CLI 00125

INFORMED CONSENT TO PARTICIPATE IN CLINICAL RESEARCH FOR ADULTS AND PARENTS/LEGAL GUARDIANS

15 November 2021

NCT03459287

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Full Study Title:	A Randomized, Double-Blinded, Controlled, Parallel Group, Non-inferiority, Phase III Study to Evaluate the Efficacy and Safety of the INTERCEPT Blood System for Red blood cells in patients undergoing Complex Cardiac Surgery Procedures (the ReCePI study)
Study Number:	CLI 00125
Sponsor:	Cerus Corporation 1220 Concord Ave. Concord, CA 94520, USA (925) 288-6000
Principal Investigator:	[Insert Name of Principal investigator]
Institution	[Insert Name of Investigational Site] [Insert Phone Number – office and after office]
Institutional Review Board/Independent Ethics Committee Approval Date	[Insert approval date]

Introduction

Red blood cells are prepared by blood centers and provided to hospitals for transfusion to subjects. Blood transfusions may cause infections in subjects who receive them if viruses, bacteria, or parasites (pathogens) are present in the transfused blood product. All blood donations are tested for some pathogens, but not all pathogens are detected by testing.

Cerus Corporation, the sponsor, has developed a device called the INTERCEPT Blood System for Red Blood Cells (INTERCEPT). This is a device that has been shown to inactivate many types of pathogens making them unable to cause infection from transfusion of red blood cells. The INTERCEPT device has previously been tested in research studies for other patient groups in the United States and some countries in Europe.

NOTE:
Throughout this document, “you” and “your” may also refer to “your child” if it is your child who is (potentially) participating in the study.

Purpose of the Research

You are being asked to participate in a research study. Your transfusion center and your hospital are conducting this research study with Cerus to test red blood cells treated with the INTERCEPT device (test product) on patients requiring red blood cell transfusions. Your hospital and Cerus are making this test product available under this study to investigate the possibility of future use of this INTERCEPT device to protect patients from receiving blood contaminated with pathogens.

During this research study, the safety and efficacy of INTERCEPT-treated Red Blood Cells will be evaluated. If you are undergoing cardiac surgery and may require a transfusion of red blood cells, you may be eligible to participate.

Duration and Enrollment

The study is being conducted to evaluate the use of the INTERCEPT device to improve the safety of blood and will include at least 292 patients enrolled with complete data. If you choose to participate, you will be transfused with study red blood cells (INTERCEPT-Treated or untreated) according to local practices for up to 7 days of transfusion support. After 7 days, you may continue to be transfused with untreated (standard) red blood cell components if needed as prescribed by your doctor. During the 28 days following your last study transfusion, you will be contacted weekly by your hospital's study team to talk about how you are feeling and what medications you are taking. You will be asked to return at 28 days and at 75 days after the last study transfusion for follow-up visits. Your participation will last approximately four months.

Participant Selection

Patients aged 11 or over with certain types of scheduled cardiac surgery will be invited to join the study. Your doctor will be informed, and you can speak to your doctor about the study.

To take part in this study you must sign this written informed consent (if you are age 18 and above or are a parent of a child 11-17 years of age). *If your child is the potential participant, their assent (agreement to participate) may also be requested if this is your local institution's (IRB) requirement. This document will be provided to your child separately.* You also must weigh a minimum of 40kg (88 lbs.) and, as determined by your doctor, be likely to require a red blood cells transfusion. If you are female of child-bearing potential, you must agree to use at least one method of birth control that results in a low failure rate (including abstinence).

Voluntary Participation

Your agreement to join in the research study is voluntary. You may refuse to participate with no penalty, and you may choose to withdraw at any time. If you choose not to participate or to withdraw from the study, your decision will in no way affect the relationship you have with the hospital or your doctor, and there will be no loss of benefits to which you are entitled if you refuse to join or withdraw from this study. Your doctor can withdraw you from the study and begin use of standard red blood cells without your consent if deemed clinically appropriate or for any other reason. If you choose to withdraw from the study or you are withdrawn by your doctor, you might be asked to come back to the hospital for follow up testing.

Procedures

If you agree to join this research study your participation will include: an initial visit (screening), a pre-operation visit, a visit 7 days following your surgery or before you go home from the hospital, a visit 28 days after your last study transfusion, and a final follow-up visit 75 days after your last study transfusion.

During the initial visit (screening) you will be given this document and your doctor will explain the study to you and respond to all your questions. If you agree to participate and you sign and date this document your doctor will perform a medical exam, obtain your vital signs (i.e., heart rate, respiratory rate, and blood pressure), and information will be collected about your general medical condition and your treatments. During this visit a blood sample will be taken (approximately 2 tablespoons) to assess your general state of health, and, for females of child-bearing potential, a urine pregnancy test will be conducted and you will be asked about the number of prior pregnancies. You will also be given an electrocardiogram (ECG) test, which will use electrodes placed on your skin to check the electrical activity of your heart. It is possible, in certain situations, for a mobile medical professional authorized by Cerus to come to your home to draw the blood.

After that, you will be randomly (like tossing a coin) assigned to one of two groups, where one group will receive transfusions with INTERCEPT treated Red Blood Cells, and the other group will receive transfusions with untreated (standard) red blood cells. Neither you nor your doctor will know which type of blood product you are receiving. INTERCEPT treated and untreated (standard) red blood cells are in similar containers, which cannot be distinguished from each other. You will receive as many red blood cells as are appropriate for your treatment during the 7-day period following your cardiac operation. The decision whether you need a transfusion of red blood cells is made by your doctor.

During this 7-day period, information will be collected about your general medical condition, your treatments, and about your response to the transfusion of red blood cells components to see if you had any side effects after the transfusion. During this period, your vital signs will be checked at least daily and blood samples will be taken (approximately 1 teaspoon daily) for laboratory examination. You may also be given an electrocardiogram (ECG) test. Your study doctor will also record information about medications that you are given and collect other information related to your surgical recovery and general health status.

All the samples listed above will be analyzed at the Hospital Laboratory and will be destroyed after analysis.

About twenty-eight days (Day 28) after your last study transfusion you will be asked to go back to your hospital for a follow up visit. Your doctor will ask you questions about your general state of health and another blood sample (about 1 teaspoon) will be taken and tested to find out if you generated an immune response “allergy” to INTERCEPT treated Red Blood Cells and to measure your general health. Your vital signs will be taken, and information will be collected about your general medical condition and your treatments. It is possible, in certain situations, for a mobile medical professional authorized by Cerus to come to your home to draw the blood.

30 days after surgery your vital status and need for Renal Replacement Therapy will be assessed. This assessment can be performed through review of your medical record, via a telephone conversation with you or a family member, or during the Day 28 visit depending on the timing of your last study transfusion.

About seventy-five days (Day 75) after your last study transfusion you will be asked to go back to your hospital for a final follow-up visit. A blood sample (1 teaspoon) will be taken and tested to find out if you generated an immune response “allergy” to INTERCEPT treated Red Blood Cells. It is possible, in certain situations, for a mobile medical professional authorized by Cerus to come to your home to draw the blood.

If it is suspected that you have developed an immune response “allergy” to INTERCEPT treated Red Blood Cells, additional tests to confirm whether or not you have had an “allergic” response will be performed, which may include weekly blood and urine samples. Two to 4 tablespoons of blood may need to be obtained weekly for up to four weeks. It is possible, in certain situations, for a mobile medical professional authorized by Cerus to come to your home to draw the blood.

The blood samples for evaluation of your immune response, i.e., potential “allergy” to INTERCEPT treated Red Blood Cells, will be obtained and processed at your hospital laboratory. If the primary DAT RBC screening panel score is positive then your RBC

screening panel will be sent to our central lab Blood Center of Wisconsin (BCW) located at 638 North 18th Street, Milwaukee, Wisconsin 53233, for further testing. These samples will be disposed of after analysis results have been obtained.

Your plasma samples will be obtained for determination of human leukocyte antigen (HLA). These samples will be stored and shipped frozen to Vitalant Research Institute (VRI) located at 270 Masonic Avenue San Francisco, CA 94118-4417, where they will be tested and stored for up to 1 year after the study has completed.

You have the right to be informed of any plans for new analyses on your retained identifiable samples that are not currently foreseen and you have the right to refuse further analyses.

All your samples will be always treated in a confidential manner.

Your samples will not be used for genetic testing or any testing unrelated to blood safety without your consent. Collaborating researchers who may perform additional testing will not have access to your personal identifiers. You will be notified by your doctor of any abnormal test results that may impact your health. You can request to have your stored sample(s) removed from the repository at any time by notifying **[Insert Investigator's Name]** at the following number **[Insert Phone Number].**

Alternative Procedures

Clinical research involves a treatment or therapy that has not yet been approved by regulatory authorities. If you choose not to join in this research study, you will continue to receive any needed transfusions of red blood cells components ordered by your doctors. The red blood cells will not have been processed or treated using INTERCEPT Blood System.

Please discuss with your doctor about the benefits and risks of this treatment.

Risks

Blood samples will be needed for this study. These samples will be drawn in the same way as all of your other blood samples for treatment of your medical condition. The taking of blood to get samples for lab tests or the use of a needle to administer the red blood cells transfusion may cause slight pain and there is some risk of bleeding from the point of injection and the possibility of local bruising. Rarely do infections arise where the needle is inserted. The blood samples are drawn by expert medical staff using measures to reduce each of these risks to a minimum.

You may have a reaction with either INTERCEPT treated or untreated (standard) red blood cells, either during or after the blood transfusion. Reactions to the transfusion may include the following symptoms:

- jaundice (yellow coloring of the skin or eyes) dark-colored urine
- shivering, violent shivering fever
- high or low blood pressure
- heat flashes skin rashes, hives, itchiness sneezing, eye inflammation
- dizziness
- difficulty breathing or cough
- sense of anxiety

An increase in reactions to the transfusions due to the INTERCEPT treatment process is not expected. However, reactions associated with transfusion of the INTERCEPT treated Red Blood Cells could occur, as they sometimes do with normal blood transfusions. During previous studies, reactions to the transfusion did not increase when subjects received transfusions of INTERCEPT treated Red Blood Cells.

In this study, the risk of receiving an incorrectly labeled unit of red blood cells is minimized by using standard procedures that ensure you will be given a transfusion with the correct unit. All processes will be conducted by personnel that have been trained for the study, both at the transfusion center involved and at the hospital where you receive therapy. Your compatibility with the blood will be checked before transfusion through an extra check that ensures you receive the correct unit of red blood cells.

In this study, the red blood cells will be treated with an investigational chemical compound called Amustaline dihydrochloride. Amustaline dihydrochloride is capable of inactivating many types of pathogens making them unable to cause infection from transfusion of red blood cells without affecting their function in your body. It is possible that the risk of transmission of diseases from the transfusion of INTERCEPT treated Red Blood Cells may be lower than that of transfusion of untreated (standard) red blood cells.

The INTERCEPT treated Red Blood Cells will be preserved in SAG-M, a sugar-salt solution regularly used in Europe for preserving red blood cells. There are no known risks associated with its use in this manner.

The INTERCEPT Blood System for Red Blood Cells consists of a series of sterile plastic containers that are connected to keep the system sterile. The plastic materials that the INTERCEPT Blood System containers are made of have been used in other medical devices approved for contact with blood products or solutions administered into the bloodstream. There are no known risk increases associated with the use of this plastic system.

A possible known risk linked to INTERCEPT treated Red Blood Cells transfusions is an immune (allergic) reaction. This type of reaction was encountered in a previous study in two patients that had received multiple red blood cells transfusions treated with a previous version (called "Original process") of the INTERCEPT Blood System for Red Blood Cells. These patients developed antibodies against a part of the amustaline dihydrochloride compound. No abnormal health effects were seen in these patients and the antibodies disappeared in 6 months. Antibodies form when a person's immune system recognizes and defends itself against foreign substances like viruses, bacteria or chemical substances. For example, some patients produce antibodies against antibiotics, like penicillin.

Tests on animals given transfusions of INTERCEPT treated red blood cells did not show any signs of immune or allergic reactions. Tests were run on human beings to assess how well the red blood cells work and survive in circulation after transfusion. These tests showed that the INTERCEPT treated red blood cells function normally. In this study and another similar Cerus study, multiple patients developed antibodies to INTERCEPT red blood cells. In response, Cerus stopped their participation in the study, followed them over time, monitored their health, and found there were no harmful side effects. Cerus notified the committee who oversee safety for the study patients (so-called the "Data Safety Monitoring Board" or DSMB). The committee reviewed the findings and determined the study could continue to enroll new patients into the study.

During this study, your doctor will decide what dose of red blood cells you will receive.

Even though the study's sponsor considers the risks linked to participation in the study minimal, it is always possible for there to be unforeseen risks or that you might experience harmful effects that were not encountered in previous studies.

Risks for Women

INTERCEPT has not been tested in pregnant women. The effects of INTERCEPT on an unborn human fetus (developing baby still in the womb) or a nursing child are unknown. If you are a woman who is able to have children, you must take precautions against becoming pregnant. You cannot participate in this study if you are pregnant or breastfeeding. If you are still able to have children, you must have a serum or urine pregnancy test with a negative result to rule out pregnancy. Also, you must use at least one method of highly effective birth control

such as implants, injectables, combined oral contraceptives, some intrauterine devices (IUDs), or sexual abstinence. You can participate if your male partner is vasectomized. Please discuss with your doctor the appropriate birth control methods to be used during the study participation.

In case you become pregnant during the study, you should immediately inform the investigator. You will be discontinued from the study however information about your pregnancy may be collected.

Risks for Men

Even though there is no indication INTERCEPT RBCs may affect your sperm or unborn child, it is recommended that if you are a man who has not had a successful vasectomy and has a partner who is able to become pregnant, you and/or your partner should use a highly effective method of contraception as described above, from at least the first day of your partner's last normal menstrual period, throughout the entire study period, and for 14 days after the last study transfusion.

Benefits

There is a possible benefit from participating in this research study, which includes being transfused with red blood cells that have been treated with INTERCEPT to reduce the ability of pathogens to cause infection. There is also a chance the risk of reactions to transfusion is reduced, since the INTERCEPT treated Red Blood Cells contain less plasma. Plasma is a part of the blood that contains the substances (proteins) your immune system could recognize as foreign and could therefore cause a reaction to the transfusion. Your participation in this study may benefit patients receiving red blood cells transfusion in the future.

Authorization To Use and Share Your Medical Information

What information may be used and given to others?

Information about you that may be collected during the study, used and given to others may include past, present and future health information. Your personal information includes but is not limited to the results of study related procedures as described in this informed consent. (e.g., medical history, medical tests, blood component transfusions and other study-related materials that are unique and specific to your participation in this clinical research study). The above information may identify you by name, address, telephone number, social security number, health plan number, study number, date of birth, dates relating to various medical procedures, and/or other identifying information. All your information will be kept confidential to the extent permitted by the applicable laws and/or regulations and your information will not be made publicly available.

There may be other information about you that is used or given to others that may not have been stated above. It is advised that you discuss this with the study doctor and/or study staff and ask any questions that you may have about the sharing of your health information.

By signing this informed consent form, you are authorizing access to your original medical records for verification of clinical trial procedures and/or data, without violating your confidentiality, to the extent permitted by the applicable laws and regulations.

Who may use and give out information about you?

The study doctor and the study staff will use and provide your information.

Who might get this information?

- The study sponsor of this research (Cerus). "Sponsor" includes any persons or companies that are working for or with or owned by the sponsors (including monitors and auditors)
- Institutional Review Board (IRB) that oversees research at your site
- Government regulatory agencies including the U.S. Food and Drug Administration

If the results of this study are made public, information that identifies you will not be used.

This study may be published on governmental health authority websites. The results of the study may also be posted on governmental health authority and/or sponsor websites. Information learned from this research may be used in reports, presentations, and publications. None of these will identify you by name nor include any information that can easily be traced back to you.

Your information will be processed electronically (that is, by a computer) or manually and analyzed to determine outcomes of this study. The sponsor may use your information for other medical/health care purposes related to biomarker testing. For this purpose, only your coded information will be used.

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.

Is my health information protected after it has been given to others?

Once your information is disclosed to the study sponsors, its agents, the IRB or government agencies as described above, there is a potential that your medical information will be re-disclosed and will no longer be protected by US federal privacy regulations. In addition to disclosures to the entities identified above, the sponsor may further electronically disclose your coded health information to others involved in the research study, such as:

- To laboratories or offsite testing facilities for clinical tests required by study protocols.
- To approved offsite storage facilities or cloud service providers to meet study record retention and storage requirements.
- To other third parties contracted by the sponsor to provide services related to studies.

The study data may be transferred to other countries for processing, including countries not covered by data protection legislation. The laws of your state may provide further protection.

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to see if the research was done right.

May I review or copy my information?

You have a right to see and copy your information, however, not while the research study is going on. Significant new findings discovered during the course of the research which may relate to your willingness to continue participation in this study will be provided to you in a timely manner.

How Long Is This Authorization In Effect?

This authorization to use and disclose your personal health information does not expire. You must notify the study doctor that you no longer want to share your information. Information collected about you prior to the termination of your authorization may still be used for study purposes. Normally no new information will be collected for the study database unless you specifically authorize that. However, the law does require that any side-effects you may suffer are documented and reported. To complete the study findings, your long-term health status may also be obtained from public sources.

If you do not agree to this authorization, you cannot participate in this study. If you decide that you no longer wish to have your personal health information shared, you may withdraw at any time. However, once you do so, you can no longer continue to participate in the study.

In addition:

- You must provide a written request to the study doctor, listed on page 1, and tell him or her that you no longer want to share your information. Revoking your authorization and choosing to no longer participate in this study does not affect your treatment or any other benefits to which you would otherwise be entitled.
- You will no longer be a part of this research study.
- The study doctor and study staff can continue to share any of the information that they already have.

Compensation and Coverage of Medical Treatments

The test product will be made available to you at no charge and you will not be required to pay for any study procedures. You or your insurance company may be billed for any standard medical care that is not required for the research study. If you choose to participate in this research study you will not receive any payment. However, you may be reimbursed for travel expenses related to the study.

It is important that you tell your study doctor, _____ [investigator's name(s)] if you feel that you have become ill or injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ [telephone number].

The Sponsor of this study will pay for the costs of medical care arising from illness or injuries that are the direct result of your participation in the research study, if such costs are not covered by your medical or hospital insurance or government programs providing such coverage. In the event of a physical injury as a direct result of study procedures, you will be referred for appropriate medical care, and you and/or your insurance company will be expected

to cover all costs. This does not preclude you from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research. You are not waiving any legal rights by signing this form, accepting medical care or accepting payment for medical expenses.

Will the personnel involved in the study receive any payment?

The [investigator] receives payment from Cerus who is the sponsor of this study.

Additional Information

The sponsor of this research study and the investigator reserve the right to discontinue your participation in the study. A summary of the results of this research study will be provided to all investigators and participating subjects upon request. In case of confirmed antibodies to INTERCEPT Red Blood Cells, subjects will be discontinued from the study and supported with untreated (standard) red blood cells.

Who has reviewed the study?

This study was given a favorable ethical opinion by the [insert full name of IRB].

Contact Information

For questions about the study, contact the study doctor at the number listed on the first page of this form.

If you believe you have suffered an injury as a result of your participation in this study, you should contact the study doctor at the number listed on the first page of this form.

For questions about your rights as a research participant, contact:

[Insert Contact Information for IRB]

CERTIFICATE OF CONSENT

PARTICIPANT SIGNATURE

I have read or someone has read to me this consent document which describes the purpose and nature of this research. I have had time to review this information and have been encouraged to ask questions and have received answers to my questions. I understand that my participation in this research study is voluntary and that I may refuse to participate or withdraw at any time without any negative experiences. I have received a copy of this signed and dated form for my records and future reference.

Print Name of Participant: _____

Signature of Participant: _____

Date: _____

If participant has a Legally Authorized Representative (LAR):

Print Name of LAR: _____

Signature of LAR: _____

Date: _____

PERSON OBTAINING CONSENT

I have read this consent document to the participant and/or the participant has read this consent document. An explanation of the research study was given and questions from the participant were solicited and answered to the participant's satisfaction. In my judgment, the participant has demonstrated comprehension of the information.

Print Name of Person Obtaining Consent: _____

Print Title of Person Obtaining Consent: _____

Signature of Person Obtaining Consent: _____

Date: _____

INSTRUCTION_PLEASE USE IF NO INSTITUTION-SPECIFIC IRB/IEC IS REQUIRED

Typically, HIPAA Authorizations are a separate form (usually requested by most participating sites that have already adopted their own HIPAA Authorization). If the institution does not have its own HIPAA Authorization, please use the following HIPAA Authorization Form.

If the institution, CRO, health authority, or IRB/IEC have a requirement for the HIPAA Authorization text to be a specific font/font size, ensure that the appropriate adjustments are made.

HIPAA Research Authorization
Authorization to Use and Disclose Health Information

I agree to permit [*insert name of Research Center*] and any of my doctors or other health care providers (together, "Providers"), Principal Investigator, and [his/her/their/its] collaborators and staff (together, "Researchers"), to obtain, use, and disclose health information about me as described below.

1. The health information that may be used and disclosed includes:
    - All information collected during the research and procedures described in the Informed Consent Form (the "Research")
    - Personal health information in my medical records that is relevant to the Research, which includes my past medical history, medical information from my primary care physician, and other medical information relating to my participation in the study
2. The Providers may disclose health information in my medical records to:
    - The Researchers
    - Representatives of government agencies, review boards, and other persons who watch over the safety, effectiveness, and conduct of research
    - The sponsor of the Research, [*insert Cerus Corporation affiliate*] and its affiliates, agents and contractors assisting in the conduct or completion of the Research (together, "Sponsor")
3. The Researchers may use and share my health information:
    - Among themselves, with the Sponsor, and with the other participating Researchers to conduct the Research
    - As permitted by the Informed Consent Form

4. The Sponsor may use and share my health information for purposes of the Research and as permitted by the Informed Consent Form.
5. Once my health information has been disclosed to a third party, federal privacy laws may no longer protect it from further disclosure.

Please note that:

- You do not have to sign this Authorization, but if you do not, you may not participate in the Research. If you do not sign this Authorization, your right to other medical treatment will not be affected.
- You may change your mind and revoke (take back) this Authorization at any time for any reason. To revoke this Authorization, you must write to the Research Study Personnel at:

NAME:	*[Insert name]*
ADDRESS:	*[Insert address]*
PHONE:	*[Insert telephone number]*

- However, if you revoke this Authorization, you will not be allowed to continue taking part in the Research. Also, even if you revoke this Authorization, the Providers, Researchers, and the Sponsor may continue to use and disclose the information they have already collected to protect the integrity of the Research or as permitted by the Informed Consent Form.
- While the Research is in process, you may not be allowed to see your health information that is created or collected during the course of the Research. After the Research is finished, however, you may see this information as described in [*insert name of Research Center*], Notice of Privacy Practices.

INSTRUCTION: For all sites outside of California use the following text:

This Authorization does not have an expiration (ending) date.

You will be given a copy of this Authorization after you have signed it.

INSTRUCTION: For California sites, use the following text:

The expiration date for this Authorization is 25 years after the study is completed.

You will be given a copy of this Authorization after you have signed it.

Print Name of Participant: _____

Signature of Participant: _____

Date: _____

If participant has a Legally Authorized Representative (LAR):

Print Name of LAR: _____

Signature of LAR: _____

Date: _____

PERSON OBTAINING CONSENT

I have read this consent document to the participant and/or the participant has read this consent document. An explanation of the research study was given and questions from the participant were solicited and answered to the participant's satisfaction. In my judgment, the participant has demonstrated comprehension of the information.

Print Name of Person Obtaining Consent: _____

Print Title of Person Obtaining Consent: _____

Signature of Person Obtaining Consent: _____

Date: _____