INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**NeuroIntact, Inc. / "Feasibility Study for VCool™ Intranasal Cooling System in Healthy Volunteers"**
Protocol Number:	**00080424**
Principal Investigator: (Study Doctor)	**Neeraj Badjatia, MD**
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KEY INFORMATION
You are invited to take part in a research study. This research study is studying the VCool™ Intranasal Cooling System as a possible treatment for body temperature reduction when cooling is medically needed. NeuroIntact, Inc., a medical device manufacturer, is sponsoring this research study.

The purpose of this study is to evaluate the performance of the VCool Intranasal Cooling System in lowering body temperature from approximately 98°F to about 96°F within 2 hours and maintaining the temperature for an additional hour. During screening you will be asked about your medical history and demographics such as age, sex race, and ethnicity. Your nasal passage will also be assessed prior to study participation to ensure you do not have a deviated septum. During the study, your height, weight, and temperature will be measured. You will also be observed for shivering and headache.

Although there are no benefits to you directly for participation in the study, the information gathered may aid future patients that require body temperature cooling. The possible side effects you may experience while participating in the study include nosebleed, shivering, cold induced-headache, irritation of your nose, or a stuffy nose.

A small plastic tube (nasal cannula) will be placed in the opening to your nose and cool air will be delivered. Temperature will be measured by an esophageal (related to the esophagus, the tube that connects your mouth to your stomach) probe which will be inserted through the nostril and down into the esophagus.

Your participation in the study will last for approximately 4 hours.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form.

BACKGROUND AND PURPOSE

You are being asked to participate in this research study because you are a healthy adult between the age of 18 and 55. The sponsor of this study is a medical device company, NeuroIntact, that has developed a device designed to reduce the body temperature of patients when medically required. The VCool™ System lowers the body temperature by delivering cool air through the nose. The VCool System has been studied in animals where it was shown to be effective in reducing temperature and did not cause any side effects.

The cooling process is referred to as Targeted Temperature Management (TTM) and there are several devices on the market that provide TTM. NeuroIntact is conducting this study on healthy volunteers to determine if the VCool device can reduce core body temperature without causing side effects. The VCool System provides cooled air delivered at high flow through a nasal cannula. A nasal cannula is typically used to provide supplemental oxygen to patients who need it. It consists of a thin, flexible tube that splits into two prongs that rest just inside the nostrils. The cannula is attached to an air delivery tube which is attached to the VCool device. The VCool device cools medical air and delivers the air via the nasal cannula to cool the nasal passages with a goal to lower the body temperature.

The study will utilize the VCool System to reduce your temperature from your starting temperature to about 96°F.

The investigational device being studied, the VCool System, provides a new approach to TTM. Current standard of care includes surface cooling where liquid or air is pumped through pads that are wrapped around the patient's body and intravascular cooling where a catheter is inserted into a large vein and cold fluids are circulated through the catheter directly cooling the blood. Both methods can produce shivering and intravascular cooling is invasive. Surface cooling is difficult to set-up and can irritate the skin.

VCool is attempting to overcome these disadvantages and provide an approach that is not invasive, easy to set-up and minimizes shivering.

The purpose of this research study is to:

- Determine if the VCool System can reduce your temperature to about 96°F within 2 hours.
- Determine if the VCool System can maintain the cooled temperature for 1 hour.
- Determine if the VCool System causes shivering or any other side effect.

This is a research study to test a new investigational device. An investigational device is one that is not approved by the United States Food and Drug Administration (FDA). This is the first time that the study device has been used on people.

About 10 subjects will participate in this study.

WHAT WILL HAPPEN DURING THE STUDY?
Your participation in this study will last approximately 4 hours and will include 1 visit to the study center.

Screening:
Before any study-related tests and procedures are performed, you will be asked to read and sign this consent document. You will be given a copy of the Informed Consent Form (ICF) to take with you. The following screening activities and procedures will then be performed to determine if you qualify to take part in this study:

- You will be asked questions about your medical history.
- You will be asked if you are taking any medications that could affect your temperature.
- Your temperature will be taken using an esophageal probe.
    - An esophageal probe is a small, flexible tube that is gently placed through your nose and down into your esophagus (the tube that connects your mouth to your stomach). This probe helps measure your body temperature from inside your body. It is similar to taking your temperature with a thermometer, but it checks from the inside, which gives a more accurate reading.

Study Treatment:
This is an open-label study. This means that you, the study doctor, the study staff, and the Sponsor will know the study treatment you are given. All 10 subjects will receive the same study treatment.

- You will be asked your age, sex, race, ethnicity, height and weight.
- A temperature probe will be placed on your forehead and your ear at the beginning and end of the study, and your arm pit continuously throughout the study.
- You will undergo magnetic resonance imaging (MRI) as part of your participation in this study.
- Your temperature will be recorded every 2 minutes.
- You will be observed for shivering, headache, and any other side effects throughout the study.
- You will lie down on your back in an inclined position and the nasal cannula will be placed in your nose. Cool air will be delivered through the cannula.
- The VCool System will be used for up to 2 hours until your body temperature reaches 95.9°F (35.5°C).
- Once your body temperature reaches 95.9°F (35.5°C), you will use the study system for another hour to determine if this temperature can be maintained.

- After the hour of maintenance cooling, the cannula will be taken off.
- You will be monitored until your temperature returns to approximately the starting temperature. The esophageal temperature probe will then be removed.
- The study is complete.

The steps below detail how the esophageal probe will be inserted into your esophagus. One of the study doctors will:

- Wash their hands and put on surgical gloves.
- Examine your nasal passages for any abnormalities.
- Have you sit in an upright position and measure the desired length of the esophageal probe to be inserted.
- Check the integrity of the probe for any signs of damage or malfunction.
- Lubricate the esophageal probe with a water-based lubricant to reduce friction and insert it into your nostril. The probe will then be gently guided into your nostril and then into your esophagus with steady, gentle pressure. Once the probe is inserted to the correct depth, the study doctor will check to make sure that you are comfortable and not experiencing coughing, gagging, or breathing difficulties.
- Secure the probe in place with medical tape.
- Regularly check on your comfort throughout the study.

If your body temperature does not reach 95.9°F (35.5°C) within 2 hours or if you develop a nosebleed or severe headache, your participation in the study will be ended.

<u>After Study Treatment</u>:
There is no planned after-study treatment.

EXPECTATIONS
If you participate in this study, you will be expected to:

- Receive cooled air via the VCool device for up to 3 hours.
- Have your temperature monitored every 2 minutes for the duration of the study treatment.
- Every 10 minutes, you will be observed for any shivering or headaches.

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS
The following temporary side effects or discomforts may occur:

Cooling Risks:

- <u>Nosebleed:</u> the cool, dry air may cause a nosebleed. VCool treatment will be stopped if this happens.
- <u>Shivering:</u> the cooling may cause your body to shiver which is the body's defense mechanism to cold.
- <u>Nasal irritation and/or congestion:</u> you may experience a stuffy or runny nose from the flow of cooled air.

- Skin irritation: you may experience skin irritation where the cannula is inserted in your nose.
- Cold-induced headache: you may experience a headache from the cooled air. If this happens, the study will be stopped.
- Overcooling: your temperature could go too low. If this happens the flow will be reduced or the study treatment will be stopped.

MRI Risks:

- Loud noise: the MRI machine produces loud knocking sounds; you will be given ear protection.
- Feeling confined: you may feel anxious or claustrophobic inside the MRI scanner.
- Metal-related injury: metal objects inside the body may move or heat; you will be screened for implants or metal before the scan.
- Discomfort from lying still: you may experience stiffness or discomfort from remaining still during the scan.

Tympanic (Ear) Temperature Probe Risks:

- Ear discomfort: insertion of the probe into the ear canal may cause mild discomfort or pressure.
- Ear canal irritation: the probe may cause temporary redness or irritation inside the ear.

Axillary (Underarm) Temperature Probe Risks:

- Skin irritation: adhesive or probe contact may cause mild skin irritation or redness.
- Mild discomfort: holding the probe in place under the arm may cause mild discomfort.

SpotOn (Forehead) Skin Temperature Probe Risks:

- Skin irritation: the adhesive sensor may cause redness or irritation on the forehead.
- Mild discomfort: you may feel slight pulling when the adhesive patch is removed.

UNFORESEEN RISKS

Since the study device is investigational, there may be other risks that are unknown.

ALTERNATIVES TO PARTICIPATION

This research study is for research purposes only. The only alternative is to not participate in this study.

NEW FINDINGS

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

BENEFIT

There is no direct benefit to you from your participation in the study. Information learned from the study may help other people in the future.

COMPENSATION FOR PARTICIPATION
You will be given a $200 Amazon Gift Card at the end of your participation in this research study.

If you have any questions regarding your compensation for participation, please contact the study staff.

CONFIDENTIALITY
Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

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.

To make sure that the health information collected in this study is accurate, it will need to be checked from time to time against your medical records. Some persons may need to see these records in order to monitor the research and verify the accuracy of the study data, including:

- A limited number of representatives from the study sponsoring drug/device company (namely its monitors and auditors),
- The research institutional review board – Advarra IRB (an independent ethics committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study subjects),
- Government regulatory authorities including the US Food and Drug Administration (FDA) and other foreign regulatory agencies.

Your study records including confidential information about you collected during the study will be kept at a secure location.

While every effort will be made to protect the privacy of your information, absolute confidentiality cannot be guaranteed. This does not limit the duty of the researchers and others to protect your privacy.

By signing this information and consent form, you consent to the collection, access, use and disclosure of your information as described above.

COMPENSATION FOR INJURY

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured then they will help you get the care you need.

If you are injured as a result of the study procedures done for the purpose of this study, the sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. By signing this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

COSTS

There will be no charge to you for your participation in this study. The study device study-related procedures, and study visit will be provided at no charge to you.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research subject;
- Eligibility to participate in the study;
- The study doctor's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

Please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, contact:

- By **mail**:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00091706.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

_____

Printed Name of the Person Conducting the Consent Discussion

_____ _____

Signature of the Person Conducting the Consent Discussion

Date

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

- Medical history.
- Demographics (age, sex, race, ethnicity)
- Information from your study visit, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of NeuroIntact
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Governmental agencies of other countries.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- A data safety monitoring board which oversees this study, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the VCool works and is safe.
- To compare the VCool to other devices.
- For other research activities related to the VCool.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____

Printed Name of Subject

_____ _____

Signature of Subject Date