Study Title	A PHASE I/II CLINICAL TRIAL TO DETERMINE SAFETY AND FEASIBILITY OF USING AN ACELLULAR AMNIOTIC FLUID APPLICATION TO EXPEDITE HEALING IN CHRONIC WOUNDS
ClinicalTrials.gov ID (NCT Number)	NCT04438174
Principal Investigator (PI)	Giavonni Lewis, MD
Document (ICF, Protocol, SAP)	ICF
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Consent and Authorization Document

BACKGROUND

You are being asked to take part in a research study. This study is "A Phase I/II Clinical Trial to determine safety and feasibility of using an acellular amniotic fluid application to expedite healing in chronic wounds". Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask the research doctor or staff if there is anything that is not clear or if you would like more information. Take time to decide whether or not to volunteer to take part in this research study.

You may be able to participate if:

- You have a chronic wound or wounds on your lower or upper extremities.
- These wounds have not healed with standard treatments (Standard of Care).
- These wound(s) have affected your quality of life and you have experienced pain, and it has limited your ability to function normally.

The purpose of the study is to find out if human amniotic fluid can improve your chronic extremity wound, decreasing the inflammation and assisting the wound(s) to heal. Amniotic fluid is the liquid that surrounds the unborn, growing baby during pregnancy. Amniotic fluid is mainly water, but also has other components like proteins and antibodies that protect the baby from infection and help growth. Some of these components have been shown to have an anti-inflammatory effect. The fluid is obtained during the delivery of the baby and processed so that it is sterile and can be injected into wounds. We hope that the beneficial components of the amniotic fluid will help your chronic wound in assisting your body to heal the wound. The Amniotic Fluid used in this research study is considered investigational and has not been approved by the Food and Drug Administration (FDA).

This study is being conducted by the Cell Therapy and Regenerative Medicine Program and by the Burn and Wound Clinic, which are part of the University of Utah.

CONFLICT OF INTEREST

In studies like this where there is a conflict of interest, an organization (called the Conflict of Interest Office) will create and manage a plan to ensure that the data from this study is accurately reported and correctly interpreted. This helps to make certain that the study is conducted correctly, and that participants in the study are treated in the most fair way possible.

The University of Utah has a significant institutional financial interest in intellectual property being used in this study (U-5650 "Amnion/Chorion Membrane as a Wound Cover to Control Adhesions and Heal Wounds, Amniotic Fluid (Supernatant) and Amniotic Fluid (Whole) to Reduce Inflammation, Heal Wounds and Stimulate Bone Growth") and a significant institutional financial interest in Eliksa (a non-publicly traded company which is licensing the technology for commercialization). This is a conflict of interest as determined by the University of Utah Institutional Conflict of Interest Officer and a

management plan has been implemented to ensure transparency, promote data integrity, and to safeguard human subjects in the research.

Investigators Dr. John Phillips and Jan Pierce have a financial interest in Eliksa, (a non-publicly traded company which is licensing the technology for commercialization), which is a conflict of interest as determined by the University of Utah Individual Conflict of Interest Committee, and a management plan has been implemented to ensure transparency, promote data integrity, and to safeguard human subjects in the research.

STUDY PROCEDURES

Once we have determined you can be part of the study, you can be enrolled in the study if you so desire. At the first follow-up, if your wound has not mostly healed you will either be given amniotic fluid injections or standard of care treatment without amniotic fluid injections. The assignment of which treatment you receive is done randomly, which means by chance. This means that a computer will decide by chance which group a person is in, not the doctors running the trial. You have a 50:50 chance of receiving the study treatment of amniotic fluid or standard treatment. The reason for this is to compare whether participants receive benefits from the amniotic fluid compared to the standard of care. The use of random assignment of treatment will help the interpretation of study results to be more reliable.

If you are chosen to have the amniotic fluid injection, you will be given the treatment during your 2nd (6 weeks after your first clinic visit) and 3rd (6 weeks after your 2nd clinic visit) clinic visit. If you are not chosen to have the amniotic fluid injection, you will be given standard of care treatment at the same timepoints. Whether or not you are chosen to have the amniotic fluid injection, you will have to see your doctor in the Burn/Wound for your 4th clinic visit approximately 6 weeks after your last treatment and then again for your 5th visit 3 months later. We will train you on how to care for your wound between clinic visits.

In this study you will be referred and screened by the Principal Investigator (PI) to participate in this research study at the Burn/Wound Clinic within the University of Utah Hospital.

The first visit is called a screening visit. This visit may be split into two visits if needed. At this visit the research coordinator and your study doctor will perform the following:

- You will be asked to read and sign this consent form before any study procedures can be done. You will receive a copy of this to take home.
- Your medical history and medications will be reviewed
- Your vital signs will be measured including height, weight, blood pressure, pulse and temperature.
- The study doctor will perform a physical exam and assess your pain level.
- Blood and urine samples may be collected.
- If you are a woman of child-bearing potential you will be asked to take a pregnancy test

- The study team will ask you to complete questionnaires about yourself and the study doctors will ask you questions.
- You must be willing to use effective contraception if you are a person of childbearing potential during the study, if you cannot agree to this, you should not consent to be on this study.

Follow Up visits include 4 in-person clinic visits and a follow-up phone call within 24 hours and 5-7 days after visits 2 and 3.

- Your medical history and medications will be reviewed
- Your vital signs will be measured including height, weight, blood pressure, pulse and temperature.
- The study doctor will perform a physical exam
- Blood and urine samples may be collected.
- The study team will ask you to complete questionnaires about yourself and the study doctors will ask you questions.

RISKS

The CTRM screens the amniotic fluid coming from donors for infectious diseases through medical and social history questionnaire, medical record review, and testing of the donor's blood for viruses including HIV, Hepatitis B & C, and others. The CTRM Medical Director reviews the records and test results to determine if the donor meets eligibility requirements. Although the risk of transmitting infectious disease is minimal, there is a potential for transmission.

Possible risks related to your participation in this study include the following:

- Cellulitis (an infection of the skin caused by bacteria)
- Bleeding
- Drainage
- Inflammation
- Rash
- Allergic Reactions
- Parvovirus B19 infection

The symptoms of Parvovirus B19 infection in immunocompromised, pregnant, and immunocompetent individuals are: Flu-like symptoms of malaise, muscle pain, and fever, rash, chronic infection and anemia. If you have these symptoms, please notify the study team. However, some people have no symptoms at all.

If you have a cellulitis infection, skin may appear red, swollen, warm to the touch, and/or may be painful. We do not anticipate that this will happen. However, if it does, please tell the investigator immediately and seek treatment.

If you are injured during the course of your study participation, you should seek medical help immediately, and contact the study doctor or study staff as soon as possible.

Participation in the study may also involve risks that are currently unforeseeable.

Participation in studies of any kind can result in a loss of confidentiality. This possibility is remote; however, we will take measures to protect you. Please see the Authorization Section below for further details regarding how we will protect your information.

BENEFITS
It is unclear whether the product will provide any benefit. The potential benefit from this treatment is to assist in the healing of your chronic wound(s). The information gained in this study will aid in the understanding of the use of amniotic fluid to heal wounds and help in the development of new approaches to its treatment in the future.

ALTERNATIVE PROCEDURES
You may choose not to be in this study. If you do not want to take part in the study, there are other choices to improve your symptoms, including:

- Standard of Care
- Surgical/procedural intervention

You may have received one or more of these treatments, and you may discuss these options with your doctor.

PERSON TO CONTACT
If you have questions, complaints or concerns about this study, you can contact Dr. Giavonni Lewis at 801-581-3050. If you think you may have been injured from being in this study, please call Dr. Lewis at 801-581-3050.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns that you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

Person to Contact:

Giavonni Lewis, M.D.
50 North Medical Drive
Salt Lake City, UT 84132
Phone: 801-581-3050

24-Hour Number:
Please call the Burn ICU at 801-581-2700

RESEARCH-RELATED INJURY
If you are injured from being in this study, medical care is available to you at University of Utah, as it is to all sick or injured people. The University of Utah has not set aside any money to pay the costs for such care. The University will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), to the study sponsor or other third party (if applicable), to the extent those parties are responsible for paying for medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research.

The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See sections 63G -7-101 to -904 of the Utah Code.

VOLUNTARY PARTICIPATION
Research studies include only people who choose to take part. You can tell us that you do not want to be in this study. You can start the study and then choose to stop the study later. We will still give you medical care and answer any questions you have. Your decision will not affect your relationship with your doctor or the study team in any way.

If you want to stop being in this study, please let the research doctor know. That way you can find out what should be done about your normal medical care outside of the study.

RIGHT OF INVESTIGATOR TO WITHDRAW PARTICIPANTS
The investigator can withdraw you without your approval. Possible reasons for withdrawal include:

- Any adverse effect that may affect you, and that in the opinion of the treating doctor justifies withdrawing you from the study.
- Noncompliance with the treatment.
- Any other unforeseeable circumstance that in the opinion of the treating doctor justifies withdrawing you from the study.

There are always reasonably foreseeable risks of participation in a study. If an adverse effect occurred during the study and you were withdrawn from it, the doctors may have to follow-up on the problem until it is resolved.

COSTS AND COMPENSATION TO PARTICIPANTS

The parts of your care that would normally be done as standard treatment such as regular doctor visits and lab work for the follow-up of your chronic wound will be billed to you or your insurance company. Anything strictly related to the study, such as the amniotic fluid or exams required by the study outside what is considered standard of care, will not be billed to you or your insurance company. The standard of care exams required by the study include your doctor visits, including exams, and your routine blood tests.

You will not be compensated for participating in this study.

NEW INFORMATION

Sometimes during the course of a research project, new information becomes available about the amniotic fluid that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study.

If you decide to withdraw at that time, your research doctor will make arrangements for your medical care to continue. Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your medical care to continue.

NUMBER OF PARTICIPANTS

We expect to enroll 60 participants at Burn/Wound Clinic, University of Utah. This study is not conducted in any other center outside the University of Utah

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION

Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study.

This is the information we will use and include in our research records:

- Demographic information like age, gender, name, address, telephone number, and email address
- Related medical information about you like allergies, current and past medications or therapies, and information from physical examinations, such as blood pressure reading, heart rate, temperature, and lab results
- All tests and procedures that will be done in the study

How we will protect and share your information:

- We will do everything we can to keep your information private but we cannot guarantee this. Study information will be kept in a secured manner and electronic records will be password protected. Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this

information as part of the regular treatment, payment, and health care operations of the hospital. We may also need to disclose information if required by law.

- A description of this clinical trial will be 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 website at any time.

- In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:
  - Members of the research team at the University of Utah Health Sciences Center.
  - The University of Utah Institutional Review Board (IRB), which reviews research involving people to make sure the study protects your rights.
  - National Institutes of Health and Food and Drug Administration
  - Independent contracted professionals to review de-identified wound digital images

- If we share your identifying information with groups outside the University of Utah Health Sciences Center, they may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.

- If you do not want us to use information about your health, you should not be part of this research. If you choose not to participate, you can still receive health care services at the Burn/Wound.

What if I decide to Not Participate after I sign the Consent and Authorization Form?
You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

You have a right to information used to make decisions about your health care. However, some information from this study will not be available during the study; it will be available after the study is finished.

CONSENT

I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I will be given a signed copy of the consent and authorization form to keep.

I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.

_____
Participant's Name

_____ _____
Participant's Signature Date

_____
Name of Person Obtaining Authorization and Consent

_____ _____
Signature of Person Obtaining Authorization and Consent Date

INTERPRETER STATEMENT: (For Non-English Speaking Participants Only): I confirm that I was present as an interpreter for the duration of the consent process for this research study. I confirm that I am qualified and have the necessary skills to provide interpretation between the participant's language and English. By signing this form, I confirm that I provided a full and complete interpretation of the exchange between the researcher obtaining consent and the participant, to the best of my ability.

_____
Name of Interpreter

_____ _____
Signature of Interpreter Date