Supplementary File 2: Consent Forms

CONSENT FORM FOR RESEARCH and

TEEN (13-17 YEARS OLD) ASSENT AND PARENTAL PERMISSION FORM FOR RESEARCH

Disclaimer: *The following is the consent form for research.*

If you are between the ages of 13 to 17, parental permission to participate in research is required and this document will serve as an assent form for research. If you are a parent/guardian of a child who may participate, "you" refers to "your child" throughout this form.

Title: RANDOMIZED-CONTROLLED TRIAL OF VIRTUAL REALITY FOR CHRONIC LOW BACK PAIN TO IMPROVE PATIENT-REPORTED OUTCOMES AND PHYSICAL ACTIVITY

SPONSOR: THE NATIONAL INSTITUTES OF HEALTH (NIH)

PRINCIPAL INVESTIGATOR: BRENNAN SPIEGEL, MD

STUDY CONTACT PHONE NUMBER AT CSMC: (310) 423-5434

AFTER HOURS CONTACT (24 HOURS): (248) 383-5346

This research study is sponsored by the NIH. The NIH only reimburses Cedars-Sinai Medical Center for the costs associated with running the study; the NIH is not providing additional compensation to Cedars-Sinai Medical Center or the Principal Investigator for their participation in the study.

KEY INFORMATION ABOUT THIS RESEARCH STUDY

We are seeking your consent to take part in this research study. Your participation in this research is voluntary. If you choose to participate, you can stop at any time. Please consider the following summary, along with the more detailed information provided throughout this consent form.

- The purpose of this study is to assess the impact of virtual reality (VR) therapy on chronic lower back pain. We want to see if using VR therapy will improve pain management, offer additional pain relief, or be an effective alternative to traditional pain medication.

- The main procedures of this study include using a virtual reality headset every day to manage your pain for 90 days. Using the headset will take about 10 minutes each day.

You will also wear a Fitbit to collect data on your daily activity. We will also ask you to complete weekly surveys over the first 30 days, then biweekly surveys until the end of the study. Surveys will be sent via email and can be completed from a computer or smartphone (Android or iOS). You will need to complete one week of screening surveys prior to being sent the virtual reality headset and other study materials. If you choose to take part in this study, it will last about 90 days.

- All research studies involve some risks. Risks or discomforts from this study may include: minor psychological distress from questionnaires regarding health and employment status, and ~5% risk of "cybersickness," presenting as short-term symptoms related to entering VR environments (vertigo, nausea, headache).

- Potential immediate benefits include reduction of chronic low back pain and overall improvements in psychological health. Potential long-term benefits include improved functionality, reduced opioid use, and improvements in overall physical health. This research will contribute to the societal knowledge about the use of digital interventions within healthcare.

- If at any point in the study you feel the need to make any changes to your prescribed medications, please talk with your prescribing physician. Making abrupt changes to medications may be unsafe and any modification in medications should occur under the guidance of your physician.

- If you choose not to participate, there may be other choices available to you. You can continue your current treatment with your providers. You will not lose any services, benefits or rights you would normally have if you choose not to participate. Please discuss your choices with the researchers.

Please take time to read this entire form and ask questions before deciding whether to participate in this study. You are encouraged to talk with family members, friends, and/or healthcare providers before you make your decision.

1. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

We are doing this study to see if using an audiovisual headset helps to manage or improve chronic lower back pain. We want to know if the use of this tool can limit the extent to which pain interferes with your life and if your overall health improves.

You are being asked to take part in this research study because you are an outpatient at Cedars- Sinai Medical Center (CSMC) with chronic lower back pain.

In this study, three different virtual reality experiences using three different software programs will be assessed for their ability to reduce pain. You will be randomized into one of three groups after the screening period. See Section 2 below for more information.

The study will enroll up to 360 people in total.

This research study is designed to use the PICO G2 Headsets and the Fitbit Charge 4 Activity Monitor. Both the VR headset and Fitbit Charge 4 activity monitor can be purchased in stores, are not currently regulated by the FDA, and pose minimal to no risks to individuals.

2. WHAT WILL HAPPEN DURING THE STUDY?

This section provides a general overview of what will happen during your participation in this study. Information included below should be considered along with the flowchart of procedures attached as an Appendix.

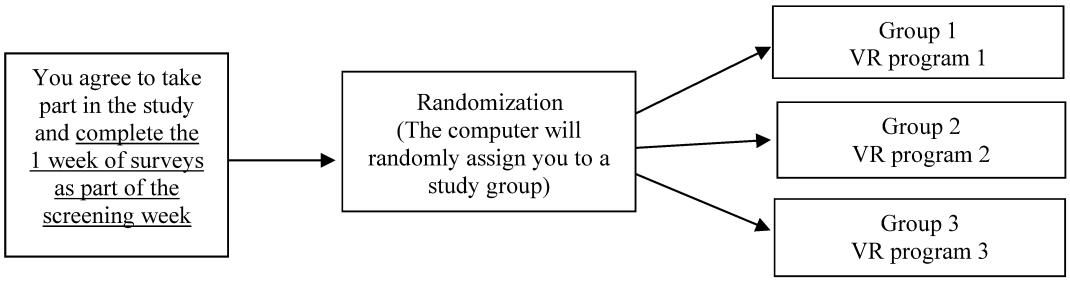
The flowchart shows a timeline for research-related procedures that are involved in your participation in this study. **Research-related procedures** are those performed solely for the research. They would not be performed if you did not take part in the study. All procedures in this study are research-related procedures.

At the start of the study, you will be sent surveys via email. Surveys can be completed on a computer or smartphone (Android or iOS). You will be trained on how to use the VR headset, Fitbit, and any related apps required for the study.

Overview of study:

This is a single-blind, randomized research study with an additional screening week. Standard (routine) care will involve treatment as prescribed by your provider for your pain condition.
Your study participation will not dictate your standard treatment or care.

- **"Single-blind"** means that the researchers will know which group you are assigned to but will not tell you which group you are participating in. Your physician will also not know which group you are in.
- "**Randomized**" means that you will be assigned to a study group by chance, like flipping a coin. You will be randomized into one of three study groups and will have an equal chance of being placed in one of the three groups described below.
- "**Screening week**" means you will receive surveys every day for a week via email. Once you complete this week of surveys, you will be eligible to be randomized.



A computer will randomly assign you to a study group. This is done because no one knows if the results experienced by the participants in one study group are better, the same, or worse

than the results experienced by participants in the other. Once you are put in one group, you cannot switch to another group. Neither you nor your doctor can choose the group in which you will be placed.

Any of these different approaches could help your condition but could also cause mild temporary side effects. This study will allow the researchers to learn whether the different software programs are better, the same, or worse than the current standard of care. Audiovisual therapy has been used in several studies at Cedars-Sinai. The results of these studies have demonstrated the device to be safe; less than 25% of patients who use the VR headset have minor, short-term side effects from the device.

If you are assigned to any group, you will be followed as you receive the care generally provided for individuals with your condition, with the addition of a wrist-worn sensor to track your physical activity, sleep quality and duration, and heart rate. This sensor is called a Fitbit. You will be asked to use the VR unit for no more than 20 minutes at least once a day and as needed during moments of pain. You will be asked to complete surveys asking questions about your pain via email.

The wrist-sensor, VR unit, and the app we install on your smartphone will collect data and periodically upload data to secure, encrypted servers at Cedars-Sinai.

You will be asked to keep your smartphone on your person and answer surveys when prompted. We will also ask you to keep the VR headset with you whenever possible and wear the sensor on your wrist at all times. You should only remove the sensor when charging the unit or prior to starting an activity that may damage the headset, such as taking a shower or swimming. In the event that any of the study equipment are lost or damaged, you will not be held responsible for the lost or damaged study equipment. However, all study equipment, whether damaged or intact, must be returned at the end of the study.

Prescription Data

As part of this study, we will be collecting prescription data from the Cedars-Sinai Medical Record as well as any prescription data available from the California Controlled Substance Utilization Review and Evaluation System (CURES), if relevant. CURES is a database that tracks controlled substances prescribed to patients in the state of California. Our study will request permission to obtain prescription data to assess whether there are any changes in medication use throughout the course of the study. The data will be collected from 90 days before enrollment until 90 days after completion of the study. The data will be requested from CURES between 9/1/2023 to 7/1/2024. As with all study data, this information will only be used for research purposes and will comply with all requirements of the California Confidentiality of Medical Information Act and the Health Insurance Portability and Accountability Act of 1996 (HIPAAA).

How long will you be in the study?

We think you will be in this study for about 90 days.

3. WHAT ARE THE POSSIBLE RISKS?

This section describes the possible risks and/or discomforts we anticipate you could experience that are related to the study procedures:

VR Intervention:
While using the VR headset, you may experience discomfort with the virtual environment, including temporary headache, vertigo, or nausea. These should be short-term and should stop soon after the headset is removed.

Fitbit Charge 4 Activity Monitor:
You may experience minor skin irritation or discomfort from wearing the activity monitor for extended periods of time.

Surveys:
It is possible that some of the items in the surveys may make you feel uncomfortable or embarrassed. You are not required to respond to any item that you do not wish to answer. The surveys will be labeled with a unique study number that will link your identity so that only the research team can recognize you.

There are no anticipated long-term risks from participating in this study.

Risks of sharing data
Even though we will protect your privacy as much as possible, there is a very small chance that the data could be identified as yours. The risk of this happening is very small, but may increase in the future as technology changes.

Research using data from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your samples and data.

If you do not want your data and samples used for other research, you should not participate in this study.

Follow-up Visit for Discontinuing Participants
While you are free to discontinue your participation at any time, we encourage you to complete the final study on the 90^{th} day.

4. ARE THERE BENEFITS IN TAKING PART IN THE STUDY?

If you agree to take part in this research study, there may or may not be direct medical benefit. The possible benefits of taking part in the research study are pain relief, improved functionality, greater satisfaction with care, and overall improvements in physical and mental health. However, no benefit is guaranteed. It is possible that your condition may remain unchanged or even get worse.

It is possible that none of the programs we are testing will provide benefit. However, you will

continue to receive standard of care treatment from you physician regardless of the group you are assigned to. However, your participation will advance scientific knowledge by helping us evaluate these VR programs.

We hope the information learned from this research study will benefit other individuals with acute or semi-acute pain in the future by helping us to learn how we can reduce pain and improve functionality, while minimizing the use of opioids.

Potential benefits of sharing of data
There is no direct benefit to you from the storage and sharing of your data, but sharing may help researchers learn more about pain management or using VR to help manage other diseases, which may help you or others in the future.

5. WHY WOULD MY PARTICIPATION BE STOPPED?

Your participation in this study may be stopped at any time by the researcher or the sponsor without your consent for any reason, including:

- The study is stopped or suspended;
- Funding for the study is reduced, stopped or withdrawn;
- If it is in your best interest;
- You do not consent to continue in the study after being told of changes in the research that may affect you;
- You do not follow the study procedures.

You may choose (or you may be required) to withdraw from certain parts of the study, but invited to continue with other parts. For example, you might stop using the audiovisual experience, but continue to fill out the surveys. Separate written consent will be requested if your continued participation will involve procedures not described in this consent form.

6. ARE THERE ANY OTHER OPTIONS?

Your participation is voluntary so you have the right to decline to participate or to withdraw from this research study at any time without any penalty or loss of benefits to which you would be entitled outside of the study. Choosing not to participate will not affect the care you receive at Cedars-Sinai Health System.

7. WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We will do our best to make sure that the personal information collected as part of this study is kept private. However, we cannot guarantee total privacy. A copy of your research consent and authorization forms may be filed in your electronic medical record at CSMC. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other identifiable personal information will not be used. Organizations that may look at and/or copy your medical records for research oversight, quality assurance, and data analysis include: accrediting agencies, government and regulatory groups (such as Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), etc.), safety monitors, companies that sponsor the study, and authorized representatives of the sponsor.

Attached to this consent form is an "Authorization Form" that outlines with whom your information may be shared for the purposes of this research and under what circumstances.

We might share your information and/or research samples collected in this study with other researchers at Cedars-Sinai, other academic institutions, or third-party commercial entities for future research without additional informed consent from you. Information that identifies you will be removed and will not be shared with other researchers or anyone outside of Cedars-Sinai.

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.

Protections from Forced Disclosures (Subpoenas) – Certificates of Confidentiality

To further protect your private identifiable information, we have obtained a Certificate of Confidentiality (Certificate) from the federal government.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law such as child abuse and neglect, or harm to self or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document such as including research data in the medical record.

Data Storage and Sharing
Your study data will be stored securely at *Cedars-Sinai or at sites NIH selects for this study. Your data will be stored indefinitely. We will do our best to protect your personal information.* Your name and other personally-identifying information will not be kept with the data. Your data will either be stored without a code linking them to you or they will have a code that links to your identifying information. If your data has a code, the key to the code will be kept at Cedars- Sinai in a separate, secure area and will not be shared outside of Cedars-Sinai.

This study is part of the NIH HEAL Initiative focused on understanding and developing new treatments for addiction and pain. Research gives us the best information and progresses more quickly when data is available from many studies and many individuals, and when many researchers can work with the data and samples and analyze them in different ways. Therefore, your data will be used for this and other NIH HEAL Initiative studies. Your stored data will also be made widely available to other researchers. The shared data may be used indefinitely for research not related to this study or the HEAL Initiative, without asking you for additional consent.

If you withdraw from this research study before it is done, we will keep and continue to use data and samples that have already been collected.

8. WHAT IF I BECOME ILL OR INJURED BECAUSE OF TAKING PART IN THIS STUDY?

You will not be in danger of any illness or injury from this research study. However, should you believe that you are ill or have been injured as a result of your participation, please contact the study team at the phone number listed on page 1 of this consent form.

9. FINANCIAL CONSIDERATIONS

Costs of Participation
You and your insurance company will not be charged for your participation in this research study. The Sponsor will cover the cost of all items, drugs and services required by this study, including any procedures required by the study that may be standard of care.

Compensation for Participating
You will be eligible for up to $225 in Amazon gift card codes at the end of the study. You will be emailed surveys throughout the course of the study. Each email will have a link to a set of surveys:

- After completing 4 of the 5 sets of surveys (80%) in the 1st month, you will be sent a $25 Amazon gift code.
- After completing 3 of the 4 sets of surveys (75%) of the surveys in the 2nd month, you will be sent another $25 Amazon code.
- Once you complete 8 of the 10 sets of surveys (80%) in the 3rd month and return the equipment, you will be sent a $175 Amazon gift code.

The $175 Amazon code will not be released until the audiovisual headset and Fitbit device has been returned.

Financial Interest in the Research
The PI and institution have no potential financial conflict of interest with respect to this study.

10. WHAT IF I HAVE QUESTIONS OR PROBLEMS?

Please contact the investigator listed on the first page of this form for questions or concerns about the research.

If you have questions, problems, or concerns that you want to discuss with someone who is not associated with this study, or want to offer suggestions or feedback, please contact:

Cedars-Sinai Human Research Protection Program
(HRPP) Phone: (310) 423-3783
Email: ResearchConcerns@cshs.org

The Cedars-Sinai HRPP has been established to protect the rights and welfare of research participants. You may also contact the Cedars-Sinai HRPP if you want to offer input or obtain information regarding the study.

11. CONSENT PROVISIONS

If you sign this form below, it means that:

(1) You have taken the time to carefully read and understand the information presented in this informed consent form; you should discuss it with others, and if appropriate seek a second opinion to make an informed decision;
(2) The information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction;
(3) You have received and understand all of the information you desire regarding your participation in the research study;
(4) You have considered the potential risks, any anticipated benefits and alternatives (and their relative risks and benefits) of participation;
(5) You are voluntarily agreeing to participate in this research study;
(6) You understand that by consenting to participate in the research, you are not giving up any of your legal rights;
(7) You understand that you have the right to be informed of significant new findings related to this research study which may affect your willingness to continue participating in this study; and
(8) You have been provided with a copy of the "Experimental Subject's Bill of Rights", if applicable to this research study, and have been provided with an opportunity to ask questions regarding the Bill of Rights.

We will give you a copy of this signed and dated consent form and the Experimental Subject's Bill of Rights.

SIGNATURE PAGE

Consent Form for Research

SIGNATURE BY THE PARTICIPANT: *I hereby agree to participate in the research study described to me during the informed consent process and described in this informed consent form.* ***You will be given a signed copy of this form.***

Name of Participant (Print)	Signature	Date Signed

If the participant is aged 13 to 17 years old, a signature from the participant's parent or guardian is required. Please complete the following if applicable:

SIGNATURE BY THE PARTICIPANT'S PARENT OR GUARDIAN: *I hereby give permission for my child to participate in the research study described to me during the informed consent process and described in this informed consent form.*

Parent/Guardian Name (Print)	Signature	Date Signed

SIGNATURE BY THE INVESTIGATOR: *I attest that all the elements of informed consent described in this form have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.*

Name of Investigator (Print)	Signature	Date Signed

APPENDIX: EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

Procedures	Pre-screening	Screening Week Day -8 to -2	Enrollment Day -1 to 0	Day 1 (+ 6 days)	Day 7 (+ 6 days)	Day 15 (+ 6 days)	Day 21 (+ 6 days)	Day 30 (+6 days)	Day 45 (+ 6 days)	Day 60 (+ 6 days)	Day 75 (+ 6 days)	Day 90 (+ 6 days)
Prospective patient identified (DEEP 6 or provider registry)	X											
Confirm eligibility and Informed Consent via telephone and REDCap	X											
Online Pain Intensity Journal (7 days)		X										X
Screening Week Online Baseline Survey		X										
Randomization			X									
Participant receives study intervention kit			X									
Technical onboarding call				X								
Intervention: Participant uses VR therapy program and wears Fitbit Charge 4 watch				X	----------							X
Online survey: NIH HEAL Minimum Dataset		X										X
Immersive Tendency Questionnaire (ITQ)[32] and Motion Sickness Propensity Survey[33]		X										
Treatment expectation question		X										
Simulator Sickness Questionnaire (SSQ)[34] and Presence Survey				X								
Online survey: Primary outcome: PROMIS® Pain Interference		X			X	X	X	X	X	X	X	X
Discontinuation of Treatment Questionnaire					X	X	X	X	X	X	X	X
PROMIS® Physical Function[35], Anxiety[35], Depression[35], Sleep disturbance[35]; Pain intensity/interference with Enjoyment of life/interference with General activity (PEG)[36], PCS-6[37]		X				X		X	X	X	X	X
EMR data: Charlson Comorbidity Index[38], CURES and EMR: Prescription Data		X										X
Perceived study arm question, treatments in the last 90 days question												X
Online survey: PHQ-2, GAD-2, PGIC, TAPS (1/2)		X										X
Remote technical support				X	----------							X
End of study procedure question												x
Event Assessment: AE, SAE and UP review and reporting				X	X	X	X	X	X	X	X	X

ITQ: Immersive Tendency Questionnaire
PEG: Pain, Enjoyment, General Activity
PCS-SF: Pain Catastrophizing Scale-Short Form 6
PHQ-2: Patient Health Questionnaire-2
GAD-2: Generalized Anxiety Disorder 2-item
PGIC: Patient Global Impression of Change
TAPS: Tobacco, Alcohol, Prescription Medication, and Other Substance Use
AE: Adverse event
SAE: Serious adverse event
UP: Unanticipated Problem

CEDARS-SINAI MEDICAL CENTER

AUTHORIZATION FOR USE AND DISCLOSURE OF IDENTIFIABLE HEALTH INFORMATION FOR RESEARCH

1. USE AND DISCLOSURE OF HEALTH INFORMATION

If you agree to this Authorization, you give permission to the Sponsor, Principal Investigator, other investigators and their research team described in the Consent Form for Research ("Research Team") to use or disclose your identifiable health information ("private information") for the research study titled "Randomized-controlled trial of virtual reality for chronic low back pain to improve patient-reported outcomes and physical activity" which is described in the Consent Form for Research ("Consent Form") to which this Authorization is attached. In particular, you authorize the research team acting under the direction of the Principal Investigator to review your medical records and collect your private information from the following sources:

☐ Laboratory tests
☐ Pathology reports
☐ Imaging reports (e.g., x-rays or scans)
☐ Photographs or videos of your image
☒ Doctor/clinic records
☒ Hospital/medical records
☐ Mental health records
☐ Billing records
☒ Other tests or other types of medical information: survey responses, CURES database

2. WHO WILL HAVE ACCESS TO YOUR PRIVATE INFORMATION?

Your private information will be used by and/or shared with the Research Team.

In addition to the research team, if applicable, the following parties may receive your private information and inspect your records:

- The reviewing Institutional Review Boards and Cedars-Sinai offices with authority to oversee research compliance.
- U.S. government agencies, such as the Food and Drug Administration and the Department of Health and Human Services.
- Researchers at other organizations who are participating in this research study.
- The Study Sponsor, its business partners, and Cedars-Sinai's business partners for matters related to research study oversight, data analysis, use of research results in product development, and payment or reimbursement.

- Representatives from regulatory agencies in other countries may join in the review of your research records, including research-related medical reports and information, with the Sponsor and/or the FDA.

Cedars-Sinai is required by law to protect your private information. However, the recipients described above may re-disclose (or share) your information with other parties unless such sharing is prohibited by law.

3. WHEN WILL MY AUTHORIZATION EXPIRE?

By signing this document, you authorize the use and sharing of your private information until the end of the research study and any related optional sub-study you choose to participate in.

4. REVOKING AUTHORIZATION

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, the research team may still use or disclose private information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to the Principal Investigator of the research study by writing to the Office of Research Compliance and Quality Improvement, 6500 Wilshire Blvd., Suite 1800, Los Angeles, Calif. 90048 and/or emailing to ResearchConcerns@cshs.org.

5. NOTICE OF RIGHTS AND OTHER INFORMATION

You do not have to agree to this Authorization, but if you do not agree, you may not participate in the research study. The Research Team may not condition (withhold or refuse) treating you on whether you agree to this Authorization.

If you agree to this Authorization, please sign on the appropriate signature line below. You will receive a copy of this Authorization.

SIGNATURE PAGE

Authorization for Use and Disclosure of Identifiable Health Information (Research)

Authorization for Use and Disclosure of Identifiable Health Information (Research): *I hereby agree that my identifiable health information may be used and/or disclosed in accordance with this "Authorization for Use and Disclosure of Identifiable Health Information (Research)" form.*

_____

Name of Participant (Print) Signature Date Signed