Informed Consent Form and HIPAA Authorization

LAY TITLE:	Study of Thrombosomes® Compared With Blood Platelets to Control Bleeding in Patients with Thrombocytopenia
TITLE:	A Prospective, Multicenter, Randomized, Open-Label Phase 2, Parallel, Dose Ranging Multidose Study of Thrombosomes® vs Liquid Stored Platelets (LSP) in Bleeding Thrombocytopenic Patients
PROTOCOL NO.:	2019-1 WIRB® Protocol #20202295
SPONSOR:	Cellphire, Inc.
INVESTIGATOR:	Name Address City, State Zip Country
STUDY-RELATED PHONE NUMBER(S):	Phone Number Phone Number (24 hours) [24 hour number is required]

Overview and Key Information

A person who takes part in a research study is called a research or study subject. In this consent form "you" always refers to the research subject. If you are a legally authorized representative, please remember that "you" means the research (study) subject.

You are being asked to participate in a research study because you have thrombocytopenia, a low concentration of platelets in your blood. Platelets help your blood form a clot, so a low concentration of platelets means you may be more likely to have bleeding that will not stop.

Researchers are required to provide a consent form to inform you about the research study, to explain that your participation is voluntary, to explain risks and benefits of participation including why you might or might not want to participate, and to help you to make a decision. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. You should feel free to discuss and ask the researchers any questions you may have. This study has been reviewed by an Institutional Review Board (IRB), also called an Ethics Committee.

This research study is looking at the use of a new product called Thrombosomes® made from human platelets that might be useful in making blood clot to help stop bleeding. Thrombosomes is investigational, also called experimental, which means that it is not approved by the Food and Drug Administration (FDA). The study will compare Thrombosomes to standard liquid stored platelets to see if Thrombosomes stop bleeding as well as standard platelets do. The duration of your participation may be about 30 days. You will be randomized to receive either Thrombosomes or standard liquid stored platelets (by chance) to treat your thrombocytopenia. If you decide not to take part in this research study, you should know that you can still receive standard care for your thrombocytopenia, which would be liquid stored platelets.

Thrombosomes may or may not work better than liquid stored platelets at stopping bleeding. Your participation in the study may help to understand how well Thrombosomes work.

The most likely risks of participating in this study are that your white blood cell count and levels of other proteins in your blood might increase, that your heart might have an abnormal rhythm or a murmur, or that you might develop antibodies to (become allergic to) your own platelets.

Thrombosomes may work better than liquid stored platelets at stopping bleeding; however, they may work the same or less well. Your participation in the study may contribute to the understanding of how well Thrombosomes work.

What am I being asked to do?

We are asking you to receive (by chance) either a new product called Thrombosomes or standard liquid stored platelets. Thrombosomes are the result of freeze-drying a small pool of platelets from 5–10 blood donors. Standard liquid stored platelets come from a single donor and contain the donor's plasma (the fluid portion of blood) while Thrombosomes contain very little plasma.

What are my rights if I take part in this study?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. Whatever choice you make, there will be no penalty to you and you will not lose any of your regular benefits. You also can also leave the study at any time. Leaving the study will not affect your medical care at [insert name of hospital]. You can still get your medical care from our institution. Your decision not to participate or to leave the study will not result in any penalty or loss of benefits to which you are otherwise entitled.

During the course of the study, you will be informed of any significant new research findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study may be re-obtained.

Why is this study being done?

This study is being done to answer the following questions:

How do Thrombosomes compare with standard liquid stored platelets in stopping bleeding in patients with thrombocytopenia? Are Thrombosomes as effective and as safe as standard liquid stored platelets?

Thrombosomes are more stable than standard platelets, they can be stored for longer time making them easier for hospitals and clinics to keep around to use when they are needed. Thrombosomes might be less likely to carry certain viruses than standard platelets.

What is the usual approach to stopping bleeding in thrombocytopenic patients?

The usual approach for patients who are not in a study is to give standard liquid stored platelets.

What are my choices if I decide not to take part in this study?

You may choose to have the usual approach described above–liquid stored platelets.

You may choose to take part in a different research study, if one is available.

You may choose not to be treated for thrombocytopenia.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either get Thrombosomes at the dose level you are randomized to for up to 3 days, or you will get liquid stored platelets for up to 3 days. If you are given Thrombosomes and they do not control your bleeding, your doctor can decide to give you standard platelets or other blood products.

After the 3 days, your doctor will continue to follow your condition for bleeding and give you standard liquid stored platelets or other blood products as they see fit. Your participation in this study will take about 30 days including the three days of treatment and follow up appointments.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care at [insert name of hospital]. You can still get your medical care from our institution.

If you decide to stop, let your study doctor know as soon as possible. If you stop, you can decide if you want the study doctor to know how you are doing.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), Department of Health and Human Services (the part of the federal government that is paying for this study) or study sponsor (Cellphire). The study sponsor is the organization who oversees the study.

Additional Important Information About the Study

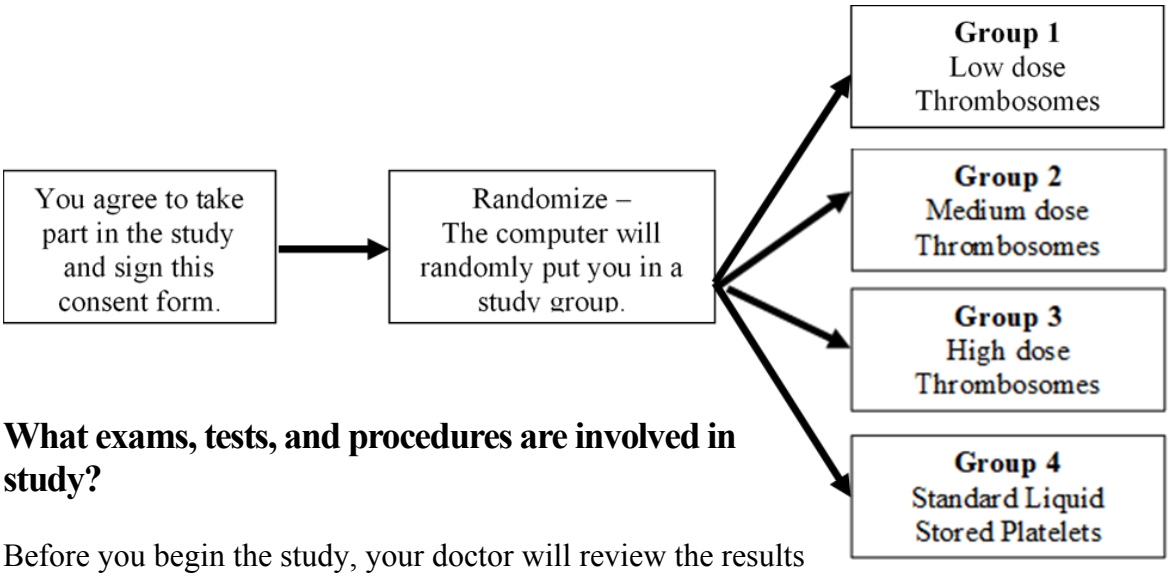
What are the study groups?

This study has four study groups. We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose, and you cannot choose which study group you are in, but you and your doctor will be told which group you are in. You will be put into a group by chance. You will have an equal chance (25%) of being in each of the four groups. There will be about 160 people taking part in this study.

- **Group 1 (about 40 people in this group)**
- If you are in this group, Thrombosomes will be injected into your vein at a low dose based on your body weight (about 1 tbsp), up to six times over 72 hours (3 days).
- **Group 2 (about 40 people in this group)**
- If you are in this group, Thrombosomes will be injected into your vein at a medium dose based on your body weight (about 3.5 tbsp), up to six times over 72 hours (3 days).
- **Group 3 (about 40 people in this group)**
- If you are in this group, Thrombosomes will be injected into your vein at a high dose based on your body weight (about 7 tbsp), up to six times over 72 hours (3 days).
- **Group 4 (about 40 people in this group)**
- If you are in this group, you will not receive any Thrombosomes, but will receive liquid stored platelets as if they were Thrombosomes (about 16 tbsp), up to six times over 72 hours (3 days).

If you are in the group that gets Thrombosomes, you will not be able to get additional doses of the product beyond the 6 doses over 72 hours (3 days), but your doctor will be able to control your bleeding by giving you standard liquid stored platelets or other blood products.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Many of these are included in the usual care you would get even if you were not in a study. This is called screening. If your doctor decides during screening that it is not safe for you to take part in the study or you do not meet the study requirements, you might be asked sometime later to repeat some of the screening tests again to see if things have changed and to see if you can join the study. It is your choice whether you want to repeat these tests.

If your screening happens more than 24 hours before you are able to be infused, some additional tests will be done and some tests that were done during screening may be repeated.

Screening Visit

Sign this consent form after you read and understand it. You will need to do this before you can participate in any part of the study, including the rest of screening. During screening the following tests will take place:

- Pregnancy test if you are a woman who could get pregnant
- Physical Exam
- Vital signs (heart rate, blood pressure, temperature, breathing rate and a measure of how much oxygen is in your blood)
- Electrocardiogram (EKG)- a provider will put 12 sticky patches in different places on your body and measure your heart rhythm
- Blood draws for testing and determining your blood type ([amount] tsp/tbsp of blood)

Baseline Visit

This will happen before you are infused. During baseline visit the following tests will take place:

- Short physical exam
- Vital signs (heart rate, blood pressure, temperature, breathing rate, and a measure of how much oxygen is in your blood)
- Blood draw for testing to see if you are still able to be in the study (will be done within 12 hours before you get your first Thrombosomes or standard liquid stored platelets) ([amount] tsp/tbsp of blood)
- Blood draw to be store for future testing ([amount] tsp/tbsp of blood)

Infusion

Depending on the group you are in your doctor will give you ("infuse" into you) Thrombosomes or liquid stored platelets. These will be delivered into a vein in your arm over less than an hour each time. You will receive Thrombosomes between one and six times up to 72 hours (3 days) depending on what your doctor thinks is necessary to control your bleeding. If at any time the doctor does not think your bleeding is being controlled well, they can stop giving Thrombosomes and can provide standard liquid stored platelets or other blood products.

After infusion the following tests/collections will take place:

- Vital signs taken at 15 minutes, 1 hour, 4 hours, 8 hours and 12 hours after each infusion; then again at 24 hours, 48 hours, 72 hours and 96 hours (if necessary)
- Blood draws for testing
    - within 15-60 minutes after each infusion ([amount] tsp/tbsp of blood)
    - at 12 hours ([amount] tsp/tbsp of blood)
    - at 24 hours ([amount] tsp/tbsp of blood)
    - every day for three more days (four days if you are still in the hospital) ([amount] tsp/tbsp of blood)
- Archive blood draw to be stored for future testing at 72 hours (3 days) after your first infusion ([amount] tsp/tbsp of blood)
- Physical exam at 12 hours, 24 hours, and then every day for three more days (four days if you are still in the hospital)

Day 7 Visit

During your Day 7 visit the following tests/assessments will take place:

- Physical exam

- Vital signs
- Blood draw for testing ([amount] tsp/tbsp of blood)

Day 30 Phone Call

About 30 days after your infusion, you will receive a phone call from the doctor's office to see how you are feeling and if you have had to return to a clinic or hospital for any emergency care.

Archive Blood Samples

Blood draws taken for future testing ("archive samples") will be stripped of information that could identify you; shipped to the study sponsor; and stored for up to one year after the study ends. Testing done on these samples may show how your blood changed because of the study treatments. No genetic testing will be done on these samples. You and your study doctor will not get the results of this testing.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

General Risks

If you choose to take part in this study, there is a risk that Thrombosomes may not be as good as liquid stored platelets at preventing bleeding.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

There is also a risk that you could have side effects from Thrombosomes. These side effects may be worse and may be different than you would get with the usual standard liquid stored platelets.

Here are important things to know about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

Side Effect Risks

During previous clinical studies some people experienced slight side effects, but it is not known if these side effects were caused by the Thrombosomes. It is possible you may experience similar side effects.

- There is a chance that transfusion of Thrombosomes might make you form a clot at an unusual site like a major vein or artery.
- There is a possibility of a heart attack due to clot in the blood vessels supplying the heart and this may result in death.
- There is also a possibility of a stroke due to a clot in the blood vessels supplying the brain and this may result in death.
- There is a possibility that you may develop an immune response to Thrombosomes. This new antibody could be directed not only against the infused Thrombosomes, but also against your own circulating platelets. This may cause a decrease in your already low platelet count.
- Other possibilities from a previous study of Thrombosomes in volunteers included changes in white blood cell count and clotting tests, minor EKG changes, heart murmur, and a minor immune reaction to the volunteer's own platelets; none of these required treatment.

Risks of receiving liquid stored platelets may include: shivering, rise in temperature, itching, skin rash, or other allergic reactions and the potential for lung injury.

There is also a risk that you could have other side effects from the study that are not yet known.

Risks from Venipuncture (placement of the needle into your vein)

A needle will need to be placed in your vein to inject the Thrombosomes or standard liquid stored platelets. The risks of this are:

- Discomfort and/or a bruise at the site.
- Lightheadedness, fainting, the formation of a small blood clot or swelling of the vein and surrounding tissue, and bleeding from the puncture site, though these are less common
- If a needle comes out of your vein but remains in your arm, blood may flow into the surrounding tissue, causing discoloration, swelling and soreness that could last for a few days.
- There is a rare chance of infection.

You can ask your study doctor questions about side effects at any time. If you notice or feel anything different, tell your study doctor. They can check to see if it is a side effect. Your study doctor will work with you to treat your side effects.

Benefits

Thrombosomes might control bleeding better than standard liquid stored platelets, but we do not know yet. You may or may not benefit from taking part in this study. Studies like this one will help find out. This study will help the study doctors learn things that may help people in the future.

What are my responsibilities in this study?

If you choose to take part in this study, you will need to:

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study or hospital
  - if you have been or are currently in another research study.
- Inform the doctor if you decide to discontinue your participation.

For women: Do not get pregnant or breastfeed while taking part in this study.

Women who are pregnant or nursing a child may not take part in this study. We do not know the effect of the Thrombosomes on a pregnant woman or her fetus. Before entering the study, you and your study doctor must agree on the method of birth control you will use during the entire study. If you think that you have gotten pregnant during the study, you must tell your study doctor immediately. Pregnant women will be withdrawn from the study and their study doctor will communicate with the doctor managing the pregnancy. You and your pregnancy will be followed to term.

For men: Do not father a baby while taking part in this study. We do not know the effect of Thrombosomes on sperm, eggs or fetuses.

What are the costs of taking part in this study?

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. You or your insurance provider will not have to pay for Thrombosomes, standard liquid stored platelets, or other blood products used as part of the study while you take part in this study. These include:

- The EKG in this study done to determine if you can take part in the study
- A pregnancy test will be done if you are female and capable of becoming pregnant to determine if you can take part in the study

- Blood tests that are for the study only
- Physical exams and measurement of your vital signs (blood pressure, temperature, etc.) that are done only for the study

You and/or your insurance plan will need to pay for the costs of standard medical care you would get as usual care for your thrombocytopenia if you were not in the study. This may include:

- the costs of tests, exams, procedures, and drugs that you would get if you were not in the study.
- your insurance co-pays and deductibles for routine care.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

Will I be paid to participate in this study?

If you enter the study, you'll receive $200 for the screening visit. If you receive any infusion of Thrombosomes or standard liquid platelets as part of the study, you will receive $200 for the baseline visit. You will be paid an additional $400 for completing the visit at Day 7, and an additional $200 for providing information at Day 30 about how you are feeling. The maximum amount you could be paid for completing the study is $1,000.

The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will pay for medical treatment for injury that is directly related to your participation in the study.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study.

For questions about the study or research-related injury, contact [insert PI's name] at [insert PI's 24-hour number here with area code].

You are not waiving any legal rights you may have by signing this form.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information or Protected Health Information (PHI) may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any PHI that goes out to others will not identify who you are.

Information about a Certificate of Confidentiality for this research:
_____ **(name of research site and investigator)** has received a Certificate of Confidentiality from the government which will help protect the privacy of research subjects. The certificate protects against the involuntary release of information about subjects collected during the course of this research. The researchers involved in this study cannot be forced to disclose any information collected in this study in any legal proceedings.

However, the subject may choose to voluntarily disclose the protected information and this certificate does not prohibit such voluntary disclosure. Furthermore, the parties listed in the Confidentiality / Authorization section of this consent form may review our records under limited circumstances and this certificate does not prohibit such disclosure.

Some of your health information, such as your response to thrombocytopenia treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. Your name and contact information are not part of this health information and will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study now or in the future. This would include any organization helping the company with the study, working for or with the sponsor, or owned by the sponsor.
- The FDA, the US Department of Health and Human Services (DHHS) agencies, and the groups it works with to review research.
- Governmental agencies and regulatory authorities like the FDA in other countries.
- Governmental agencies to whom certain diseases (reportable diseases) must be reported.
- Ethics committees called Institutional Review Boards that review research to protect your rights.

The Sponsor of this study may use and share your health information collected during this study. Once your health information has been disclosed to the Study Sponsor or their agent, or any other groups listed above, the federal privacy laws may no longer protect it from being shared among a wider audience.

If your information is transferred outside of the United States, different privacy laws may apply. Additionally, if one of the companies or institutions listed above merges with, or is purchased by, another company or institution, this authorization to use and disclose protected health information in the research will extend to the successor company or institution.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Will my authorization expire?

This Authorization to use or disclose protected health information does not have an expiration (ending) date.

Please note that:

- You do not have to consent to this Authorization to use or disclose protected health information, but if you do not, you will not be allowed to participate in the Research.
- You (or your legally authorized representative) may change your mind and cancel this authorization at any time. To cancel your authorization to use or disclose protected health information, you must write to:

  [Insert Principal Investigator's Name]
  [Insert Full Address (no P.O. Box)]

However, if this Authorization to use or disclose protected health information is canceled, you will no longer be allowed to participate in the Research. Also, even if this Authorization to use or disclose protected health information is canceled, the information already obtained by the Researchers and the Sponsor of this study may be used and disclosed as permitted by this Authorization and the Informed Consent.

May I review or copy the information obtained or created about me for this study?

Yes. You have the right to review and copy your health information. However, you may have to wait until the study is finished.

If you decide to leave the study or withdraw your authorization, you will still be able to review and copy your health information.

Where can I get more information?

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.

You can talk to the study doctor about any questions, complaints, or concerns you have about this study or to report side effects or injuries. Your study doctor will explain your options and tell you where to get treatment. Contact the study doctor [insert name of study doctor[s]] at [insert telephone number (24 hours), and email address if appropriate].

For questions, complaints, or concerns about your rights while in this study, call the Institutional Review Board at (800) 562-4789.

Signature and consent/permission to take part in the study

- All patients that are unable to consent and need to use an LAR, are required to assent, unless the investigator determines that the capability of the patient is so limited that the patient cannot reasonably be consulted.
- If assent is obtained, have the person obtaining assent document assent on the consent form.

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the study.

Participant:

By signing this consent form, you indicate that you are voluntarily choosing to take part in this research.

_____	_____	_____
Printed Name	Signature	Date

Participant's Legally Authorized Representative (LAR):

By signing below, you indicate that you give permission for the participant to take part in this research. Signature by a participant's Legally Authorized Representative (LAR) is required only for people unable to give consent for themselves.

_____
Printed Name of Legally Authorized Representative

_____	_____
Signature of Legally Authorized Representative	Date

_____
Description of Legally Authorized Representative's Authority to Act for Participant

Person Explaining the Research and Obtaining Informed Consent:

Your signature below means that you have explained the research to the participant/participant representative and have answered any questions he/she has about the research.

_____	_____	_____
Printed Name	Signature	Date

****For Sites in California****

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

Who may use and give out information about you?
The study doctor and the study staff. [They may also share the research information with [enter SMO company name], an agent for the study doctor. delete if the site does not have an SMO]

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:

- working for or with the sponsor, or
- owned by the sponsor.

Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- The institution where the research is being done,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Institutional Review Board (IRB)

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

- to do the research,
- to study the results, and
- to make sure that the research was done right.

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

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This permission will be good until December 31, 2070.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

Authorization:
I have been given the information about the use and disclosure of my health information for this research study. My questions have been answered.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

AUTHORIZATION SIGNATURE:

Signature of Subject or Legally Authorized Representative	**Date**