Consent and Authorization Document

You are being asked to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask the research doctor or staff if there is anything that is not clear or if you would like more information. Take time to decide whether or not to volunteer to take part in this research study.

The purpose of the study is to evaluate the effect of supplementing vitamin D3 (cholecalciferol) in neurocritical care patients with vitamin D deficiency in order to evaluate clinical outcomes. The study is being conducted by the Drs. Michael Karsy and Sarah T. Menacho of the Department of Neurosurgery at the University of Utah. This is a multi-center study coordinated from the University of Utah.

A research trial usually involves comparing different treatments. In a trial, one group will get one treatment and another group will get a different treatment. In a "randomized trial" people are put in one group or the other by random chance. This means that a computer will decide by chance which group a person is in, not the doctors running the trial. In a blind trial you will not know which treatment group you are in. A placebo is a dummy treatment such as a pill, which looks like the pill that contains the study drug but is not. Placebos contain no drugs or active ingredients. Study participants are given placebos so that the effects of a drug can be compared against no drug. Use of placebos also prevents the participant and the doctor from knowing whether or not the subject is getting the drug.

This is a phase II/III trial done on a larger number of human subjects to see if a drug is safe, find out how the drug works and if it does what it is supposed to do.

BACKGROUND

The purpose of the study is to examine the effectiveness of vitamin D supplementation on patients with low vitamin D level in the Neurocritical Care Unit (NCCU). Neurocritical care providers face the constant challenge of improving patient outcomes, including shorter hospital stays, lower rates of neurological deficit, and improved lifespan, after admission to the critical care unit for unexpected diseases. Vitamin D is a low-cost medication with potential benefit in improving outcome in a variety of diseases including, asthma, acute respiratory distress syndrome, dementia and medical critical care environments. We previously published a observational study of vitamin D levels in the neurocritical care environment and found that low vitamin D levels predicted worsen length-of-stay, and in-hospital mortality. This was the first study evaluating vitamin D levels in a neurocritical unit. This study was limited in not being a randomized clinical trial and thus limiting the use of the data.

STUDY PROCEDURES

A research trial usually involves comparing different treatments. In a trial, one group will get one treatment and another group will get a different treatment. In a "randomized trial" people are put in one group or the other by random chance. This means that a computer will decide by chance which group a person is in, not the doctors running the trial. The trial is double blind, which means neither you

nor your doctor will know which treatment group you are in (although, if your doctor needs to find out for important medical reasons, he/she can do so).

You have been identified as a patient with low vitamin D levels (<20ng/mL) and eligible for this study. You will be randomly assigned (similar to flipping a coin) to one of two groups being compared in this study. You will either cholecalciferol/vitamin D3 supplementation (540,000 IU once orally or by feeding tube) or an oral sugar pill (placebo).

A placebo is a dummy treatment such as a pill which looks like the pill that contains the study drug but is not. Placebos contain no drugs or active ingredients. Study participants are given placebos so that the effects of a drug can be compared against no drug. Use of placebos also prevents the participant and the doctor from knowing whether or not the subject is getting the drug.

Regardless of what group you are assigned to, your clinical exam, clinical course and laboratory studies will be closely monitored. This will be used for the study and to ensure patient safety. Prior to discharge you will receive a quality-of-life survey, a standardized metric for evaluating the impact of a disease on your health. This will be repeated at your followup appointment, 3 months and 6 months.

RISKS

Rare adverse risks of vitamin D include hypercalcemia, or high calcium in the blood stream, impairment of kidney function, calcification of the soft tissues, osteoporosis, nausea, constipation, and anemia. Vitamin D is an over-the-counter medication and we prescribe it as a standard-of-care for patients in the Neurocritical care unit. Our observational study of 823 patients did not show any adverse effect for vitamin D supplementation. Nor has any record of adverse effect at the dosages used in this study been reported. Nevertheless, patients in this study will be closely monitored by the ICU and neurosurgery/neurology teams, and, in the event that an adverse effect associated with the study medication is seen, the patient will be promptly discontinued from the trial.

REPRODUCTIVE RISKS

There are no known risks of vitamin D supplementation in pregnant women and daily supplementation is recommended. However, patients that are pregnant will not be eligible for this trial because the doses used are higher than the recommended daily supplementation rate and the risks to the baby are unknown at this dose. Women who are at risk of pregnancy will be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. There will be no need for birth control for this research project. As the treatment is a single dose, it will not affect future risks to the embryo or fetus. For studies involving possible reproductive risks, please include a section that includes the following:

UNFORESEEABLE RISKS

In addition to the risks listed above, you may experience a previously unknown risk or side effect.

BENEFITS

We cannot promise any benefits to you from your being in the study. However, possible benefits may include a improved neurological outcome, shorter hospital stay and increased lifespan. We hope that this study will help you, however, this cannot be guaranteed. In addition we hope this study will help future patients admitted to the neurocritical care unit.

ALTERNATIVE PROCEDURES

You may choose not to participate in this study. If you do not want to take part in the study you will continue to be monitored for the effects of low vitamin D. Patients with very low vitamin D levels (<10 ng/mL) will received vitamin D supplementation based on the standard practice in the neurocritical care unit. You will not be contacted by the research team any further.

PERSON TO CONTACT

If you have questions, complaints or concerns about this study, or if you think you may have been injured from being in this study, you can contact Dr. Michael Karsy, principal investigator, or Dr. Sarah T. Menacho, study sponsor, through the hospital operator 801-581-2121. In the case of an emergency, call (801) 581-2121 and ask for the Neurosurgery resident on call.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

RESEARCH-RELATED INJURY

If you are injured from being in this study, medical care is available to you at the University of Utah, as it is to all sick or injured people. The University of Utah has not set aside any money to pay the costs for such care. The University will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), to the study sponsor or other third party (if applicable), to the extent those parties are responsible for paying for medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research.

The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See sections 63G -7-101 to -904 of the Utah Code.

VOLUNTARY PARTICIPATION

It is up to you to decide whether or not to take part in this study. If you decide to take part you are still free to withdraw at any time and without giving a reason. Refusal to participate or the decision to withdraw from this study will involve no penalty or loss of benefits to which you are otherwise entitled. If you don't take part, you can still receive all standard care that is available to you. This will not affect the relationship you have with your doctor or other staff, nor decrease the standard of care that you receive as a patient.

If you want to stop being in this study, please let the research doctor know. That way you can find out what should be done about your routine care outside of the study.

RIGHT OF INVESTIGATOR TO WITHDRAW PARTICIPANTS
The study doctor may stop your participation in this study at any time without your consent if they feel it is in your best interest.

COSTS AND COMPENSATION TO PARTICIPANTS
Procedures that are done only for the study, such as vitamin D level draws and vitamin D supplementation are standard-of-care treatments for patients admitted to the neurocritical care unit at the University Hospital. You will not be charged for the study drug or its dispensing.

You or your insurance company may be billed for any standard medical care given during this research study in the ordinary manner.

You will not be paid to participate in this study.

NEW INFORMATION
During this study, you will be told about anything new that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

NUMBER OF PARTICIPANTS
We expect to enroll 436 participants, namely 218 experimental and 218 control patients, at the University of Utah.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION
Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study.

This is the information we will use and include in our research records:

-Demographic and identifying information like name, medical record number, date of birth, gender, diagnosis, ethnicity/race, dates of admission and discharge

-Related medical information about you like past medical history, past surgical history, current and past medications or therapies, information from physical examinations, vital signs, and lab results.

-All tests and procedures that will be done in the study.

How we will protect and share your information:

- We will do everything we can to keep your information private but we cannot guarantee this. Study information will be kept in a secured manner and electronic records will be password protected. Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and health care operations of the hospital. We may also need to disclose information if required by law.

- All investigators on this trial have signed conflicts-of-interest disclosures and confidentiality agreements that are available on file with the IRB and FDA.

- 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.

- In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:
    - Members of the research team and the University of Utah Health Sciences Center*;*
    - The University of Utah Institutional Review Board (IRB), which reviews research involving people to make sure the study protects your rights;
    - The Food and Drug Administration reviews data from all clinical trials in the U.S. to ensure data quality and patient safety.

- If you do not want us to use information about your health, you should not be part of this research. If you choose not to participate, you can still receive health care services at University of Utah Health Sciences Center.

- If we share your identifying information with groups outside of the University of Utah Health Sciences Center, they may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.

What if I decide to Not Participate after I sign the Consent and Authorization Form?

You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

You have a right to information used to make decisions about your health care. However, your information from this study will not be available during the study; it will be available after the study is finished.

CONSENT

I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I will be given a signed copy of the consent and authorization form to keep.

I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.

_____
Participant's Name

_____ _____
Participant's Signature Date

_____
Name of Person Obtaining Authorization and Consent

_____ _____
Signature of Person Obtaining Authorization and Consent Date

WITNESS STATEMENT:

The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is illiterate
☐ The participant is visually impaired
☐ The participant is physically unable to sign the consent form. Please describe:
_____

☐ Other *(please specify)*: _____

I confirm that I was present as a witness for the consent process for this study. I confirm that the participant named above was read the information in the consent document and that the participant has agreed to take part in the research study.

_____
Name of Witness

_____ _____
Signature of Witness Date

If the participant is unable to give consent and authorization, consent and authorization is given by the authorized personal representative of the individual:

LEGALLY AUTHORIZED REPRESENTATIVE CONSENT STATEMENT:
I confirm that I have read this consent and authorization document. I have had the opportunity to ask questions and those questions have been answered to my satisfaction. I am willing and authorized to serve as a surrogate decision maker for

_____.
Participant's Name

I have been informed of my role and my obligation to protect the rights and welfare of the participant. I understand that my obligation as a surrogate decision maker is to try to determine what the participant would decide if the participant were able to make such decisions or, if the participant's wishes cannot be determined, what is in the participant's best interests. I will be given a signed copy of the consent and authorization form to keep.

_____
Name of Authorized Personal Representative

_____ _____
Signature of Authorized Personal Representative Date

Indicate the legal representative's authority to act for the individual:
☐ Spouse
☐ Individual with power of attorney
☐ Guardian appointed to make medical decisions for individuals who are incapacitated