**RESEARCH SUBJECT CONSENT FORM**

**(Screening Interview)**

**Title of Research Study:**

Are Pathogenetic Coagulation Proteins Operative in the Development of Osteonecrosis of the Jaw?

**Protocol No.:**

Methodist Hospitals’ IRB Study #\_\_\_\_\_

**Sponsor:**

Oral Surgery Group, Inc, Merrillville, IN

Amer Assoc Oral Maxfac Surg Foundation

Maxillofacial Center, Morgantown, WV

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Initials: \_\_\_\_

You are being asked to participate in a clinical research study. You are being asked to take part in this study because you have recently been diagnosed with osteonecrosis of the jaw (ONJ). This informed consent form (ICF) describes what is involved in this research study. It explains the tests and other details of what will happen to you if you decide to participate. Please read this information carefully. Ask your study doctor or a member of the research team to explain anything that you do not understand or want to know more about. Before deciding whether or not to take part, you may want to discuss this with a relative, friend or your family doctor.

Your participation in this research study is voluntary—if you do not want to take part, you do not have to and it will not affect the care you receive in any way.

If you decide to participate, please sign and date this ICF on the last page. By signing it, you are telling us that you:

* Understand what you have read
* Consent to take part in the research study
* Consent to have blood drawn for specialized testing
* Consent to the use of your personal and health information as needed

You may withdraw your consent at any time. You do not need to give a reason and your medical care will not be affected.

Oral Surgery Group, Inc. is the sponsor of this research study and is providing financial support for the research.

**WHY IS THIS STUDY BEING DONE?**

The purpose of this research study is to determine whether patients with osteonecrosis of the jaw (ONJ) have inherited the abnormal ability to form “super” blood clots that may impair the circulation of blood in their jaw. You understand that your blood will be tested for abnormal clotting factors which could help in the management of your jaw disease.

**HOW DO I QUALIFY FOR THE STUDY?**

* If you have already been treated for ONJ we will need copies of the surgery reports and pathology reports, and pertinent photographs and/or radiographs to support the diagnosis.
* If you have not been treated for ONJ and you have areas of exposed jawbone or non-healing dental extraction sockets that have been present for more than eight weeks, you qualify for the study.

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**WHAT WOULD EXCLUDE OR DISQUALIFY ME FROM THE STUDY?**

* History of radiation treatment to jaws or head and neck.
* If the investigators determine by analyzing your completed Medical and Dental Questionnaire there is not enough evidence to support a diagnosis of ONJ.
* Failure to complete the consent document and three (3) questionnaires in a timely fashion—2 weeks.
* Unable to provide an adequate blood sample for the required tests.

**ARE THERE BENEFITS TO TAKING PART IN THE STUDY?**

Taking part in this study may or may not improve your jaw condition. However, if it is discovered that you have inherited the abnormal ability to form blood clots, it may help explain why you developed ONJ. Also, we may be able to stall the progression of the disease by recommending a period of anticoagulation.

Also, in certain clinical situations (prolonged bed rest, long distance traveling, use of birth control pills, et cetera), you and some of your blood relatives may have an increased risk of forming leg clots which could travel to the lungs or brain. These findings might also shed light on the unexplored causes of other clot dilemmas that your siblings, parents and grandparents have had, or, are dealing with now.

**WHAT ARE THE POSSIBLE RISKS OF BEING IN THE STUDY?**

**BLOOD DRAWING RISKS**

During this study, a small amount of blood (4 tablespoons) will be drawn from a vein to perform tests that allow your doctors to see if you have abnormal clotting factors in your blood.

Drawing blood may cause pain where the needle is inserted. There is a small risk of bruising and/or infection at the site where the needle is inserted. Some people experience dizziness, upset stomach, or fainting when their blood is drawn. To insure the safest and best experience for our patients, we will insist that only certified phlebotomist or licensed medical technologists draw the blood (when possible). These individuals are highly trained in recognizing and preventing potential complications of a venipuncture procedure, which minimizes the risks. The risks associated with the venipuncture procedure are negligible in the hands of skilled laboratory personnel. If you have a fear of needles and may faint, let the technician know so she can take extra precautions.

**PSYCHOLOGICAL RISKS**

Some patients who are aware that they may have a potential clotting disorder can develop excessive fear of having a stroke, heart attack, etc. But just the opposite is true, i.e. the

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knowledge that you have these abnormal clotting factors can be useful to your Doctor in treating you with the proper therapy (in certain clinical situations), so as to prevent these blood clots. So patients should be reassured.

You will be reassured and educated about the implications for your disorder. Many of these clotting events will only be clinically evident under specific circumstances, such as prolonged bed rest after surgery, during long distance traveling, etc.

If you test positive for a clotting factor, you or your blood relatives may be advised to avoid use of hormonal therapy, such as Birth Control pills, fertility medications, and testosterone therapy so as to avoid risk of abnormal blood clot formation. The risk of blood clots in these situations is high and can be avoided with proper recommendations and/or therapy.

**SOCIAL RISKS**

There is concern that you might blame your parents for inheriting a mutated gene, which could potentially have serious clinical implications to you.

Also, there is concern that if you are a parent, you m ay feel guilty because you passed on a mutated gene to your offspring. This information could have serious clinical implications for your offspring and other blood relatives.

**CONFIDENTIALITY RISKS**

* There are few risks to you when your blood specimens and data are used for this type of research. The greatest risk, although rare, is the loss of confidentiality caused by unauthorized release or misuse of information from your research records. We will do everything possible to make sure that the information in your research records are kept private and locked up.
* Risk from participating in genetic research: Your genetic information is unique to you. You do share some genetic information with your family members. Although rare, there are examples where health insurers or employers have denied insurance or employment based on results from genetic testing. Many states currently have laws to protect against genetic discrimination by employers or insurance companies.

A new federal law called the Genetic Information Non-Discrimination Act, or GINA is in effect. This law helps to lower the risk of health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. To learn more about the GINA Law, please check the Internet or ask the study staff.

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* How we will address these risks: We have several safeguards in place to prevent misuse of research results by any third party including insurers or employers: your research results will only be discussed with you. With your permission, your doctor will be allowed to share in the results. Insurers or employers will not be authorized to view any
* research records; and all information will be coded. We believe that the risks to you and your family are very low.

**HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?**

At least 65 adults will take part in this study. We hope to locate them from Northwest Indiana, Indianapolis area and Chicagoland.

**WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY AND HOW LONG WILL I BE IN THE STUDY?**

The ONJ Research Protocol is divided into three (3) Time Periods.

1. **The Screening Period** is designed to locate patients with “bona fide” ONJ. Your dentist or oral surgeon is convinced you have ONJ, or, that you might be developing it. We will need to do a complete oral evaluation of you, review any dental x-rays, CT scans or other radiographic studies to determine if he/she is right and that you qualify for the study. To help us in this endeavor, you will be asked to complete three questionnaires regarding the risk factors pertaining to ONJ. They are:
   1. Medical Risk Factor Questionnaire
   2. Medication Risk Factor Questionnaire
   3. Dental Risk Factor Questionnaire

If you have difficulty completing any of the questionnaires, we encourage you to seek help from a family member, caregiver or your private doctor or their nurse.

These questionnaires must be completed and returned to the Investigator within a 21 day period called the Screening Period. The Investigator will review these completed questionnaires with you and will assign you a Patient Number.

1. **The Study Period** is time set aside for patients we have deemed acceptable candidates for the ONJ study.
2. “Yes” patients (designated with a “Y”) already have well established biopsy proven ONJ. They will be given five (5) additional attachments to complete within a three week period:
   * + Patient’s Contact Information sheet
     + Patient Instruction sheet
     + A HIPAA Form for your signature only. This gives us permission to have your health care provider(s) release medical and dental records to us, so

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that we can search for risk factors that may be operative in your ONJ condition.

* + - Consent for blood draw. Collection of 4 to 5 tablespoons of blood for special laboratory tests to determine if you have inherited an abnormal ability to form “super” blood clots. Results from these tests will only be used for assessing and classifying your disease. Samples will not be stored or used for further testing or evaluation.
    - Doctor’s Order/Lab Instruction Sheet. “Yes” patient should have the results of their blood studies within two weeks of the blood draw.

1. “Questionable” patients (designated with a “Q”) do not yet have a definitive ONJ diagnosis. They may have the earliest stage of ONJ, Stage 0, which is difficult to diagnose without enforcing a strict waiting period since the progression to Stage 1 can take weeks, even months to reveal itself. (Stage 1 is when the gum has retracted away from the dead bone and becomes visible on examination of your teeth and gums.)

Thus, Stage 0 could well be called Stage of Confusion because often the patient may have had recurrent jaw pain and/or dental infections with some relief with antibiotics and, despite numerous extractions and/or root canal treatments, still may suffer significant pain.

“Q” patients will be instructed to:

* Sign the HIPAA form to release additional medical/dental records, so that the Investigator can continue to study the risk factors that may relate to your case of jaw osteonecrosis (ONJ)
* Have a follow-up appointment at Oral Surgery Group (OSG) in 4-6 weeks, and, every 4-6 week periods thereafter, until it is ascertained the patient has “bona fide” ONJ, or, he/she does not and will receive a “N” designator.

1. “No” patients receive the “N” designator which disqualifies them from having the blood studies. These can continue with periodic follow-up visits with OSG, and are encouraged to bring any new information or findings to the investigators.
2. **The Results Period** is the time period it takes to get together with you to discuss the results of your blood tests and their implications for you and your blood relatives. This period is limited to 14 days.

**CAN I STOP BEING IN THE STUDY?**

Yes. You can decide to stop at any time. Tell the doctor if you are thinking about stopping or decide to stop. This will allow discussion of what (if any) follow-up care could be helpful for you.

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**WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?**

Your other choices may include:

* Getting treatment or care for your ONJ without being in a study.
* Taking part in another study.
* Supportive care to try to stop the advance of the osteonecrosis.

Talk to your doctor about your choices before you decide if you will take part in this study.

**WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?**

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you. Leaving the study will not affect your medical care.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

**WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?**

Your medical information will be kept as confidential as possible within the limits of the law. Your medical information may be given out if required by law. If information from this study is published in a medical journal or presented at scientific meetings, you will not be identified by name, picture, or any other personally identifying information.

The following people and groups of people may look at and/or copy your medical records to make sure that the study is being done properly and to check the quality of the data:

* Oral Surgery Group, Inc. (OSG) personnel
* The Institutional Review Board is responsible for protecting the rights and safety of the patients who take part in research studies at Methodist Hospitals.

**HOW WILL MY HEALTH INFORMATION BE USED AND DISCLOSED?**

If you sign this document, you give permission to OSG to use or disclose (share) your health information that identifies you. This information may be shared for the following reasons:

* Purposes of this research study
* Research directly related to ONJ and related diseases

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Your health information includes all that has been and will be created or received by OSG. This information is in your medical record kept by OSG.

You do not have to sign this consent form. If you choose not to sign it, you may not take part in this research study. You are free at any time to limit OSG’s use and sharing of your health information, without penalty or loss of benefits to which you are otherwise entitled. If at any time you choose to limit OSG’s use and sharing of your health information that is necessary for the completion of this research study, you may not be allowed to take part, or continue to take part in this research study.

You have the right to see and get a copy of your medical records kept by OSG that are related to the study. However, the results of the trial will not be available until the trial is fully completed.

You may change your mind and withdraw from the study at any time. If you choose to withdraw from the study, no new health information will be collected about you. However, the Sponsor will still be able to use and disclose any health information about you from this research study that has already been collected.

Your authorization (permission) to use and disclose (share) your health information will continue indefinitely, but that use and sharing will only be for the purposes described in this Informed Consent Form.

**WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?**

You can talk to your study doctor about any questions or concerns you have about this study. If you have any questions about your rights as a research subject, you may contact the Methodist Hospitals Institution Review Board at 219-738-5891. 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 any time.

Contact your study doctor:

Dr. McMahon, at phone: (O) 219-757-5700

or

Dr. Hajjar at Phone: (O) 219-757-5700

**WILL I BE PAID IF I TAKE PART IN THIS STUDY?**

You will not be paid for being in this study and you will not be reimbursed for expenses (for example, child care or travel expenses) related to your participation in the study.

You will not receive a cash reward for participating.

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**WILL IT COST ME ANYTHING TO BE IN THE STUDY?**

No. The battery of coagulation tests will be performed at no cost to you. Also, there is no charge for the initial screening interview.

For subsequent office visits, there will be a charge that is customary for the visit, and if imaging studies and other diagnostic procedures are necessary to establish a definitive diagnosis, then these fees and fees generated for surgery at Oral Surgery Group or Methodist Hospitals will be charged by the doctors, according to their usual and customary rates.

You and/or your health plan/insurance company will need to pay for some or all of the costs of actually treating your jaw osteonecrosis in this study. Some health plans will not pay the costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting the regular treatments for ONJ.

You will not be paid for taking part in this study.

**HOW LONG WILL I BE IN THE STUDY?**

The total time from the screen interview to the completion of our discussion of your blood results will take approximately 1-2 months.

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**SIGNATURE**

I have been given a copy of all 10 pages of this Informed Consent Form document. I have read its contents and this information has been explained to me. I have been given an opportunity to ask my questions in private as well as to meet with a study doctor to discuss this study. I have asked the staff any questions I may have had, and I have had enough time to decide if I want to take part in this study. I hereby voluntarily agree to take part in this research study, and authorize OSG to use and disclose (share) my health information as described in this Informed Consent Form.

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Patient Name (print)

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If applicable—Name of Patient’s Legally Authorized Relationship to Patient

Representative (print)

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Patient Signature or Patient’s Legally Authorized Date

Representative Signature

I, the undersigned, have fully explained this informed consent to the patient named above and/or the patient’s legally authorized representative.

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Name of person conducting informed consent Date

Discussion (print)

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