PARTICIPANT INFORMATION AND CONSENT FORM

TITLE:	The Sonic Incytes Liver Incyte System, assessment of liver fibrosis and steatosis
PROTOCOL NO.:	SI-CLIN-01 WIRB® Protocol #20182643
SPONSOR:	Sonic Incytes
QUALIFIED INVESTIGATOR:	

SPONSOR CONTACTS: Sonic Incytes

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You are being invited to participate in this study because you have shown interest in volunteering your time for imaging.

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant. Two hundred subjects will take part in the study.

1. YOUR PARTICIPATION IS VOLUNTARY

Your participation is voluntary. You have the right to refuse to participate in this study. If you decide to participate, you may still choose to withdraw from the study at any time without any negative consequences to the medical care, education, or other services to which you are entitled or are presently receiving.

You should be aware that there is a difference for both you and your doctor between being a patient and being a research participant.

As a patient all medical procedures and treatments are carried out for your benefit only according to standard accepted practice. As a research participant you and your doctor also must take into account the Requirements for the research study. These may include procedures and treatments that are not part of standard practice or are not yet proven.

This consent form describes the diagnostic and treatment procedures that are being carried out for research purposes. Please review the consent document carefully when deciding whether or not you wish to be part of the research and sign this consent only if you accept being a research participant.

If you wish to participate in this study, you will be asked to sign this form.

Please take time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

2. WHAT SHOULD I KNOW ABOUT THIS RESEARCH?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

3. WHY IS THIS RESEARCH BEING DONE?

The mechanical properties of human tissue can change due to many different reasons. The liver can show a dramatic change when affected by viruses, genetics, alcoholism, or a fatty diet. For this reason, finding a low-risk way to evaluate tissue stiffness is useful. As the liver increases in stiffness, the structure of it changes becoming more fibrous, which is called fibrosis. If fibrosis continues to increase significantly, it can lead to cirrhosis, a disease which occurs when the liver becomes severely damaged. This can result in death or various cancers. If dramatic increases in liver stiffness from fibrosis can be caught at an early stage, treatment can be tailored for the patient and results can be monitored to reduce the damaging effects. Currently, the degree of damage is often assessed using biopsy, where a needle is inserted into the liver to remove a tissue sample. This process can be uncomfortable, painful, and can carry associated risks like bleeding and in rare cases mortality. This is why finding a non-invasive technique is important.

Elastography is a technique to estimate soft tissue stiffness. A vibrating mechanism is applied externally to the skin while images are taken. Various elastography methods have been developed and applied to the liver. Transient elastography, FibroScan (Echosens, Paris), is the most common type of elastography currently applied to the liver. It uses ultrasound technology. It is applied between two lower ribs on the right side of the body. It has become standard of care in some clinics worldwide as an affordable device that is diagnostically good. Although it is pain-free, quick, and convenient, it is only able to collect a very small sample from the right lobe of the liver so cannot capture any regions that may have differing stiffness values and may misrepresent the state of the whole organ. As well, stiffness values obtained from FibroScan readings have not been able to correlate with Magnetic Resonance Elastography values in any direct comparison in the literature, and they result in less reliable results for earlier stages of fibrosis.

Another method of ultrasound elastography is shear wave elastography currently commercially available on some ultrasound machines, such as the Philips EPIQ machines. This technique using the acoustic power of the ultrasound probe to create a tiny push on the liver tissue. The resulting wave is then tracked using ultrasound imaging techniques. This method is used more often used in radiology imaging clinics and performed during routine abdominal ultrasound procedures.

Magnetic Resonance Elastography (MRE) is another type of elastography applied to the liver. It is accurate at estimating the extent of fibrosis development and is used in some private clinics, primarily in the United States. It allows greater flexibility in the location and frequencies applied. It shows consistent results and is often effective in patients with higher BMIs. The high costs associated with MRI scans restrict its usefulness in many areas affected by liver disease. The MRE procedure is very similar to a standard MRI procedure, except for the addition of a vibration device applied to the chest, and up to 20 minutes of additional time. It is non-invasive and does not cause any pain.

Our method, Vibro-elastography (VE) is an ultrasound method that will produce two and three-dimensional images, allowing for full visualization of the liver. It is an adjustable technique that can apply multiple frequencies and can display the wave propagation in the tissues while the scan is taking place. It is affordable and feasible in widespread clinical settings due to the simple hardware needs of an ultrasound device. The Vibro-elastography scan is very similar to a standard ultrasound examination with the addition of a vibrational applied device to the abdomen. It is non-invasive and does not cause any pain.

4. WHAT IS THE PURPOSE OF THE STUDY?

The main purpose of this study is to compare the effectiveness of various non-invasive elastography techniques at determining liver stiffness measures in human subjects. Specifically, FibroScan, Shear wave elastography (SWE), our approach, Vibroelastography (VE), and optionally Magnetic Resonance Elastography (MRE), will be included. These techniques are used to measure mechanical properties of soft tissue. The MRE studies will be optional and compared with the FibroScan or SWE and VE results. As part of a usability study, several trained users may scan you with the VE approach.

5. HOW LONG WILL I BE IN THIS RESEARCH?

We expect that your taking part in this research will last 90 minutes, including the screening discussion and ultrasound scans. There will be no follow-up to this study. As part of a user study, you may be scanned with the VE system by several trained users.
The optional MRE study will take approximately 60 minutes and can either be performed on the same day or within a 2 week window of the ultrasound based scans.

6. WHAT HAPPENS TO ME IF I AGREE TO TAKE PART IN THIS RESEARCH?

Both volunteers with no history of liver disease and those with diagnoses chronic liver disease will participate in this study. You will be assigned to the study arm that correlates to your medical history.

	Screening	Study Visits	
		Visit 1	Visit 2[5]
Procedure	**(-4 to 1 weeks)**	**(Day 1, Week 1)**	**(Day 5 ± 4, Week 1)**
Informed consent form	X		
Eligibility criteria	X	X	
Demographics[1]	X		
Medical and social history	X		
Physical Exam[2]	X		
Pregnancy Test[3]	X		
FibroScan/SWE measurement		X	
Liver Incyte measurement[4]		X	
Liver Incyte session questionnaire		X	
MRE[5]			X
Concomitant medication		X	X

	Screening	Study Visits	
		Visit 1	Visit 2[5]
Procedure	**(-4 to 1 weeks)**	**(Day 1, Week 1)**	**(Day 5 ± 4, Week 1)**
AE collection		X	X

[1] DOB, gender, height and weight
[2] For Cohort 2 participants
[3]For Women of childbearing potential
[4]Participants at VCID and Beth Israel sites will be evaluated with Model B only. Participants at LAIR Centre site will be evaluated using Model B followed by Model A
[5]Optional procedure for participants who consent

As part of the screening process, you will be asked several questions about your medical history. If needed, you may be asked to take a pregnancy test.

Volunteers who have agreed to participate in the study will have their liver scanned using the FibroScan/SWE, and VE techniques. You will be asked to fast (not eat) for 3-4 hours before your scheduled scan time.

FibroScan or SWE takes less than 15 minutes. It involves a short ultrasonic scan using a simple transducer. The transducer creates a short impulse, transmitted through the ribs into the liver. You will be asked to lie on your back and breathe shallowly during the exam. Ten valid measurements will be taken during the exam. The entire procedure is painless.

The VE scan will take up to 30 minutes. You will be lying on your back for the entire scan. The sonographer will acquire both regular ultrasound and VE images of your liver. A voice coil, or speaker, will be placed on a board (2 feet by 5 inches, 0.5 inches thick) between your back and the bed and will apply low-amplitude vibrations at various frequencies between 40 and 70 Hz. It feels much like a massage chair. Six VE scans wills will be taken during the exam. While the scans are taken, you will be asked to hold your breath for approximately 10 to 14 seconds.

VE is investigational, which means that it is not approved by Health Canada or the U.S. Food and Drug Administration (FDA). The device is not commercially available, so will not be accessible after the study is completed.

The scheduling of the FibroScan, VE and MRE scans is dependent on availability at the scanning facilities. They will take place during business hours or soon before or after business hours during the week.

All participants in this study will undergo the same procedures. This will be the only time you will be asked to participate in this study. There will not be any follow-ups or extensions of this study. The investigational device will not yet be readily available at the end of the study.

The study will finish at the end of the first visit. There is no planned future follow-up as part of this study.

We will answer any questions about this process to ensure that you are fully informed.

7. WHAT ARE MY RESPONSIBILITIES?

- Participants are expected to attend the appointments they have set up and remember to fast for at least 3-4 hours before hand.
- Participants are expected to report any side effects to your physician, otherwise go about your regular routine.

8. COULD BEING IN THIS RESEARCH HURT ME?

The only difference of this study relative to the standard treatment is the application of a mild vibration to the skin during a portion of the ultrasound exam. Given the mild vibration, there is no potential risk to you from participating in this study. The only side effect associated with Vibro-elastography is a slight chance of discomfort, and there is no risk associated with FibroScan or SWE.

In addition to these risks, taking part in this research may harm you in unknown ways.

9. WHAT ARE THE POTENTIAL BENEFITS OF PARTICIPATING?

You will not directly benefit from participating in this study. We hope that the information learned from this study can be used in the future to benefit other people.

10. WHAT WILL THE STUDY COST ME?

All research-related medical care and treatment and any related tests that you will receive during your participation in this study will be provided at no cost to you.

11. WILL I BE PAID FOR TAKING PART IN THIS RESEARCH?

For taking part in this research, you may be paid up to a total of $ 30. Your compensation will be broken down as follows:

- You will be given $30 at the end of the ultrasound scan visit
- In the event that you decide to withdrawal from the study before the scanning has begun, you will not receive payment.

The results from this study may lead to new commercial products or tests. If this happens you will not receive any compensation.

12. ARE THERE ANY DISCLOSURES?

Dr. Edward Tam is a member of the Clinical Advisory Board for the sponsor. Please feel free to ask any further questions you might have about this matter.

13. WHAT ARE THE ALTERNATIVES TO THE STUDY TREATMENT?

This research is not designed to diagnose, treat or prevent any disease. Your alternative is to not take part in the research.

14. WHAT IF NEW INFORMATION BECOMES AVAILABLE THAT MAY AFFECT MY DECISION TO PARTICIPATE?

You will be informed if any information becomes available that could affect your decision to remain in the study. If there are unanticipated findings you will be referred to your physician.

15. WHAT HAPPENS IF I DECIDE TO WITHDRAW MY CONSENT TO PARTICIPATE?

You may withdraw from this study at any time without giving reasons. If you decide to enter the study and to withdraw at any time in the future, there will be no penalty or loss of benefits to which you are otherwise entitled.

16. HOW WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Your confidentiality will be respected.

You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that

contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor
- People who work with the research sponsor
- Government agencies, such as Health Canada and the U.S. Food and Drug Administration
- The Research Ethics Board (REB) or Western Institutional Review Board (WIRB) that reviewed this research

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

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.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected. You also have the legal right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor. The information collected from you will be kept for 25 years.

The data gathered from this study, with information identifying you removed, will be used to compare liver stiffness results in healthy volunteers, as well as to improve our technology. The information will be shared *with trial sponsors*, governmental regulatory agencies that oversee such research, WIRB, the investigators who have conducted this trial and other doctors and researchers through publication of the results of this study.

If you decide to be in this study, the study doctor and study staff will collect information about you. This may include your name or initials, date of birth, gender, ethnic origin, medical history and health-related information such as results imaging, physical examinations, and medical records.

There is no expiration for your permission. You may take away your permission to collect, use and share information about you at any time by providing reasonable notice to the study doctor. If you do this, you will not be able to stay in this study. No new information about you will be gathered after that date. However, the information about you that has already been gathered may still be used and given to others as described in this

17. WHAT IF I AM INJURED BECAUSE OF TAKING PART IN THIS RESEARCH?

If you are injured or get sick because of being in this research, call the study doctor immediately. The study doctor will provide emergency medical treatment. You, your Provincial Health Plan, or your private insurance may be billed for this treatment. The sponsor will pay any charges that are not covered by your private insurance policy or the government, provided the injury was not due to your underlying illness or condition and was not caused by you or some other third party. No other payment is routinely available from the study doctor or sponsor.

You have not waived any of your rights to legal recourse, including if you are harmed as a result of the research, by participating in the research.

18. CAN I BE REMOVED FROM THIS RESEARCH WITHOUT MY APPROVAL?

The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- It is in your best interest
- You have a side effect that requires stopping the research
- You need a treatment not allowed in this research
- You become pregnant
- The research is canceled by Health Canada or the FDA, WIRB or the sponsor
- You are unable to keep your scheduled appointments

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

19. WHO DO I CONTACT IF I HAVE ANY QUESTIONS OR CONCERNS ABOUT MY RIGHT AS A PARTICIPANT?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by WIRB. WIRB is a group of people who perform independent review of research studies. You may talk to them at (800) 562-4789, help@wirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

20. AFTER THE STUDY IS FINISHED

Once the study is completed, we will be analyzing the data, and results should be published in the following year. Participant data may be used in future studies, while maintaining confidentiality. If you wish, you can contact Sonic Incytes (info@sonicincytes.com) to request information about progress or results.

21. SIGNATURES

The Sonic Incytes Liver Incyte System, assessment of liver fibrosis and steatosis

Participant Consent

I understand that participation in this study is entirely voluntary. I may choose not to participate or I may withdraw from the study at any time. I understand that I may ask questions about this study in the future. I will receive a signed copy of this consent form including all attachments, for my own records.

My signature on this consent form means:

- *I have read and understood the subject information and consent form.*
- *I have had sufficient time to consider the information provided and to ask for advice if necessary.*
- *I have had been able to ask questions and have had satisfactory responses to my questions.*
- *I understand that my participation in this study is voluntary*
- *I understand that I am completely free to refuse to participate or to withdraw from this study at any time without changing in any way the quality of care that I receive.*
- *I understand that I am not waiving any of my legal rights as a result of signing this consent form.*
- *I understand that there is no guarantee that this study will provide any benefit to me.*
- *I have read this form and I freely consent to participate in this study.*
- *I have been told that I will receive a dated and signed copy of this form.*

Signature of the Subject	Printed name	Date

Signature of Person Obtaining Consent	Printed name	Study Role	Date