

## INFORMED CONSENT DOCUMENT

**Project Title:** Nicotinamide riboside (NR) in Paclitaxel-induced Peripheral Neuropathy

**Principal Investigator:** Donna Hammond, PhD

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**Other Research Team Members:** Mark Karwal, MD; Sneha Phadke, DO; Mary Schall, RN

This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

### **WHAT IS THE PURPOSE OF THIS STUDY?**

This is a research study. We are inviting you to participate in this research study because you have stage 4 breast cancer, are being treated for your breast cancer with Paclitaxel, and are experiencing peripheral neuropathy. The symptoms of peripheral neuropathy include numbness or tingling, pricking sensations or muscle weakness, usually in the hands or feet. However, peripheral neuropathy can also affect other areas of your body.

The purpose of this research study is find out if nicotinamide riboside (NR), a nutritional supplement and type of vitamin B3, can prevent the progression of peripheral neuropathy in people with breast cancer being treated with Paclitaxel.

Nicotinamide riboside is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration as it is being used in this research study. Nicotinamide riboside is currently used to increase levels of NAD<sup>+</sup>, a substance in the blood which is important in converting blood glucose into energy. Increased NAD<sup>+</sup> levels may also play a part in delaying the effects of aging, obesity and disease.

### **HOW MANY PEOPLE WILL PARTICIPATE?**

A total of approximately 39 people will take part in this study conducted by investigators at the  
Consent Version 1; Protocol dated 10.26.16

University of Iowa and Wake Forest University.

### **HOW LONG WILL I BE IN THIS STUDY?**

If you agree to take part in this study, your involvement will last approximately 9 months. This includes up to 12 weeks of treatment with NR, with a weekly visit on each occasion you receive chemotherapy during treatment, then follow-up visits at the following time points:

- 7-14 days after the end of treatment
- 30-37 days after the end of treatment (may be done by telephone)
- 12-14 weeks after the end of treatment (may be done by clinic visit or telephone)
- 24-26 weeks after the end of treatment (may be done by clinic visit or telephone)

Each visit during treatment will last between 1-2 hours. Each follow-up visit will also last between 1-2 hours.

### **WHAT WILL HAPPEN DURING THIS STUDY?**

#### **Before you begin the study:**

If you choose to take part in this study, you will need to have the following procedures to find out if you can continue in the study. Most of these procedures are part of your regular cancer care and would be done even if you do not join the study.

- A complete physical examination, including assessment of vital signs (temperature, height, weight, heart rate, blood pressure, and respirations or breathing rate).
- Blood tests (approximately 3-4 teaspoons of blood will be drawn and studied for kidney function, liver function, white cells, red cells, and platelets).
- Pregnancy test for females of childbearing potential.
- Questionnaire 1 – one page which asks 11 brief questions about how you're feeling.
- Questionnaire 2 – one page which asks 7 brief questions about the type of your neuropathy

#### **During study treatment:**

You will take the study drug, NR, by mouth twice a day while you're receiving chemotherapy in this study. If the initial dose of NR is well-tolerated during the first week, the dose will be increased for all subsequent weeks.. You will take NR twice a day each day you are in the study. You will stop taking NR one week after your last infusion of Paclitaxel.

You will have 12 planned infusions of Paclitaxel as part of your regular cancer care. You will visit the hospital each week for your infusion of Paclitaxel. Once you've started taking the study drug, NR, the following tests and procedures will be done at each weekly visit:

- Complete physical exam (only on weeks 3, 6 and 9).
- Assessment of vital signs (temperature, weight, heart rate, blood pressure, and respirations or breathing rate).
- Blood tests (approximately 3-4 teaspoons of blood will be drawn and studied for kidney function, liver function, white cells, red cells, and platelets).

- Blood for research tests (approximately 3 teaspoons of blood will be drawn to check the level of Paclitaxel and NAD<sup>+</sup> in your blood.) If your chemotherapy drug levels get too high or too low from taking the study drug, you may be removed from this study.
- Questionnaire 1 – one page which asks 11 brief questions about how you're feeling.

We will ask you to complete questionnaire 1 each time you visit. This questionnaire will ask specific questions about how you've been feeling. We will ask you to fill out a form each day about the amount and types of dairy products you eat (a dairy product diary). We will also ask you to fill out a form to record when you took NR (a drug diary). We will provide you forms to keep track of the study drug that you take each day, and how much dairy you eat each day. We will ask you to bring the dairy product diary, the drug diary, and any remaining pills with you to each weekly visit. Once a month, you will be asked to fill out questionnaire 2 about the type of neuropathy you are experiencing.

**After study treatment:**

After you've finished taking NR, you will have a follow-up visit 7-14 days after your last dose. The following tests and procedures will be done:

- A complete physical examination, including assessment of vital signs (temperature, weight, heart rate, blood pressure, and respirations or breathing rate).
- Blood tests (approximately 3-4 teaspoons of blood will be drawn and studied for kidney function, liver function, white cells, red cells, and platelets).
- Questionnaire – one page which asks 11 brief questions about how you're feeling.

You will also have follow-up scheduled at the time points listed below. These may be done by a telephone call to see how you're doing.

- 30-37 days after the end of treatment.
- 12-14 weeks after the end of treatment.
- 24-26 weeks after the end of treatment.

**Follow-up Contact Plan:**

If we aren't able to successfully contact you by telephone, we may send you a certified letter to your last known address, requesting a return receipt.

**WHAT ARE THE RISKS OF THIS STUDY?**

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

There is a risk that NR will increase or decrease the level of paclitaxel in the blood. An increase in levels of paclitaxel could result in increased peripheral neuropathy and decreased levels of white blood cells and red blood cells. A decrease in levels of paclitaxel could decrease the effectiveness of this chemotherapy. Your levels will be monitored weekly.

There is also a very small risk that NR will cause flushing. You may also experience headache, nausea, vomiting, fatigue, dizziness, or loose stool.

You will be required to take appropriate precautions to avoid pregnancy from screening through follow-up because the effects of NR on the fetus are unknown. Males must agree to take appropriate precautions to avoid fathering a child from screening through follow-up. Any of the following methods have been determined to be more than 99% effective (<1% failure rate per year when used consistently and correctly)

- Complete abstinence from sexual intercourse
- Double barrier methods:
  - Condom with spermicide in conjunction with use of an intrauterine device
  - Condom with spermicide in conjunction with use of a diaphragm
- Surgical sterilization (bilateral removal of ovaries with or without hysterectomy, tubal ligation or vasectomy) at least 6 weeks prior to starting the study.
- Non-hormonal intrauterine device (IUD)

### **WHAT ARE THE BENEFITS OF THIS STUDY?**

We don't know if you will benefit from being in this study. We hope that, in the future, other people might benefit from this study because of the information gained. The information gained might help to develop better treatments for peripheral neuropathy that occurs during chemotherapy.

### **WHAT OTHER TREATMENT OPTIONS ARE THERE?**

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could choose to have no treatment for your peripheral neuropathy, or choose to take part in a different research study, if one is available.

### **WILL IT COST ME ANYTHING TO BE IN THIS STUDY?**

You will not have any additional costs for being in this research study. The study drug, nicotinamide riboside is being supplied by the maker of the drug, ChromaDex, Inc. The cost of blood draws that are done for research only will not be the responsibility of you or your insurance company.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

### **WILL I BE PAID FOR PARTICIPATING?**

You will not be paid for being in this research study.

## **WHO IS FUNDING THIS STUDY?**

The National Institutes of Health (NIH) is funding this research study. This means that the University of Iowa is receiving payments from the NIH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from the NIH for conducting this study.

## **WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?**

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

## **WHAT ABOUT CONFIDENTIALITY?**

It is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- the U.S. Food and Drug Administration and the sponsor, the NIH
- ChromaDex, Inc, the maker of the study drug may also inspect any part of your medical record for the purposes of auditing the conduct of the study.
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will conduct research interventions in private rooms, limit data collection, and store research documents in locked offices and on password-protected computers. Study data will not list your name, but will identify you by a code number. **A Record of Informed Consent document will be placed in your UIHC medical record to show that you have participated in this research study.**

If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). This Certificate means that the researchers cannot be forced (for example by court subpoena) to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding. However, a Certificate of Confidentiality does not prohibit the researcher from disclosing information about you or your involvement in this research that you have agreed to disclose or make available. For example, if you **if**

**applicable: or your legally authorized representative]** request in writing that information about you or your participation in the research be released to an insurance company, the researcher may not use the Certificate of Confidentiality to withhold this information. This means that you and your family should actively protect your own privacy. Finally, the researcher is not prevented from taking steps, including reporting to appropriate authorities, to prevent serious harm to yourself or others. You may receive a copy of the Certificate of Confidentiality upon request.

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.

### **WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?**

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires your health care provider to obtain your permission for the research team to access or create “protected health information” about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once your health care provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under “Confidentiality.”

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff, the NIH, and ChromaDex, Inc., the maker of the study drug.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes your health care provider to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to:

**Donna Hammond, PhD  
University of Iowa Hospitals and Clinics  
200 Hawkins Drive, 3000 ML  
Iowa City, IA 52242**

However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will

receive a copy of this signed document.

### **IS BEING IN THIS STUDY VOLUNTARY?**

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

### **What if I Decide to Drop Out of the Study?**

If you decide to leave the study early, we will ask you to talk to the study doctor as soon as possible so that you can stop safely. If you leave the study before the final planned study visit, the study doctor may ask you to complete the final visits.

### **Will I Receive New Information About the Study while Participating?**

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

### **Can Someone Else End my Participation in this Study?**

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because in our judgment it would not be safe for you to continue, because your condition has become worse, because you are or became pregnant, or because funding for the research study has ended. This might also happen if your Paclitaxel levels go too high or too low.

### **WHAT IF I HAVE QUESTIONS?**

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Donna Hammond, PhD at 319-335-9595. If you experience a research-related injury, please contact: Donna Hammond, PhD at 319-335-9595.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail [irb@uiowa.edu](mailto:irb@uiowa.edu). General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, <http://hso.research.uiowa.edu/>. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

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This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): \_\_\_\_\_

**Do not sign this form if today's date is on or after EXPIRATION DATE: 09/17/19.**

\_\_\_\_\_  
(Signature of Subject)

\_\_\_\_\_  
(Date)

**Statement of Person Who Obtained Consent**

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

\_\_\_\_\_  
(Signature of Person who Obtained Consent)

\_\_\_\_\_  
(Date)