Washington University in St. Louis

INFORMED CONSENT DOCUMENT

Project Title: **Intranasal Theophylline Irrigation for Treatment of Post-Viral Olfactory Dysfunction**

Principal Investigator: Jake Lee

Research Team Contact: **Jake Lee, MD**
314-362-9475

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you have been diagnosed with difficulty smelling (olfactory dysfunction) of 6 months to 36 months duration after a presumed viral upper respiratory infection.

The purpose of this research study is to evaluate the effectiveness of the addition of theophylline to low-pressure, high-volume saline nasal irrigation (similar to the "Neti-Pot") for patients with olfactory dysfunction without polyps who have not undergone sinus surgery.

For this study, oral theophylline capsules will be opened and their contents mixed into a saline (salt water) nasal irrigation. The mixture may improve the delivery of theophylline to the sinuses.

Theophylline in the oral form is approved by the U.S. Food and Drug Administration for the treatment of chronic asthma and other chronic lung diseases (e.g, emphysema and chronic bronchitis). However, the use of theophylline is considered investigational in this study.

You will also be given sodium chloride & sodium bicarbonate mixture packets. The sodium chloride & sodium bicarbonate mixture is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

The theophylline nasal irrigation will be compared to a placebo nasal irrigation. A placebo is something that looks like a drug, but contains no active ingredients of the drug.

WHAT WILL HAPPEN DURING THIS STUDY?

If you had a nasal endoscopy or rhinoscopy as part of your clinical exam we will record the results for research purposes. If not, a nasal endoscopy (scope in your nose) will be performed to see whether or not you have polyps.

You will be randomly assigned to perform either 1) nasal saline irrigation with theophylline powder (12 mg/capsule) or 2) nasal saline irrigation with a placebo product containing lactose powder. A placebo is something that looks like a drug, but contains no active ingredients of the drug. Randomly assigned means the study treatment you receive will be determined purely by chance, like flipping a coin. You have a 50% chance of being in either group.

The study doctor and study team will not know whether you are receiving the theophylline capsule or the placebo capsule.

You will be provided with a 6-week supply of the 8-ounce (240 ml) NeilMed Sinus Rinse Regular Bottle Kits and the pharmaceutical grade Sodium Chloride & Sodium Bicarbonate Mixture (pH balanced, Isotonic & Preservative & Iodine Free) commercially prepared packets. You will need to purchase distilled water or boil tap water for five minutes for use with the saline irrigation.

You will be required to dissolve the contents of the capsule into the 8-ounce (240 ml) NeilMed Sinus Rinse Regular Bottle along with the saline rinse. You will irrigate both right and left nasal cavities with one-half of the contents of the nasal rinse. You will perform this twice daily for 6 weeks.

At the beginning of the study and your final visit, you will complete questionnaires about your symptoms and quality of life. This should take no longer than 10 minutes to complete and you are free to skip any questions you do not want to answer.

You will be presented with a booklet with a distinct “scratch and sniff” smell on each page. You will be asked to circle one of four options to identify each smell. This should take no longer than 15 minutes and will be completed at the baseline (first) visit and final visit (week 6 (+/- 10 days)).

If you are one of the first ten participants enrolled, you will have a blood sample drawn to measure your blood theophylline levels at the end of week 1. You will need to return to the clinic for your blood to be drawn. Depending on the results seen in these first ten participants, we may also collect samples in another 10 participants. The amount of blood drawn will be approximately 1 teaspoon.

During Weeks 2, 4, and 6, the study team will call you to ask you about your sense of smell and how you are doing with the study medication.

During Week 6, you will be seen in the clinic for a routine follow up visit. During this visit, you will complete the same tests and questionnaires that you completed at the first visit. After this visit, your active participation in the study is complete. If you are unable to make the clinic visit in person due to distance or unforeseen circumstances, you will be presented the option of completing the smell testing by mail. The study team will mail you the questionnaires and "scratch and sniff" test along with a pre-stamped and pre-addressed envelope. After completing the questionnaires and tests, you will put all the

forms into the pre-stamped and pre-addressed envelope and mail it back to the study office. Upon receipt, the study team will call you to discuss your results. After the call, your active participation in the study is complete. There is no long term follow up for the study.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining data from you. We would like to use this data for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding olfactory dysfunction or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your data you give up any property rights you may have in the data.

We will share your data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

If you change your mind and do not want us to store and use your data for future research you should contact the research team member identified at the top of this document. The data will no longer be used for research purposes. However, if some research with your data has already been completed, the information from that research may still be used. Also, if the data has been shared with other researchers it might not be possible to withdraw the data to the extent it has been shared.

Please place your initials in the blank next to Yes or No for the question below:

My data may be stored and used for future research as described above.

_____ Yes **_____ No**
Initials **Initials**

Identifiers may be removed from your private information including data and used for future research or shared with others. If this occurs, we will not ask you for additional consent.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 40 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for six weeks. The study questionnaires will be completed during your visits to the ENT office (today and in approximately 6 weeks). The approximate length of time for each visit will be 30 minutes.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. The possible risks below are for oral theophylline, which is absorbed throughout your body. Theophylline delivered to the nose is less absorbed. One study showed no side effects in 10 patients. However, you may still experience one or more of the risks related to oral theophylline indicated below from being in the study. Although rare, if severe, some of these risks may cause death. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Theophylline

Likely / Common

Mild

- Upset stomach
- Stomach pain
- Diarrhea
- Headache
- Restlessness, nervousness
- Insomnia (difficulty sleeping)
- Irritability
- Tremors
- Drug interactions – theophylline is known to interact with certain medications. Please let the study team know if you are taking any medications.

Rare

- Vomiting
- Increased or rapid heart rate
- Irregular heartbeat
- Disorientation
- Seizures
- Skin rash
- Changes in the blood levels of potassium or glucose

Sodium Chloride (commonly known as salt) & Sodium Bicarbonate (commonly known as baking soda) Mixture – Saline solution for irrigation and moisturizing of the nasal passages

Rare

For the most part, sodium chloride and sodium bicarbonate isn't a health hazard, but in excessive amounts it can irritate your:

- eyes

- skin
- airways
- stomach

Nasal Endoscopy
Rare

- Nosebleed
- Fainting
- Harmful reaction to the decongestant or anesthetic such as rapid heartrate, increase in blood pressure, numbness of the mouth or throat, or allergic reactions.

Blood Drawing
The blood draw may cause bleeding, bruising, or pain. Some people become dizzy or feel faint. There is also a rare risk of infection.

Women Capable of Becoming Pregnant
If you are a woman capable of becoming pregnant, you must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the doctor if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

Breach of Confidentiality
One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study. However, we hope that, in the future, other people might benefit from this study because further information about the management of olfactory dysfunction will be known.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could receive oral capsules containing theophylline outside of the study or do nothing at all.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will have costs for being in this research study. You may have costs if you choose to purchase distilled water needed for the nasal irrigation.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

You will receive $40 for completing Visit 1 (baseline) and $40 for study completion at week 6. If you are one of the participants who has the blood draw, you will receive $40 for the completion of the blood draw at week 1. You can expect to receive a check approximately two weeks after each visit.

WHO IS FUNDING THIS STUDY?

The University and the research team are not receiving payment from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator, Jake Lee, MD, at 314-362-9475 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Hospital or University representatives to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records

and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.

To help protect your confidentiality, we will code your data using an assigned study ID in place of your name. If you provide a blood sample, they will be labeled with your study ID and date/time of draw only. The master list linking your name to your study ID will be kept separately from the information collected for the research. The master list will be accessible to the study team members only. Paper records and blood samples will be stored in a secure environment. Electronic records will be password protected. Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others. Sharing this information will allow others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

A description of this clinical trial will be available on 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.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.

- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
  - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
    - **If you revoke your authorization:**
      - The research team may only use and share information already collected for the study.
      - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
      - You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgment it would not be safe for you to continue, or because your condition has become worse.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Jake Lee, MD at 314-362-9475. If you experience a research-related injury, please contact: Jake Lee, MD at 314-362-9450 or Jay Piccirillo, MD at 314-362-8641.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 01/14/22.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)