SHRINERS HOSPITALS FOR CHILDREN

CINCINNATI HOSPITAL

INFORMED CONSENT TO PARTICIPATE IN RESEARCH PROJECT OR STUDY

Subject Name: _____ **Date of Birth**: ____/____/____

Principal Investigator Richard Kagan, MD

Human Studies Committee Approval Number 95-7-26-1

Title of Project or Study:

Skin Repair with Cultured Cells and Biopolymers

If you are acting on behalf of a child or adolescent, the words "you" and "your" as used in this explanation mean that child or adolescent.

You have been invited to join this research study. Before you agree to join, it is important that you read and understand the following information. It tells how and why the study will be done. It also tells about the good things that could be learned from the study. Possible risks or things that may hurt or be uncomfortable are described and the different kinds of medical treatment that may also help you are explained.

It is important to know that no promises can be made about the results of the study. You can drop out of the study at any time and no one will be upset.

Please ask questions about anything that you do not understand before deciding whether or not to participate.

1. PURPOSE:

I agree to the participation of _____ in this study being conducted by Richard Kagan, M.D. and/or certain of his assistants. This study involves research and the investigators hope to learn the following:

The purpose of this research study is to evaluate the effectiveness of cultured skin substitutes made from either my own skin, skin from a cadaver donor, or a combination of both, for covering:

- excised burn wounds or burn scars,
- giant hairy nevus, or
- skin that must be removed surgically because it is severely injured or diseased.

For burns, the areas of your body that are treated with cultured skin substitutes will be compared to similar areas treated with your own donor skin (split-thickness skin autograft) to evaluate wound closure, infection, the amount of skin needed to heal the wounds, cosmetic appearance (color, softness, smoothness), skin strength and the amount of scar at each grafted area. Comparative areas treated with cultured skin substitutes, or your own skin, will be the same size (about 3 H 9 inches). For burn scars, giant hairy nevus or other skin conditions, cultured skin substitutes may be used as the only treatment if your doctor feels it is beneficial. Cultured skin may be applied at more than one operative procedure if your doctor feels it is beneficial.

You have been asked to participate because you have:

- burns over 50% or more of your body, or,
- burn scars that require skin grafting after recovery from burns over 50% or more of your body, or,
- skin that is abnormal, diseased, or injured and requires skin grafting.

You will not be able to participate if you are pregnant.

2. PROCEDURE:

If you agree to participate, we will ask you to:

- sign this informed consent
- have a small, thin layer of your skin (about the size of a silver dollar) taken after appropriate anesthesia either in the operating room or at your bedside in the burn unit from an unburned area of your body, and taken to a laboratory and placed in culture. This donor site will heal on its own. Due to the serious nature of your injury, you will undergo surgical debridement or scar release and skin grafting whether or not you choose to enter the study. Because the

sample of skin is so small, the fact that it is used for a tissue culture and not immediately as a skin graft will not affect your progress toward recovery.

- have a teaspoon of blood collected before application of the cultured skin and again at 28 days after application to test for allergic reaction of the cultured skin. The cultured skin substitutes will be applied to your skin wound, beginning about one month after injury, during operative procedures where your burn wounds are prepared as they would be for standard skin grafting. After application to the wound bed, the skin substitute will be covered with a sterile non-adhesive dressing, fastened with skin staples or sutures to the wound bed, and dressed according to conventional methods. You will be monitored closely by the burn physicians, the principal investigator, and the clinical research nurse for graft healing, incidence of infection, bleeding, adverse results, and cosmetic appearance. During the healing process, photographs will be taken approximately weekly, and treated areas will be traced during the first month after treatment to measure the size of the areas. Treated areas will be traced and photographed at one year and periodically between three and five years post-grafting.

- have wound biopsies performed with a skin punch (about 1/8 inch diameter) following injection of a numbing medication, and closed with stitches if necessary. Biopsies will be collected at certain times after application from both the cultured skin and healed autograft sites. There will be no greater than 6 biopsies total, nor 5% of the healed area of cultured skin. Biopsies will be collected both during your hospitalization, and at certain routine clinic visits after your discharge. Biopsies of the healed skin will allow microscopic comparison of normal skin to treatment with cultured skin.

- have measurements performed with instruments and/or clinical examination that follow the course of the healing process. Measurements with these instruments do not delay healing of the skin, and should not cause discomfort. Measurements may include one or more of the following properties of the skin: protective barrier, softness, color, sensation or blood flow. Joint Range of Motion will be recorded when applicable.

- have a skin test performed to evaluate whether cultured skin may be used for treatment of burn scars after treatment of original burns with cultured skin. The skin test consists of an injection of a few drops of cultured skin extract under healthy skin to determine if an allergic reaction (red bump) develops. A teaspoon of blood will also be collected at the time of the skin test, and again at the time of discharge from the hospital after treatment with cultured skin.

Parent/Participant Initial Here _____

3. EXPERIMENTAL PROCEDURES:

Some of the procedures used in this study are used regularly to diagnose or treat your medical condition. Other procedures are not usually used for these reasons and they are considered to be experimental. The experimental procedures used in this study are:

- grafting with cultured skin substitutes of burn wounds, burn scars, giant nevus or other skin wounds.

- measurements of healing skin with instruments.

4. RISKS:

Because this is a research study, discomforts and side-effects associated with the treatments or procedures are not fully understood. These risks and discomforts may include:

- a possibility of contamination of the cultured skin in the laboratory. Sterile technique, specialized equipment, and addition of antibiotics to culture medium minimize infection (bacteria, yeast fungi) of cultured skin in the laboratory. With these procedures, infected cultures of skin cells occur only rarely (about 1 in 500). Any infected skin cells cultures are destroyed, and not included in cultured skin grafts. Although it is possible that cultured skin may contain very small amounts of infection, the possibility is considered remote. Each preparation of cultured skin substitutes is tested before clinical use, and must be negative for infection.

- a risk of sensitization (allergic reaction) and irritation caused by the skin substitute, specifically the polymer (fabric) component to the dermal substitute. The polymer fabric, and other materials used in the preparation of the cultured skin substitute are from bovine sources (cows or beef). Allergic reactions may include temporary redness, swelling or itching at the site of cultured skin, but this risk is lower than 1 in 100. Because the fabric contains collagen, a protein found in tissues of the body, an immune response theoretically could cause an autoimmune disease. However, in 15 years (approximately 125 patients) of experience with cultured skin substitutes, no incidence of autoimmune disease has been observed. If the patient is known to be allergic to beef, s/he should not be treated with cultured skin substitutes.

- allergic reactions to several drugs used for preparation and application of the cultured skin could occur. These drugs include penicillin, streptomycin, neomycin, polymyxin B, mupirocin, ciprofloxacin, amphotericin B, hydrocortisone and insulin. If the patient is known to be allergic to these drugs, s/he should not be treated with cultured skin substitutes.

Parent/Participant Initial Here _____

- an allergic reaction and loss of cultured skin grafts could occur from the treatment of burn scars, if the original burns were treated with cultured skin. Specific tests will be performed to determine whether a risk of allergic reaction may occur for treatment of burn scars.
- a chance of rejection of the skin substitute, if allogeneic cells from cadaver skin are used. The chance of rejection of cultured allografts (cadaver skin cells) is no greater than the chance of rejection of cadaver skin that is routinely used as a temporary wound cover.
- a chance of infection and loosening of the skin substitute, and scarring of the wound covered by the skin substitute is possible, but these risks are very similar to those associated with normal human skin grafts. Infections derived from the laboratory procedures are possible, but the chances of this kind of infection are very small. Cultured skin made from cadaver skin will only be used if it has tested negative for HIV (AIDS) and hepatitis, and also has satisfied all other safety standards that are required for tissue banking.
- a risk that the cultured skin substitute may not be effective, which could necessitate additional surgery for debridement and skin grafting.

In addition, there may also be risks and discomforts which are not yet known.

5. DURATION:

Your participation in the study will continue through the hospitalization phase of treatment, and for subsequent clinic visits for approximately a year after treatment with cultured skin substitutes. After one year, the participant will be seen periodically thereafter.

6. ALTERNATIVES:

An alternative procedure or course of treatment available that might be helpful to you is the harvesting of skin autograft from donor sites, and grafting to prepared wounds.

7. BENEFITS:

No promises are being made that you personally will benefit from this study. Possible benefits to you or to others that might result from this research are:

- reduced requirements for harvesting of donor skin to complete grafting and healing of your skin wounds, burn scars, or diseased skin.
- fewer surgeries to complete grafting and healing of your skin wounds, burn scars, or diseased skin.
- complete closure and healing of your skin at an earlier time during hospitalization.

Parent/Participant Initial Here _____

8. CONFIDENTIALITY:

Your participation in this study and your medical records will be kept confidential in accordance with applicable state and federal laws. No information identifying you will be released without your permission unless it is subject to a subpoena or court order.

A statistical report of this research project or study, which may include slides or photographs that do not identify you, may be printed in a scientific paper.

If a research study involves the use of investigational drug(s) or devices(s), the U. S. Food and Drug Administration and the investigational sponsors, the University of Cincinnati and Shriners Hospitals for Children are permitted to have access to your medical records and to the data produced by this study for audit purposes. The Human Studies Committee at the University of Cincinnati is also permitted to have access to these records. They all are, however, required to keep your records confidential.

9. QUESTIONS:

If you have any questions, please ask us. If you have any questions later, please call Dr. Richard Kagan at (513)872-6000.

You can contact study investigators with questions about the research project. You can contact any of the investigators at (513) 872-6000 or the Chairperson of the University of Cincinnati Institutional Review Board at (513) 558-5259 for answers to pertinent questions about research, your rights as a research participant, and in the event of an adverse reaction or a research related injury.

10. COMPENSATION:

Neither you nor your parents will receive any cash, gifts or other financial compensation for taking part in this study.

In the event of injury or undesirable reaction from participation in research-related activities, Shriners Hospitals for Children can only provide those medical services available at this Hospital. If you believe you have been injured as a result of research contact Dr. Kagan at the above numbers. No financial compensation will be paid by Shriners Hospitals for Children for a research-related injury or an undesirable reaction. By signing this informed consent statement, you are not waiving the right to seek any legal options to which you are entitled.

11. WITHDRAWAL FROM THE STUDY:

Your participation in this research study is voluntary. If you decide not to participate, there will be no penalty and you will not lose any benefits you would otherwise receive. If you change your mind after you volunteer for this study, you may withdraw from this study and

Parent/Participant Initial Here _____

stop participating at any time without penalty or loss of benefits you would otherwise receive. No one will be upset if you end your participation in this study. You will continue to receive your usual treatment at Shriners Hospitals for Children, Cincinnati Hospital.

The consequences of your decision to withdraw from the research study are: You will be asked to complete a final examination by the study doctor as part of the process of leaving the study. This will be done to insure your safety. Your decision not to participate or to withdraw from the study at any time will not affect the medical care to which you are entitled.

If you wish to withdraw from this study, please contact Dr. Kagan at 513-872-6000.

12. The procedures involved in this study may involve risks to you or to your fetus (unborn child) if you are now or become pregnant while participating in this study. If you are pregnant now, could become pregnant now, or become pregnant during this study, it is important that your immediately tell one of the investigators referred to in paragraph 9 above. *If you are a woman of child-bearing potential, you will not be included in the study if you are pregnant.*

If you are a woman of childbearing potential, you will not participate in the research study unless you have a negative pregnancy test, and with the investigator=s knowledge and approval, are employing a form of birth control approved by Dr. Kagan, the medical investigator directing this study. You agree to inform the investigator immediately if: 1) You have any reason to suspect pregnancy; 2) find that circumstances have changed and that there is now a risk of becoming pregnant; or, 3) have stopped using the approved form of birth control.

13. COMMERCIAL PRODUCTS:

Samples taken during this study may be used for research and development purposes not related to your treatment or condition. You will not have any property rights or ownership interest in products or data which may result from your participation in this study. There is a possibility that this research may result in the development of a commercially valuable product or procedure. The investigators, sponsor and/or the institutions may benefit from the sale of such product or procedure.

Dr. Steven Boyce, a sub-investigator on this study, has received payments from the company that owns the rights to the process used in this study. This disclosure is made so that you can decide if this relationship will affect your willingness to participate in this study.

Parent/Participant Initial Here _____

14. GENERAL INFORMATION:

If the investigator feels that this study is not appropriate for you or that you have not followed directions for hospital tests, outpatient follow-up visits, or directions for taking medicine or test drugs, you will be dropped from the study.

15. You will be advised if significant information is developed during the course of this research that may affect your willingness to continue to participate.

16. There will be approximately 180 participants involved in this study at 5 institutions across the country.

17. Are you currently participating in any other human research study?

Yes _____ No _____

If yes, please write the name of the principal investigator (PI), the IRB approval number (IRB#) and the title of the study in the space provided below.

PI	IRB#	Study Title

Your signature, below, will indicate that you have decided to volunteer as a research participant, that you have had an opportunity to ask questions and all of your questions have been answered, and that you have read and understood the information provided above. You will be given a signed copy of this informed consent form which is yours to keep.

Signature of Witness	Date	Signature of Parent or Legal Guardian	Date
		Relationship to Participant (Parent, Legal Guardian, etc.)	
Signature of Witness	Date	Signature of Parent or Legal Guardian	Date
		Relationship to Participant (Parent, Legal Guardian, etc.)	
Signature of Witness	Date	Signature of Participant	Date

PI RICHARD KAGAN, MD
PROTOCOL NO. 95-07-210-01
APPROVED 6-17-09
EXPIRES ON 6-17-10
SIGNED _____ Chairperson/Designee UC IRB

Parent/Participant Initial Here _____

(Signature of both parents should be obtained where possible and signature of patient should be requested if 14 years of age or over.)

.....

Using language that is understandable and appropriate, I have discussed this project and the items listed above with the participant and/or his authorized representative.

_____ _____

Signature of Principal Investigator or Co-Investigator Date

The undersigned interpreted, to the best of my ability, the informed consent discussion between the investigator and the patient and/or the patient's parent(s) or legal guardian(s).

_____ _____

Signature of Interpreter Date

_____ _____

Printed Name Title

PI RICHARD KAGAN, MD
PROTOCOL NO. 95-07-260-01
APPROVED 10-17-09
EXPIRES ON 10-17-10
SIGNED _____
Chairperson/Designee UC IRB

Parent/Participant Initial Here _____