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Wake Forest®
School of Medicine

Wake Forest Institute for Regenerative Medicine &
Department Of Plastic and Reconstructive Surgery

A PHASE 1 SAFETY STUDY OF HUMAN AMNION MEMBRANE POWDER FOR ENHANCED WOUND HEALING

Informed Consent Form to Participate in Research
Joseph Molnar, MD., PhD Principal Investigator

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you require an **autologous primary skin graft with two donor sites**. "Autologous" means that the graft is taken *from your own tissue.* Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family. The study was originally funded through the Department of Defense and is now funded by Wake Forest University Health Sciences

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to find out if human amnion membrane powder can be safely used as a covering for wounds and can improve the condition of skin graft donor sites. The amnion powder product is composed of "lyophilized" (freeze-dried), "gamma irradiation sterilized" (exposed to bacteria killing radiation) fragments of amniotic membrane.

Split thickness grafting procedures are commonly performed to close wounds resulting from trauma, burns, ulcers or tumor removal. Skin donor graft sites are notoriously painful and can have potential complications resulting in fluid loss, delayed healing, infection, and hypertrophic scarring, particularly in patients with severe burns or traumatic injury. Effective healing relies on management of wound bacteria, reduction of inflammation and restoration of perfusion.

In this study, two donor sites will be selected on your body. One will be called "A" and the other site "B". The prepared amnion membrane product will be applied to site A and then covered with a standard of care (that we normally use at this hospital) dressing. The donor site B will just be covered with the standard of care dressing. These two donor sites will then be compared for wound closure in 2 weeks and 4 weeks after surgery to see how they are healing.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

We will enroll 10 subjects at Wake Forest Baptist Medical Center to take part in the study. We may need to consent up to 20 subjects to account for screen failures.

How Long Will I Be in the Study?

You will be in the study for up to 26 weeks. After the surgery you will return for up to 8 times for study follow-up. These visits will be scheduled during visits that you would normally be returning to see your doctor if possible.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

WHAT IS INVOLVED IN THE STUDY?

If you take part in this study, you will have some tests and procedures that are being done only because you are in the study. However, many of the things you will be doing you would normally do as part of regular care for people requiring an autologous primary split-thickness skin graft.

I. Procedures performed before Surgery

Visit 1 :Screening/Baseline Visit

To ensure that you qualify for the study, we will perform:

- Evaluation of inclusion and exclusion criteria
- Review of demographic/ medical information and relevant medical history
- Complete physical examination
- History of original wound /injury that requires skin grafting and any treatments already received for the injury

- Assessment of any concomitant medications
- Blood draw for Complete Blood Count (CBC) and blood chemistry tests

II. Surgical Procedures

Visit 2: Treatment Visit

On the treatment day, before your surgery, you will be asked what your pain level is and have your vital signs taken for the study. You will be taken to the Operating Room. Once you are asleep, the two donor sites will be identified and photographed. If you have donor sites on two different sides of your body, the amnion product will be placed on your right side.

Once you are asleep, two skin grafts will be taken from the designated areas – the surgical procedure performed would be the same whether or not you are in the study. The only thing that is different from the standard of care is the that the amnion product will be placed on Donor Site A while the standard of care dressing will be placed on Donor Site B. Photographs will be taken of both of your donor sites following tissue removal and then the donor sites will be covered with a film dressing. The primary dressings will stay on for 6-8 days until the next study visit.

Visits 3- 7: 1, 2, 4, 8 and 12 Week Post-Treatment Visits

You will return to our clinic 1, 2, 4, 8, and 12 weeks after your surgery for the following:

- History, physical exam and vital signs
- List of any medications pertaining to wound healing
- Photographs of the donor sites
- An assessment by clinician for healing status, infection, inflammation and allergic response.
- An assessment of pain at both sites and any other non-study related sites
- A blood draw will occur at the Week 1 and Week 4 post treatment visits to determine your general blood chemistry and CBC

3 Week Post-Treatment Phone Call

You will receive a phone call from a member of the study team 3 weeks after your surgery. You will be asked about your pain, how you are healing, what medications you are taking, and about any other issues you are having. If you are having problems, the study doctor may ask you to come in this week to be evaluated.

Visits 8-9: 16 and 26 Week Post-Treatment Visits

You will return to our clinic 16 and 26 weeks after your surgery for the following:

- History, physical exam and vital signs
- List of any medications pertaining to wound healing
- Photographs of the donor sites
- An assessment by clinician for healing status, infection, inflammation and allergic response.
- An assessment of pain at both sites and any other non-study related sites
- An assessment of scarring will be undertaken called the Vancouver Scar Scale (VSS) for both sites, and non-study wound sites and if necessary, treatment for scarring will be applied

Blood Draws

You will have approximately 10 teaspoons of blood withdrawn from a vein during each of the following visits: screening visit, week 1 post-treatment visit and Week 4-post-treatmentvisit. The total amount of blood drawn during the study will be about 30 teaspoons..

Photography/Videotaping

As part of this research study, you may be photographed/videotaped/audiotaped. This is being done to document the surgical procedure for future review learning purposes. You understand that you may request the filming or recording be stopped at any time during the course of the research study. You can also withdraw your consent to use and disclose the photograph/videotape/audiotape before it is used. You should also understand that you will not be able to inspect, review, or approve the photographs, videotapes, audiotapes or other media (including articles containing such) before they are used in this study.

Please choose one of the following regarding the use and disclosure of the photograph/videotape/audiotape used in this research study:

_____ I would like the photographs/videotapes/audiotapes of me to be destroyed once their use in this study is finished.

____ The photographs/videotapes/audiotapes of me can be kept for use in future studies provided they are kept secure and any future study will be reviewed by an IRB. I understand that I will not be able to inspect, review or approve their future use.

We can send copies of your test results and surgical records to your personal physician. Even if you do not wish to have any of your medical information sent to your physician, you can still

participate in this research study.

Do you request that we send important medical findings from your study tests/exams to your personal physician?

[ ] Yes [ ] No _____ Initials

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the amnion membrane product we are studying include:

- Allergic reaction to the Amnion Membrane Powder and wound covering – this may look like a rash in the area around the donor site(s), or the area may be red, blistered and/or itchy. You should tell the research staff if you experience any symptoms like these around your donor site wounds or anything else unusual anywhere else on your body.

- Infection at one of the donor sites

- Because the amnion powder comes from human placentas there is a very low risk of infectious disease transmission from the amnion wound covering to you. All donors of the amnions were screened and tested negative for infectious diseases (including HIV and Hepatitis).

- There is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

- You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: reduced pain and increased satisfaction with appearance of one of the donor sites.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you can have all of your donor sites for the autologous skin graft covered with the standard of care dressings.

The most common risks associated with the standard of care therapy (regular wound covering over donor graft site) are infection and potential allergic reaction or irritation to the dressing

The benefit of standard of care therapy would be that this wound covering has been used at this institution for many years and we do not expect there to be any potential infectious disease risk.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, including the surgery, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the safety and effectiveness of the Amnion Membrane product; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

If photographs or video recordings have been taken, they will be stored by Dr. Molnar or a member of the study team in a locked cabinet. They will be retained for up to 10 years. If you decide you do not want us to have the photos or recordings, you may request that they be destroyed at any time.

If you choose to participate in this study, your medical record at Wake Forest University Baptist

Medical Center will indicate that you are enrolled in a research study. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive a $50 VISA gift card at the completion of each follow-up visit (Weeks 1, 2, 4, 8, 12, 16, & 26 - total of $350 in gift cards) for taking part in this study. Any parking costs for the return visits will be paid for by the study also. To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

The study is sponsored by Wake Forest University Health Sciences. The investigational product (human amnion membrane powder) was developed by researchers at WFUHS. This means the Wake Forest University Health Sciences and the researchers have a financial interest in the product and could financially profit from the study if the investigational product is approved for use related to this research.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the Wake Forest Baptist Medical Center Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness.

Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Joseph Molnar at [redacted].

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** your medical history and physical exams, lab work.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

1) Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

2) Representatives from government agencies such as the US Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS), Office for Human Research Protections, and other similar agencies

3) Representatives from companies that may own or acquire the study technology in the future may be granted access to de-identified information/records for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept indefinitely. This authorization does not expire. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Molnar that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Joseph Molnar, M.D., Ph.D.

[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study. This will not affect the medical care that is being given to you.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and Wake Forest Baptist Medical Center. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. Dr. Molnar also has the right to stop your participation in the study at any time. He might do so for any reason including: if he feels that your health or life may seriously be

jeopardized by the continuation of treatment, for example, allergic reaction to Amnion Product; if you do not attend regularly scheduled appointments including follow up visits; if you do not have required lab tests performed; or if you refuse to follow other instructions given in regard to caring for yourself after surgery. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent. You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Joseph Molnar at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a copy of this signed consent form.

CAN I PARTICIPATE IN OTHER RESEARCH STUDIES WHILE I AM ENROLLED IN THIS RESEARCH STUDY?

You should not take part in this study if you are currently in another research study without the consent of Dr. Molnar. It is important to let your doctor know if you are in another research study.

WHAT ARE MY RESPONSIBILITIES AS A PARTICIPANT IN THIS STUDY?

Your patient responsibilities include:

- Taking any medication as ordered.
- Attending all required follow up visits.
- Having required lab studies done.
- Following all post-operative instructions.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm