NCT 04060212

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Consent Form

Study Title: Microbial Mechanisms of Methylmercury Metabolism in Humans.

Principal Investigator: Matthew Rand, Ph.D.

This consent form describes a research study, what you may expect if you decide to take part and important information to help you make your decision. Please read this form carefully and ask questions about anything that is not clear before you agree to participate. You may take this consent form home to think about and discuss with family or friends.

Key Information

- Being in this research study is voluntary – it is your choice.
- You are being asked to take part in this study because you may represent a healthy individual who is likely to eat fish.
- The purpose of this study is evaluate how quickly the trace levels of mercury in fish are removed from your body.
- Your participation in this study will last for 10 months.
- Procedures will include providing information on your height, weight and eating habits, eating fish, submitting samples of stool and hair, and taking a prebiotic supplement.
- There are risks from participating.
    - The most common risk is digestive discomfort from prebiotic.
    - One of the most serious risks is exposure to mercury. See the "Risks of Participation" section in this consent form for more information. You should discuss these risks in detail with the study team.
- You will not benefit from being in this research study.
- If you do not want to take part in this study you may opt out at any time.

Purpose of Study:

The purpose of this study is to evaluate how the bacteria in your gut can improve the break-down and de-toxification of non-harmful levels of a naturally occurring form of mercury (methylmercury) that comes with eating fish. This research could help scientists and doctors understand whether or not mercury in fish that we are likely to eat poses any concern for the health of people.

Description of study procedures:
Overview: The study will take place over approximately 10 months. Study activities will occur in two study "Periods", each lasting approximately 75 days, and separated by four months in between. In the first Period (Period 1) you will start by eating three fish meals at home within the first two weeks. Then, you must not eat any more fish or seafood for the following two months. During those two months, we will ask you to collect a stool sample and submit it to us, or we'll pick it up. You will also return to the study site after these two months and we will collect several hair strands from your head. Next, you will allow four months to go by and then return for a visit to receive more fish meals and supplies to repeat this entire process in Period 2. However, this time you will take a prebiotic supplement each day for approximately two and a half months during the study Period. Unlike "probiotic", which is live bacteria, prebiotic is a natural plant fiber in a powder form that is slightly sweet and easily taken with food or drink. Also, for this Period 2, you will collect and submit two stool samples, one at the beginning and one in the middle of the Period, so we can tell if the prebiotic is working. After a final visit for another collection of hair strands you will be done.

Altogether there are four in-person study visits, at the start and end of each study Period. At three other times during the study, you will collect stool samples at home and either drop them off or ship them to our lab or we will arrange for a pick-up from you.

Also, so as not to interfere with the hair samples, you will not be permitted to have your hair dyed during the Period 1 and 2 of the study. Finally, you will need to avoid any pre- or probiotic supplements outside of what we provide to you in the study.

The Specifics:
Visit 1, Start of Period 1: This visit will occur at the Rand laboratory located at the University of Rochester Medical Center (URMC). A visitor parking pass will be provided to you if needed. The study will be explained to you, including your responsibilities, risks and benefits. We will measure your height and weight so that we can appropriately calculate the size of the fish meals to give you and know that any mercury you get that is naturally in the fish will be well below any level of concern. We will ask you about what medicines you are currently taking. You will be given three frozen tuna steaks that have been prepared at a local market in individually wrapped portions and are to be eaten at home. You will be given a styrofoam freezer box and freezer blocks to transport the tuna home. The styrofoam freezer box will also be used later for shipping or transporting your stool samples back to the Rand laboratory. We will give you instructions to defrost the tuna and suggestions for how to prepare the tuna meals; however, you can prepare the tuna any way you like. In addition, you will be given a notebook binder "food diary" to fill in and record the food types you eat, and what you drink, at each meal starting with the first fish meal and extending through two and a half months of each study Period. You will also be asked to make notes on your health and well-being over the course of the two study Periods, for example, it will be helpful to know if you get sick or experience unusual stresses. This first visit should take about 30-45 minutes.

Fish eating and sample collection: For each of the two study Periods, you will eat tuna meals on Days 0, 7 and 14 of the study. This will be done at home and according to your own preference of cooking and eating. You are not to eat any other fish or seafood during these 14 days. You cannot eat any fish or other seafood for the 60 days following the final fish meal on day 14. This includes not eating, for example, canned tuna or shrimp in a sandwich or salad. Approximately four weeks after your last fish meal you will collect a stool sample in a container using a kit we provide with instructions. In addition, you will also take a small sample from your stool and put it in a separate tube that has a solution to preserve the bacteria DNA in the stool. You will then double-bag your sealed stool container and freeze it. You will then ship the frozen stool and the small tube with the preserved stool sample back to the Rand laboratory using the styrofoam box and freezer blocks provided. Alternatively, we will pick it up.

Visit 2, hair collection: On or around 60 days after the final fish meal (Day 74 of the study) you will come to the Rand laboratory for hair sample collection. A visitor parking pass will be provided if you need it. Hair sampling will be done by the Dr. Rand or a study staff member in laboratory. Samples of 4-8 strands at a time will be briskly tugged from your scalp, which can cause a mild but brief discomfort. A total of approximately 25 hairs will be collected (three to four separate tugs). We will collect your food diary at that time as well. We will also schedule your return visit for approximately 4 months later to begin the second study Period. This visit should take about 30 minutes.

Visit 3, Start of Period 2. Approximately four months after your prior visit you will come to the Rand laboratory and we will ask you for updates about any sickness, stresses or change in medicines you experienced in the last four months. As you did in Period 1, you will be given three frozen tuna steaks to be eaten at home provided in a styrofoam box and freezer blocks to transport home. In addition, you will be provided with two kits for stool collection and bacterial DNA sampling. You will also be provided with an 11-week supply of a Prebiotic powder, which will come in single dose pouches and with instructions for how to take it. You will also receive a new food diary to fill in.

Taking prebiotic: *(*note; you will need to collect a stool sample prior to, or on the first day of taking Prebiotic and submit it to study staff*) You will begin taking prebiotic one week before you eat the first fish meals for Period 2. Prebiotic will be taken once per day at a meal time. You can take the prebiotic in a drink or sprinkled on food. You will need to continue to take the prebiotic every day for the remainder of the study Period, and will cease taking the prebiotic on the day you return for the final visit we will remind you when it is time to stop taking the prebiotic.

Fish eating and sample collection: You will eat the three fish meals (days 0, 7, and 14 of Study Period 2), and perform the stool sampling as you did in Period 1. Note, you will need to collect a stool and a bacterial DNA sample before starting the prebiotic, and submit this to study staff. Then, you will collect another stool and bacterial DNA sample approximately four weeks after the last fish meal. You will come in for a final visit and collection of hair strands by study staff 60 days after the last fish meal. At that time we will also collect your food diary.

	Study Period 1						Study Period 2					
Activity	Day: 0	7	14	44#	74$	4 months	(-7)	0	7	14	44#	74$
consume fish meal at home	X	X	X					X	X	X		
washout period						X						
fecal sample				X			X				X	
hair sample					X							X
consume prebiotic at home&							X	X	X	X	X	X

Fecal samples can be collected within 2-3 days of this target date.
$ Hair samples can be collected within 2-3 days of this target date.
& Prebiotic is consumed daily at home from days -7 to 74 of Period 2.

Numbers of Subjects:
Approximately 46 people will participate in this study.

Duration of the Study:
Your participation in the study will last about 10 months total.

Risks of Participation:
Methylmercury is a well-studied neurotoxicant that people commonly encounter with consumption of fish. In general, the levels of fish eaten by Americans today do not approach levels of concern for methylmercury toxicity. The amount of fish you will eat with this protocol will be carefully calculated ahead of time. The methylmercury levels in your system will stay below any level of concern for risk as defined by a widely accepted reference dose (RfD) level established by the US Environmental Protection Agency (EPA). We will measure the levels of mercury in the fish prior to giving it to you in order to calculate your fish portion size in accordance with your body weight to avoid any risk from methylmercury.

You will receive fresh frozen tuna in individually wrapped portions. As with any fish intended for eating there is a risk of food poisoning, particularly if uncooked fish is left at room temperature for an extended period (e.g. >2hrs). You will be provided with instruction for preparation of tuna for consumption to avoid risks of illness from fish consumption.

You will be advised on what to expect with taking a prebiotic, including possible feelings of bloating and excess flatulence that are harmless yet may produce some annoyance. Where any adverse event related to the study arises, you are advised to contact study staff at with contact information below.

Collection of your hair samples may cause a mild but brief discomfort. Your hair samples will be sent to a Trace Element Analysis Lab for analysis of mercury levels. These samples will only be labeled with a code number, and none of your personal information will be included.

Because this study involves collecting personal, identifiable information about you, there is a potential for invasion of privacy or breach in confidentiality. To minimize this risk, we will assign you a study code number instead of labeling the information we collect from you with your name. All of the information we collect will be stored in a secure manner and only study team members will have access to it.

The study team may be notified if you receive other health care services at URMC or its Affiliates (e.g., visit to the emergency room). In addition, the following individuals may know you participated in research and may see results of testing conducted for this study:

- Staff at the University of Rochester Medical Center and its Affiliates (e.g., Strong Memorial Hospital, Highland Hospital, URMC primary care, specialist physician offices) who have a reason to access your electronic health record.
- Health care providers who are involved in your care at a facility that is not part of the University of Rochester Medical Center and its Affiliates and who have reason to access your electronic health record.

Individuals who request a copy of information from your health record for activities such as treatment or payment (e.g., medical insurance companies, worker's compensation).

Benefits of Participation:
You will not benefit from being in this research study.

Sponsor Support:
The University of Rochester is receiving payment from the National Institute of Environmental Health Sciences (NIH, NIEHS) for conducting this research study.

Costs:
There will be no cost to you to participate in this study.

Payment:
If you complete the entire study (Periods 1 and 2) you will receive a total of $75 in the form of Wegman's gift cards. A $25 card will be awarded at the end of Period 1 and a $50 card awarded upon completion of Period 2.

Circumstances for Dismissal from this Study:
You may be withdrawn from the study if you do not keep appointments for study visits or if you cannot complete study activities.

Confidentiality of Records and Authorization to Use and Disclose Information for Research Purposes:
The University of Rochester makes every effort to keep the information collected from you private. In order to do so, we will store your information in a secure manner using locked

cabinets or password-protected encrypted hard drives that only the study personnel will have access to. Sometimes, however, researchers need to share information that may identify you with people that work for the University, regulators or the study sponsor.

If you have never received a copy of the University of Rochester Medical Center (URMC) and Affiliates Notice of Privacy Practices, please ask the investigator for one.

What information may be used and given to others?
The study investigator will get your personal and medical information. For example:

- Research records
- Records about phone calls made as part of this research
- Records about your study visits

Who may use and give out information about you?

- The study investigator and the study staff
- URMC and Affiliates

Your information may be given to:

- The Department of Health and Human Services
- The University of Rochester
- Montana State University
- The study sponsor, the National Institute of Environmental Health Sciences (part of the National Institutes of Health)
- Dartmouth College: Hair samples will be analyzed at the Trace Element Analysis Lab at Dartmouth College, New Hampshire.

Why will this information be used and/or given to others?

- to do the research
- to analyze the study results, and
- to see if the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

How long will this be permission be valid?
This permission will last indefinitely.

May I cancel my permission to use and disclose information?
Yes. You may cancel your permission to use and disclose your health information at any time. You do this by sending written notice to the study investigator. Upon receiving the written notice, the study team will no longer use or disclose your health information and you

will not be able to stay in this study. Information that has already been gathered may need to be used and given to others for the validity of the study.

May I withdraw from the study?
Yes. If you withdraw your permission to be in the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
No. There is a risk that your information will be given to others without your permission.

Where else will this study be reported?
In accordance with the funding agency (NIH) this study will be registered as a "Clinical Trial" and a description of this study 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 website at any time.

Certificate of Confidentiality:
To help us further protect your privacy, the investigators have a Certificate of Confidentiality from the Department of Health and Human Services (DHHS).

With this Certificate, the investigators cannot be forced (for example, by court subpoena) to disclose or use research information, documents, or samples that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, other proceedings, or be used as evidence. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes, or to other government agencies related to communicable diseases.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your consent to receive research information, then the investigator may not use the Certificate to withhold that information. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

Contact Persons:
For more information concerning this research or if you feel that your participation has resulted in any research related injury, emotional or physical discomfort, please contact**:**
Matthew Rand, Ph.D. at 585-275-5459.

Please contact the University of Rochester Research Subjects Review Board at 265 Crittenden Blvd., CU 420315, Rochester, NY 14642-8315, Telephone (585) 276-0005 or (877) 449-4441 for the following reasons:

- You wish to talk to someone other than the research staff about your rights as a research subject;
- To voice concerns about the research;
- To provide input concerning the research process;
- In the event the study staff could not be reached.

Voluntary Participation:

Taking part in this study is voluntary. You are free to not take part or to withdraw at any time, for whatever reason. No matter what decision you make, there will be no penalty or loss of benefit to which you are entitled. In the event that you do withdraw from this study, the information you have already provided will be kept in a confidential manner.

If you are a student at the University of Rochester: This will not affect your class standing or grades at the University of Rochester. You will not be offered or receive any special consideration if you take part in this research.

If you are an employee at the University of Rochester: Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

SIGNATURE/DATES

After reading and discussing the information in this consent form you should understand:

- Why this study is being done;
- What will happen during the study;
- Any possible risks and benefits to you;
- Other options you may have instead of being in the study;
- How your personal information will be protected;
- What to do if you have problems or questions about this study.

Storing samples for Future Non-genetic Research:

It is likely that new methods will be discovered in the future that could assist in analysis of mercury metabolism and elimination processes. Therefore, we would like to store remaining samples of your hair and stool for future studies. If you allow us to save your samples, they will be kept indefinitely, as long as they are useful for research. If you decide that you don't want us to keep your samples, let us know and we will destroy them. If you decide now that we can keep your extra samples for future research, you can change your mind at any time. You will need to let the study team know, in writing, that you want to withdraw your consent. Then, the samples not already used for research will be destroyed. Information gathered prior to study withdrawal will remain in the database. We can be reached at: Dr. Matthew Rand, Dept of Environmental Medicine Box EHSC, University of Rochester, Rochester, NY 14622, (585)-275-5459. Please indicate whether you are willing to let us store samples for future research by putting your initials here:

_____ Yes, I am willing to let you save my hair and stool samples for future non-genetic research.

_____ No, I do not want my extra hair and stool samples saved for future non-genetic research.

Other Future Studies:

We are continually trying to understand the mechanisms of methylmercury toxicity. We expect that we will have new studies in the future investigating methylmercury behavior in people. We would like to know whether you would be willing to be contacted about future studies. Only the Principal Investigator (Dr. Rand) or a Study Coordinator would contact you. If you are willing to be contacted about new studies in the future, please initial and date the line below.

_____ Yes, I am willing to be contacted about future studies related to mercury. The best way to contact me is: _____.

_____ No, please do not contact me about future studies related to mercury.

Subject Consent

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I agree to participate in this study. I have received (or will receive) a signed copy of this form for my records and future reference.

_____

Subject Name (Printed by Subject)

_____ _____

Signature of Subject Date

Person Obtaining Consent

I have read this form to the subject and/or the subject has read this form. I will provide the subject with a signed copy of this consent form. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information. I have given the subject adequate opportunity to read the consent before signing.

_____

Name and Title (Print)

_____ _____

Signature of Person Obtaining Consent Date