP and the other will have SRP with minocycline HCl microspheres, 1 mg.

All study visits will be in the Oral Health Clinical Research Clinic (OHCRC) at the UMN SoD. Blood draws will be collected at the M Health Clinical Research Unit (CRU). You will be escorted there by a study team member and can get there by the second floor of the UMN SoD.

Screening (V0)

The study details, risks, benefits, and time commitment will be discussed with you. You will have time to read the informed consent form (ICF) and have the opportunity to ask a study team member questions. If you elect to sign the ICF to participate, we will have a study team member confirm inclusion and exclusion criteria before research activities begin. You may proceed to the baseline (BL) visit immediately if you elect. **This visit will take approximately 1-2 hours.**

Enrollment/Baseline (V1)

Your demographic information including age, gender, ethnicity, and education level will be collected. Your medical history will be reviewed and your vitals will be recorded (blood pressure and heart rate). Saliva, fluid around your teeth, and measurements of your gums will be collected. You will be escorted to CRU by a study team member to have your blood drawn. After the blood draw, you will have SRP or SRP with minocycline HCl microspheres, 1 mg depending on your assigned group. Both groups will have a standard of care treatment for gum disease. Minocycline HCl microspheres, 1 mg is Food and Drug Administration (FDA) approved to use with SRP and is commonly practiced at a regular dental visit. **This visit will take approximately 2.5-3 hours.**

1 month follow-up (V2)

Your medical history will be reviewed and your vitals will be recorded (blood pressure and heart rate). Saliva, fluid around your teeth, and measurements of your gums will be collected. You will be escorted to CRU by a study team member to have your blood drawn. At the conclusion of V2 you will get a $50 gift card. **This visit will take approximately 1-1.5 hours.**

3 month follow-up (V3)

Your medical history will be reviewed and your vitals will be recorded (blood pressure and heart rate). Saliva, fluid around your teeth, and measurements of your gums will be collected. You will be escorted to CRU by a study team member to have your blood drawn. After the blood draw, a periodontal maintenance (teeth cleaning) will be completed for both groups. The test group will have minocycline HCl microspheres, 1 mg placed in the same sites as the BL visit. At the conclusion of V3 you will get a $50 gift card. **This visit will take approximately 1.5-2 hours**

6 month follow-up (V4)

Research activities will be the same as V2. In addition, both groups will have a periodontal maintenance (teeth cleaning). At the conclusion of V4 you will get a $100 gift card for completing ALL research visits. You may also elect a portfolio of your oral pathogenic bacteria and inflammatory markers identified during the study. **These visits will take approximately 1.5-2 hours**

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for:

- Complying with the study protocol and research activities
- Attending your research visits that will be scheduled in advance
- Being on time for your research visits
- Giving advance notice if you need to reschedule within your research window for each visit.

What happens if I say "Yes", but I change my mind later?

You can leave the research study at any time and no one will be upset by your decision.

If you decide to leave the research study, contact the investigator so that the investigator can properly store your research information.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means that your choice not to be in this study will not negatively affect your right to any present or future dental care, your academic standing as a student, or your present or future employment.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

Risk associated with SRP, clinical measurements and teeth cleaning

You should experience no more discomfort related to having SRP, clinical measurements of your gum tissue, having your teeth cleaned, or having minocycline HCl microspheres, 1 mg placed than you would compared to your regular dental visit. The researchers will try to minimize these risks by utilizing standard of care methods.

Risks associated with saliva, fluid around teeth, and blood draw

Saliva and fluid around your teeth is non-invasion and not painful. You should experience no more discomfort or risks related to having your blood drawn than you would compared to any other medical appointment. You may experience bruising, dizziness, faintness, or on a rare occasion an infection.

Risks of placement of minocycline HCl microspheres, 1 mg

You should experience no more discomfort related to having minocycline HCl microspheres, 1 mg placed than you would compared to your regular dental visit. The researchers will try to minimize these risks by utilizing standard of care methods. The following side effects have been reported with minocycline products: swelling, rash, papules, reddening, difficulty breathing, or other signs and symptoms of possible hypersensitivity may occur.

There are additional risks for pregnant women and mothers who are breastfeeding; therefore these individuals will not be eligible to participate in this study.

As with any research study, there may be additional risks that are unknown or unexpected.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you. If you are enrolled in the study, you will get a parking pass for the Washington Avenue parking ramp.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services are performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and dental records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance. Other organizations that will have access to your information include Fairview clinical laboratory, Access Genetics laboratory, and Bausch Health Companies, Inc.

Data or Specimens Collected

Your information or de-identified data as part of this research may be used for future research studies. Samples that are collected will not be distributed.

The sponsor, monitors, auditors, the IRB, the UMN Compliance Office and other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Genetic Information

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.
- Be aware that this federal law does not protect you against genetic discrimination by companies

that sell life insurance, disability insurance, or long-term care insurance.

Will I receive research test results?

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the investigators will contact you to let you know what they have found. You will have the choice of receiving a portfolio of your oral pathogenic burden after the last study visit for completing all study visits.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 or go to https://research.umn.edu/units/hrpp/research-participants/questions-concerns. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

Can I be removed from the research?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include:

- The researcher believes that it is not the best interest of the participant to stay in the study
- If the participant becomes ineligible to participate based on the exclusion criteria
- If the participant's medical condition requires interventions which preclude involvement in the study (antibiotic therapy or diagnosis of cardiaccondition)
- If the participant does not follow study related instructions
- The study is suspended or canceled

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Will I be compensated for my participation?

If you agree to take part in this research study, you will receive a $50 gift card after completion of the 1 month and 3 month visits. You will also get a $100 gift card for completing ALL research visits and for your time and effort after the 6 month visit. The total you could receive is $200 for all research visits.

Payment you receive as compensation for participation in research is considered taxable income. If payment to an individual equals or exceeds $600 in any one calendar year, the UMN is required to report this information to the Internal Revenue Service (IRS). Research payments to study participants that equal or exceed $600 during any calendar year will result in a FORM 1099 (Miscellaneous Income) being issued to you and a copy sent to the IRS.

Use of Identifiable Health Information

We are committed to respecting your privacy and to keeping your personal information confidential. When choosing to take part in this study, you are giving us permission to use your personal health information which includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the 1099 Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Optional research activity

The research study that you are participating might have optional research activities associated with it, meaning that you do not have to agree to these activities in order to participate in the research study. Please indicate your willingness to participate in these optional activities and authorize use of your information from these optional activities as described below by placing your initials next to each activity.

Yes, **I agree**	**No,** **I disagree**
☐	☐

The investigator for this research may contact me in the future to see whether I am interested in participating in other research studies by the investigator.

Consent Form

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent