**Informed Consent Cover Page for FDAAA consent posting:**

| | |
|---|---|
| **Official Title:** | Pilot Study to Evaluate the Effect of Nicotinamide Riboside on Immune Activation in Psoriasis |
| **NCT number:** | NCT04271735 |
| **Document Type:** | Informed Consent Form |
| **Document Date:** | 4/16/2021 |

**PRINCIPAL INVESTIGATOR:** Michael N. Sack, MD, Ph.D.

**STUDY TITLE: Pilot Study to Evaluate the Effect of Nicotinamide Riboside on Immune Activation in Psoriasis**

**STUDY SITE: NIH CC, NHLBI**

Cohort: *Standard*

Consent Version: 04/16/2021

## WHO DO YOU CONTACT ABOUT THIS STUDY?

*Michael Sack, M.D. 301-402-9259, sackm@nhlbi.nih.gov*

*Becky Huffstutler CRNP 301-594-1281, rebecca.huffstutler@nih.gov*

## KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

We are interested in the effect of a dietary supplement called nicotinamide riboside (NR) versus a placebo pill on patients who have diseases that cause chronic inflammation in the body. Psoriasis is one of those diseases and we want to test whether NR can decrease some markers of inflammation in the blood and skin of patients with mild to moderate psoriasis who are not using any other psoriasis treatments. We have shown in other research studies that NR can improve immune system function in healthy patients and now we want to see if it has the same effect on patients with psoriasis.

Nicotinamide Riboside is a form of vitamin B3 that can be purchased off the internet or at health food stores. This supplement has been used in other research studies at much higher doses in healthy patients and patients with other diseases. We have not had any safety problems so far with this supplement. This form of Vitamin B3 is found in small quantities in foods like milk, and beer.

Your study participation on this study will last approximately 5 to 23 weeks. During the initial visit which we will call your screening visit, you will speak with one or more members of the study team about the nature of this study, your medical history and drugs that you are taking (prescription and non-prescription). Once you have signed the consent, we will perform a further work-up that may involve the following: review of medical history, physical examination, we may measure your vital signs (blood pressure, heart rate, and temperature), your body mass index, examine your skin, and take some blood or urine for tests. After we have completed these evaluations, we will decide if you qualify for the study. After your screening visit, which may

take up to 4 months, we will perform visit 1 which may involve a physical examination, vital signs (blood pressure, heart rate and temperature), blood and urine sample for tests, an optional skin biopsy and dispense the study capsules to you. Neither the study team or you will know whether you are getting the supplement or the placebo during your participation in the study. We will provide instructions on how to take the capsules and what to do if a dose is missed. You will take the study capsules for 4 weeks and we will ask you to return to the NIH for your visit 2 at this time. During this visit, we may perform the following: a physical examination and ask about any side effects you may have occurred while you were taking the study medication, vital signs (blood pressure, heart rate and temperature), blood and urine sample for tests, optional skin biopsy and ask you to return the study medication. We also may call you on the phone in between these visits to ensure you are taking the study capsules correctly. This visit would be your final study visit. We ask that if you develop any symptoms or illnesses in the 7 days following completion of the study capsules, you notify the study team. We may ask you to come in for an additional, unscheduled study visit in this situation evaluate your symptoms if we feel this is necessary.

The general risks associated with this study pertain to the following: blood draw, the study medication, (NR or placebo) and the skin biopsy. These are described further in this consent.

You will be offered compensation for your time and inconvenience for participation in this research study.

There is no immediate benefit to you by taking part in this study but it could help others in the future.

You can discuss with your doctor to see if there are other alternative studies that you can participate in if you decide not to participate in this one.

The remaining document will now describe more about the research study. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

## IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

## WHY IS THIS STUDY BEING DONE?

This is a research study. The purpose of this research study is to test if the dietary supplement Nicotinamide Riboside (NR), which is a Vitamin B3 supplement, can improve immune system function in the blood and skin of patients with mild to moderate psoriasis. This information might

lead to more treatment options to treat the inflamed skin and blood vessels in patients with psoriasis.

We are asking you to join this research study because you have mild to moderate psoriasis and are not currently being treated with biological therapy.

**WHAT WILL HAPPEN DURING THE STUDY?**

If you decide to take part in this study, you will be asked to come to the NIH Clinical Center for 2-3 outpatient visits which are described below.

Screening visit: At the first visit, you will speak with one or more members of the study team about the nature of this study, your medical history and drugs that you are taking (prescription and non-prescription). We will tell you about the study, answer your questions and determine if you are eligible for this study. At this point you will sign a consent form. You may undergo a brief history and physical examination, we may measure your vital signs (blood pressure, heart rate, and temperature), your body mass index, and take some blood or urine for tests. If you are female under the age of 55, and potentially eligible for this study, you will have a pregnancy test (a positive pregnancy test will require that you be excluded from the study). After we have completed these evaluations, we will decide if you qualify for the study. There is a chance that you may not qualify to continue in the study if we find problems that would exclude your participation.

Visit 1: Visit 1 may be combined with the Screening visit in which case all the procedures listed above under screening visit will be performed. If you qualify for the study after screening is complete, the following procedures may be done during Visit 1:

Research Blood Draw:

We will take blood from a vein in your arm using a needle during your outpatient visits. The amount of blood drawn is considered a safe amount for adults per NIH guidelines, which will not exceed 10.5 mL/kg or 550 mL (approximately 2 cups), whichever is smaller, over an eight-week period. The blood will be used for research and clinical testing.

Skin Biopsies:

If you agree to it and have psoriasis lesions in places we can safely biopsy, we will collect two skin biopsies each at baseline and visit 2 for a total of 4 biopsies. One biopsy will be from a psoriasis lesion and the other will be from an unaffected area of the skin. We will clean your skin in both areas and then inject a local numbing medicine. This may sting a little. After we have numbed your skin in both areas, we will use a round cutting device to remove a small piece of skin from both areas. The biopsies are small enough that they do not require sutures. We will put a clean dressing on the areas and ask you to keep them dry for 48 hours at which point you can shower. You will need to clean the biopsy sites with soap and water every day after the first 48 hours and put a new bandage on to minimize the chance of infection. The skin biopsy will be used for research only.

If Visit 1 is a separate visit from the screening visit, then we may repeat the blood baseline blood tests if it has been greater than four weeks from the screening visit, reconfirm your eligibility (including pregnancy test for females) and perform a brief history and physical exam.

Dispense Study Supplement or placebo:

We will dispense the study supplement, Nicotinamide Riboside or a matching placebo. You will start taking the capsules the following morning. You will take 500mg (two capsules) twice daily for a total of 4 weeks. Capsules must be taken whole and may be taken with or without food. If you miss the morning dose you can take it at a later time. However, you should wait 6 hours after the first dose of the day before you take your evening dose. If you miss the evening dose, do not take an extra dose to catch up. If you miss too many doses you will be withdrawn from the study. We may contact you by telephone or secure email between your first and second visit to see how you are doing on the supplement and make sure you are remembering to take the capsules. Neither the study team or you will know whether you are getting the supplement or the placebo during your participation in the study.

Visit 2: Your second visit will be scheduled approximately 4 weeks after your first visit. The visit will take place in an outpatient clinic or day hospital. After meeting with a member of the research team, you will have a repeat blood draw and skin biopsies (if obtained at Visit 1) as described above. We ask that you bring your capsule bottles to this visit (including any empty bottles). We will perform a capsule count and ask you about any missed doses of the study capsules. This would be your final study visit. We ask that if you develop any symptoms or illnesses in the 7 days following completion of the study pills, you notify the study team. We may ask you to come in for an additional, unscheduled study visit in this situation evaluate your symptoms if we feel this is necessary.

In case if you are not able to come to NIH we may see you virtually using NIH approved TeleMedicine platform. If you were recruited from a source outside the NIH then the screening and/or baseline visit #1 will be in person in NIH. The remainder of the visits may be via telehealth.

## HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for approximately 5 to 23 weeks, depending on how fast we can complete the screening visit. The study consists of a total of outpatient 2-3 visits to the NIH Clinical Center. Each outpatient visit will last for approximately 2- 3 hours.

## HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 40 people participate in this study at the NIH.

**WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?**

**Study Supplement, Nicotinamide Riboside:** Niagen™ is a commercially available form of nicotinamide riboside (NR). It has been sold as a dietary supplement since 2013. A careful review of all the information available on Niagen™ has not revealed any potential serious safety concerns or side effects. The label recommends taking 250 mg daily. We are using 1000 mg daily. We believe our dose of NR will cause higher and longer-lasting blood levels of NR. There have not been any reports of serious side effects after taking a single dose of 1000 mg of NR to 12 human subjects. There was recently a study at the University of Washington using NR 1000 mg twice a day in heart failure patients. It is also similar to a substance called nicotinamide which has a lot of safety data available. Nicotinamide has been given to Type 1 diabetic patients. The doses are equal to 3000 mg daily and was given up to 3 years without any significant side effects. Based on these studies, we do not expect that 1000 mg of NR daily for 4 weeks should raise any serious safety concerns.

**Placebo:** There is no risk to taking a placebo pill.

**Blood Draw:** A needle will be put into a vein of your arm to draw blood during your outpatient visits. You may feel some pain at the needle entry site. There is a slight risk of bleeding around the site. This is not dangerous, but it could result in a bruise. Some people feel lightheaded or dizzy and may even faint during or after having blood drawn. To reduce your risk of falling, we will monitor you closely and may ask you about these symptoms before we allow you to stand up.

**Skin biopsy**: Pain at the biopsy site should be minimal. Bleeding and infections are rare. Biopsy wounds heal with a very small, nearly unnoticeable scar. Sometimes a raised scar (keloid) or visible lump may result. The numbing medicine is used to reduce the pain of the biopsies. However, there is some burning pain caused by the injection of the numbing medicine. The pain may not be eliminated completely. You may experience mild pain and tenderness at the biopsy site for up to 1 week after the skin biopsy. In rare cases, allergic reactions to the numbing medication have been reported. Please tell one of the healthcare providers, if you ever have had an allergic reaction to any medications. It is also possible that the biopsy site can become infected and need additional treatment. If you develop signs of infection at the biopsy site such as expanding redness, swelling, or discharge, please seek medical attention and notify the research team.

**What are the risks related to pregnancy?**

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. If you think or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible.

If you are a sexually active person with a partner capable of becoming pregnant, it is important that your partner not become pregnant during your participation in this study. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant

during your participation in this study, please contact the research team member identified at the top of this document as soon as possible.

**WHAT ARE THE BENEFITS OF BEING IN THE STUDY?**

You will not benefit from being in this study.

**Are there any potential benefits to others that might result from the study?**

In the future, other people might benefit from this study because of the knowledge gained in understanding the impact of NR on inflammation in people with psoriasis

**WHAT OTHER OPTIONS ARE THERE FOR YOU?**

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could

- Choose not to enroll in this study.

- Choose to withdraw from this study. If you decide to withdraw from the study, you can do it at any time. In this case. we will keep your study results in order to properly analyze it along with the other participants. If you, at any time, decide to withdraw, please speak with members of your research team.

**DISCUSSION OF FINDINGS**

**New information about the study**

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

**Return of research results**

We do not plan to return any results from this study to you except for any clinical blood tests which are collected for screening. Any research papers written based on the study findings will be available at the website clinicaltrials.gov. We may notify you by email or mail when study findings are reported on ClinicalTrials.gov or are published.

**EARLY WITHDRAWAL FROM THE STUDY**

If new, previously undisclosed information emerges during the study that would exclude you from the study, the investigators will discuss this with you, and you may be excluded. If you miss too many study pills, you will be withdrawn from the study.

## STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

**Will your specimens or data be saved for use in other research studies?**

As part of this study, we are obtaining blood samples, skin samples and data from you. We plan to use these samples and data for studies going on right now, as well as studies in the future. These studies may provide additional information that will be helpful in understanding psoriasis, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you. By agreeing to let us use your blood, tissue and data, you give the NIH any rights you may have in the samples and data.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

**Will your specimens or data be shared for use in other research studies?**

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. These researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

**How long will your specimens and data be stored by the NIH?**

Your specimens and data may be stored by the NIH indefinitely.

**Risks of storage and sharing of specimens and data**

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

**COMPENSATION, REIMBURSEMENT, AND PAYMENT**

**Will you receive compensation for participation in the study?**

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

If you are unable to finish the study, you will receive compensation for the parts you completed.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A “Form 1099-Other Income” will be sent to you if your total payments for research participation are $600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

We will pay you for participating in this research study by check or direct deposit at the end of the study or at the time of study withdrawal for the procedures completed. Payment will typically be received within 2 months of the last study visit. The amount will be dependent on the tests performed. We calculate your compensation based on the inconvenience we will cause you for the hours you spend participating on this study, for the procedures and other forms of participation in the study up to a total of $895.

| Procedures | Inconvenience Units | Compensation per procedure | Frequency | Total Compensation |
|---|---|---|---|---|
| Medical History and physical examination | 2.5 | $25.00 | 1 | $25.00 |
| Screening Blood Draw (if needed) | 1 | $10.00 | 1 | $10.00 |
| Research Blood Draw | 5 | $50.00 | 2 | 100.00 |
| Research skin biopsy | 5 | $50.00 | 4 | $200.00 |
| Drug administration, General | 2 | $20.00 | 28 | $560 |
| | | | **Maximum Compensation:** | $895.00 |

**Will you receive reimbursement or direct payment by NIH as part of your participation?**

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH and NHLBI policies and guidelines.

You will only receive compensation as noted in the table above.

This study does not offer reimbursement for, or payment of, travel, lodging or meals.

**Will taking part in this research study cost you anything?**

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

**CONFLICT OF INTEREST (COI)**

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The NIH and the research team for this study are using Niagen developed by Chromadex through a collaboration between your study team and the company.

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

## CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

## CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information.

The research study team plans to collect social security numbers from research participants for purposes of compensation. Participants can withhold their social security numbers and still participate in the research study; however, you may not be able to receive compensation if you do so**.**

### Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

### Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

**Privacy Act**

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

**POLICY REGARDING RESEARCH-RELATED INJURIES**

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

**PROBLEMS OR QUESTIONS**

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Michael Sack, MD, PhD, sackm@nhlbi.nih.gov, 301-402-9259. *Other researchers you may call are:* Rebecca Huffstutler CRNP, Rebecca.huffstutler@nih.gov, 301-594-1281. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

**CONSENT DOCUMENT**

Please keep a copy of this document in case you want to read it again.

**Adult Research Participant:** I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

| Signature of Research Participant | Print Name of Research Participant | Date |
|---|---|---|

**Investigator:**

| Signature of Investigator | Print Name of Investigator | Date |
|---|---|---|

**Witness to the oral short-form consent process only:** This section is only required if you are doing the oral short-consent process with a non-English speaking subject and this English consent form has been approved by the IRB for use as the basis of translation.

**Witness:**

| Signature of Witness* | Print Name of Witness | Date |
|---|---|---|

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.