RUTGERS
School of Public Health

CONSENT TO TAKE PART IN A RESEARCH STUDY

Main Study

TITLE OF STUDY: Activated Macrophages and Ozone Toxicity
Principal Investigator: Howard Kipen, MD, MPH

This consent form is part of an informed consent process for a research study and it will provide information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

After all of your questions have been answered, if you still wish to take part in the study, you will be asked to sign this informed consent form.

The principal investigator or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

SPONSOR OF THE STUDY: National Institutes of Health (NIH)

NIH is the sponsor of this research study. The principal investigator is being paid to conduct this study according to a budget that will cover the costs of the study. The costs that are usually covered include things such as: physical examinations, laboratory tests required by the study, and the costs of collecting all of the information required by the study.

Why is this study being done?

The study is being done to learn about how ozone affects the lungs. Ozone is a common air pollutant and is especially high in the summer. High levels of ozone can irritate the lungs. These levels may also cause breathing problems, particularly in people with asthma or other diseases. This study will measure the types of cells in lung to see how they change after ozone exposure. The study will also examine if different genes affect the response to ozone. Genes are parts of a cell that control which proteins are made. The proteins control how the body functions.

Why have you been asked to take part in this study?

You have been asked to take part in the study because you are a healthy adult who expressed interest in the study.

Who may take part in this study? And who may not?

Healthy non-smoking and smoking adults between the ages of 18 and 40 may take part in the study.

People with the following conditions may not take part in the study:

- Cardiovascular disease
- Respiratory disease
- Recent (within 4 weeks) respiratory or COVID-19 symptoms
- Diabetes
- Pregnancy
- HIV Infection
- Orthopedic or rheumatologic conditions which would interfere with bicycle use
- Inability to produce a sputum plug
- Daily use of antioxidants such as selenium, Vitamin C, Vitamin E or one of the carotenoid vitamins which include beta-carotene, lycopene, lutein, zeaxanthin (excluding a multivitamin)
- Daily use of certain herbal supplements including ginkgo biloba

You must be fully vaccinated for COVID-19 at the time of testing. You are considered fully vaccinated for COVID-19 at least 2 weeks after you have received the second dose in a 2-dose series (such as Pfizer-BioNTech or Moderna), or at least 2 weeks after you have received a single-dose vaccine (such as Johnson and Johnson). You will be asked to provide proof of vaccination.

If you take any of these supplements at least once a week, take other supplements, or have any questions about your eligibility, please tell the study investigator. The principal investigator will determine if you are eligible for the study.

How long will the study take and how many subjects will participate?

80 subjects will participate in the study. Each subject will make 5 visits to the Environmental and Occupational Health Sciences Institute (EOHSI). The visits will range between 2 to 5 hours. The total time for the study will be approximately 12 hours.

What will you be asked to do if you take part in this research study?

You will be asked to come to EOHSI for 5 visits. The visits will include 1 screening visit, 2 exposure visits, and 2 follow-up visits. The follow-up visits will take place either 1, 2, or 3 days after the exposure visit. You will be randomly assigned to either 1, 2 or 3 days (like the flip of a coin) for the follow-up visit.

Visit 1/Screening:

You will be asked to refrain from eating 2 hours prior to this visit.
This visit will include:

- A physical examination – including measurement of your height, weight, pulse rate, blood pressure and oral body temperature. If you have any cold or respiratory symptoms, the visit will be rescheduled.
- You will be asked about your smoking history and/or history of tobacco use, if any
- Your medical history will be reviewed
- Collection of breath samples (by breathing in a cooled tube for 10 minutes)
- Collection of an oral wash (rinsing your mouth)
- Collection of a throat swab
- Collection of a urine sample
- Women will be given a urine pregnancy test
- Spirometry and impulse oscillometry (breathing tests)
- Blood tests – about 20 mL (about 1 tablespoons). The blood will be used for clinical tests, and research purposes. Electrocardiogram (ECG – heart tracing)
- You will be tested to see if you can produce a sputum sample. Before the test starts, you will be given a medication (albuterol) using an inhaler. Albuterol is an FDA-approved drug that relaxes muscles in the airways and increases air flow to the lungs. You will be asked to inhale a saline (salt) mist through a nebulizer machine for a period of approximately 20 minutes. You will be asked to cough and spit the sputum into a cup periodically. If you cannot produce a sputum sample, you will **not** be eligible for the study.
- You will be given a brief tour of the exposure room and asked to try the exercise bicycle. The resistance on the bicycle will be adjusted so that you can reach the correct exercise rate more easily.

This visit will last about 2.5 hours.

After the visit, a study physician will review your physical exam and blood tests to see if you are healthy enough for the study. If you are not eligible for the study, you will be told the reason.

If you are eligible for the study, Visit 2 will be scheduled.

Visit 2 and Visit 4/Exposure

You will be asked to refrain from eating 2 hours prior to the visit.

- You will be asked about any changes to your health since the screening visit. If you have a cold or any respiratory symptoms, the visit will be rescheduled.
- Women will be given a urine pregnancy test.
- Your blood pressure, pulse rate, and oral temperature will be checked.
- Spirometry and impulse oscillometry (breathing tests)
- Collection of breath samples (by breathing in a cooled tube for 10 minutes)
- Collection of an oral wash (rinsing your mouth)
- Collection of a throat swab
- Collection of urine samples
- Blood samples will be collected – about 20 ml (about 1 tablespoon). The samples will be analyzed in the future.
- You will be placed in the exposure room and exposed to either clean air or 0.2 ppm (parts per million) ozone for 3 hours. During this time, you will be asked to exercise for 15 minutes then rest for 15 minutes. The exercise schedule may be changed during the session for your comfort. The study staff will monitor your heart rate continuously to ensure your safety.
- You will be asked to complete questionnaires about how you feel.

These visits will last about 5 hours.

Visit 3 and Visit 5/Follow Up

You will be asked to refrain from eating 2 hours prior to this visit.

- You will be asked about any changes to your health since the exposure visit.
- Your blood pressure, pulse rate, and oral temperature will be checked.
- Spirometry and impulse oscillometry (breathing tests)
- Collection of sputum sample (described in screening visit).
- Collection of a breath sample (by breathing in a cooled tube for 10 minutes)
- Collection of an oral wash (rinsing your mouth)
- Collection of a throat swab
- Collection of a urine sample
- Blood samples will be collected – about 20 ml (about 1 tablespoon). The samples will be analyzed in the future and for genetic testing. If you do not wish to have the genetic testing done, you may **not** take part in the study.
- A questionnaire about how you feel.

These visits will last about 2 hours.

If you are unable to produce a sputum sample at your first follow-up visit (Visit 3), you may not be eligible to complete the study. The study investigators will tell you if you may continue in the study.

What are the risks and/or discomforts you might experience if you take part in this study?

1. Ozone: The proposed exposure concentration of ozone (0.2 ppm, 3 hours) is almost twice maximal levels reported in the world's most polluted cities (i.e., Mexico City); however, this concentration and higher concentrations (up to 0.4 ppm, 2 hours) with exercise have been used extensively for similar studies at United States Environmental Protection Agency (USEPA), University of Southern California (USC), UC San Francisco, and other institutions for over 40 years with no adverse effects reported. In this study, your exposure will be limited to 3 hours and will only occur once. You may experience irritation of the eye, nose or throat, cough or headache, but these are expected to be mild and dissipate within an hour after the exposure ends. During the exposure sessions, you will be able to use an intercom to tell the study staff if you are not feeling well. Your heart rate will be monitored. If you are not feeling well or if any problems with your heart or breathing are observed, the session will be stopped.

   Before and after each exposure session, you will complete a symptom questionnaire. This questionnaire will be reviewed by the clinical technician and a physician to ensure that you are ready to resume daily activities. If you develop any symptoms of chest pain, dizziness, or other symptoms of concern to either yourself or the physician, the exposure will be terminated. The covering physician will examine you and make an appropriate treatment decision, including referral to the emergency department. You may or may not be eligible to continue in the study.

   At the end of the exposure visit, you will be given the phone number of the pulmonary division of Robert Wood Johnson Medical School and a standard rescue inhaler. If you have any breathing problems after you leave the EOHSI clinic, you should call the pulmonary division. A physician will be available 24 hours per day/7 days per week. The responding physician will speak with you and may instruct you to use the rescue inhaler or to go to the hospital. If you have a reaction and need to use the inhaler, you will still be requested to come to the EOHSI clinic for your scheduled follow up appointment. If you have not yet completed both exposures, you may or may not be eligible to continue with the study. The study doctor will review your records and discuss this with you.

   You will be contacted to complete the symptom questionnaire the next day. If you report any symptoms, you will be referred to the study physician.

2. Spirometry: The spirometry procedure poses minimal risk to the subject. The breathing maneuvers may occasionally cause dizziness and very rarely, actual fainting.

3. Impulse Oscillometry (IOS): IOS is a noninvasive procedure. You may briefly feel lightheaded during the measurement.

4. Albuterol: Albuterol is a medicine widely used to treat breathing problems such as asthma by relaxing the smooth muscles. It is routinely used prior to sputum induction. In this study, it is given by inhalation. Common side effects are tremor (shaking), palpitations (sensation of your heartbeat), and headache. These effects may last four to six hours.

5. Sputum induction: The saline mist may make you cough causing a shortness of breath. If you develop problems with your breathing, the procedure will be stopped. You may be given albuterol to help your breathing.

6. Venipuncture: When your blood is drawn, there may be a bruise, bleeding, or infection at the place where your blood is drawn. However, infection is rare.

7. Oral wash: No increased risks are expected from the collection of the oral wash other than your tasting slightly salty water.

8. Throat swab: The throat swab may cause minor discomfort, including gagging.

9. Genetic testing: Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Therefore, your genetic information potentially could be used in ways that could cause you or your family economic stress. There are state and federal laws that protect against genetic discrimination. A federal law, the Genetic Information Nondiscrimination Act, makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: (1) health insurance companies and group health plans may not request your genetic information that we get from this research; (2) health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums; and (3) employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Are there any benefits for you if you choose to take part in this research study?

You will receive no direct benefit of taking part in the study. Your participation will help scientists better understand how ozone and possibly other air pollutants injure the body. This knowledge may lead to new strategies to control exposures or treat lung injury or disease.

What are your alternatives if you don't want to take part in this study?

This is not a treatment study. Your alternative is not to take part in this study.

How will you know if new information is learned that may affect whether you are willing to stay in this research study?

During the course of the study, you will be updated about any new information that may affect whether you are willing to continue taking part in the study. If new information is learned that may affect you after the study or your follow-up is completed, you will be contacted.

Will there be any cost to you to take part in this study?

There will be no cost for you to participate in the study.

Will you be paid to take part in this study?

You will be paid, in cash, up to $450 to take part in the study. You will be paid according to the visits you complete:

- Screening visit - $50
- Exposure visit (2) - $125 each
- Follow-up visit (for sputum collection) (2) - $75 each

You will be paid, in cash, upon the completion of your screening visit, and if applicable, the remaining compensation at the end of the study, according to the pro-rated schedule above.

How will information about you be kept private or confidential?

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers will use this Certificate to legally refuse to disclose any information, documents or biospecimens that may identify you from disclosure, including a court order. This means that research material collected about you for this study will not be released to anyone who is not connected with this study unless:

- …you request or consent to its release;

- …a law requires its release (such as reporting communicable diseases or child abuse to State agencies);

- …it is used for other scientific research, as allowed by federal regulations protecting subjects; or

…it is requested by the U.S. federal or state agency sponsoring the research that is needed for auditing or program evaluation or to meet the requirements of the Food and Drug Administration (FDA)."

All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. In addition to key members of the research team, the following people will be allowed to inspect parts of your research records related to this study:

- The Institutional Review Board (a committee that reviews research studies to protect people who are in them)
- Officials of Rutgers University
- NIH which is the sponsor of this study
- Department of Health and Human Services-government agency that oversees and funds research involving human beings.

By taking part in this study, you should understand that the study collects demographic data and data on your health. This data will be recorded by the study doctor/investigator who may store and process your data with electronic data processing systems. The data will be kept as long as the study is being conducted and for 6 years after.

Your personal identity, that is your name, address, and other identifiers, will be kept confidential. You will have a code number and your actual full name will not be used on questionnaires and related data. Only your study doctor and designated research study staff will be able to link the code number to your name and will keep this information during the study. When the study is finished, the link will be destroyed.

Your data may be used in scientific publications. If the findings from the study are published, you will not be identified by name. Your identity will be kept confidential.

A description of this clinical trial will be available on 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.

What will happen if you are injured during this study?

Subjects in this study will be exposed to certain risks of personal injury, which include exposure to high levels of ozone. In addition, it is possible that during the course of this study, new adverse effects of ozone that result in personal injury may be discovered. The University will make appropriate referrals for medical and/or dental treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University.

What will happen if you do not wish to take part in the study or if you later decide not to stay in the study?

Participation in this study is voluntary. You may choose not to participate or you may change your mind at any time.

If you do not want to enter the study or decide to stop participating, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to Dr. Howard Kipen, 170 Frelinghuysen Road, Piscataway, New Jersey 08854.

Who can you call if you have any questions?

If you have any questions about taking part in this study or if you feel you may have suffered a research related injury, you can call the study doctor:

Dr. Howard Kipen
Department of Environmental and Occupational Health
848-445-6091

If you have any questions about your rights as a research subject, you can call:

IRB Director
(732)-235-9806 New Brunswick/Piscataway

What are your rights if you decide to take part in this research study?

You have the right to ask questions about any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered. I **agree** to have genetic testing done on my blood sample.

Subject Name:_____

Subject Signature:_____ Date:_____

Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject and those of his/her parent or legal guardian have been accurately answered.

Investigator/Person Obtaining Consent:_____

Signature:_____ Date: _____

Addendum: Request to Store Tissue and/or Health Information for Future Research Use
We ask your permission to store some of your tissue (blood, urine, and breath samples) and health information collected about you during the main study Activated Macrophages and Ozone Toxicity (IRB# Pro20140001089) for future research. Following are details about our request. Please know that you may not participate in the main study if you say no to this request to store tissue for future research

How and where will your tissue and health information be stored and by whom?

Your blood, urine and breath samples will be stored at the Environmental and Occupational Health Sciences Institute. Only study investigators will have access to these samples. The investigators may analyze these samples to better understand health effects of air pollution.

How will tissue samples and information be collected?

The sample collection is part of the main study, discussed previously.

What are the risks of harm to you?

Psychological or Social Risks Associated with Loss of Privacy:

- While the databases developed for this project will be coded to protect your personal information, people may develop ways in the future that would allow someone to link your medical information back to you. It is also possible that there could be violations to the security of the computer systems.
- There also may be other privacy risks that we have not foreseen.

What are the benefits of participation?

You will not benefit personally from providing a sample and information because research usually takes a long time to produce meaningful results. However, your participation may help investigators understand, prevent, or treat the diseases and conditions studied in the future.

How will information about you and your tissue samples be kept private and confidential?

Information obtained from this research with material obtained from your sample(s) will be kept confidential so that neither the investigator nor the Sponsor can link your individual research results with your identity.

Your sample(s), and materials derived from your sample(s), will be given a code number, and only information related to your age, sex, race, health condition and other relevant clinical information collected in the main study will be linked with the sample's code number. Your name, date of birth, address, or other personal identifying information, will not be linked with the sample(s) you give.

Is there other important information to consider?

Yes. There is no cost to you to allow us to store and use your tissue and information for future research. Nor will you be paid to participate in this repository. Should any products or services result from research using your samples and information, there is no plan to share any of the profits with you.

The research we are doing is only a stepping stone in understanding disease. It may take a long time for our research to produce useful health-related information. Therefore, tests done for our research using your samples and information will not be useful in directing your medical care. Information from our research will not be returned to you, your family members, your doctor, or outside parties. It is possible, however, that members of regulatory authorities, such as the U.S. Food and Drug Administration, Rutgers Institutional Review Board, or other persons required by law may be allowed to look at this information.

What are your rights if you agree to the storage and use of your tissue for future research?

You have the right to ask questions about any part of our storage and future research at any time. You should not sign this form unless you have a chance to ask questions and have been given answers to all of your questions. Your participation in this study is voluntary. You do not have to participate. If you do, you can change your mind at any time.

What are the procedures for withdrawing consent?

If you wish to allow us to store your samples for future use, but change your mind later, you can write to Dr. Kipen at 170 Frelinghuysen Road, Piscataway, New Jersey 08854 and tell him to destroy any remaining tissue samples and data of yours that are currently being stored in the repository. You may also tell him to destroy any personal and private health information that you provided, along with the code linking you to the information you provided.
However, please note that it may not be possible to destroy samples, information and data created from your samples that may have already been used in research studies prior to your request. Dr. Kipen will keep records linking your identity with the blood/tissue sample(s) until the end of the study. Until those records are destroyed, you may ask that your blood/tissue sample(s) and materials obtained from your sample(s) be destroyed.

Permission to Contact You with Additional Requests to Participate in Research

Please tell us if we may contact you in the future to tell you about other ways you may participate in this research or other research we are conducting by initialing next to your choice.

The investigators may contact me in the future to ask me to take part in more research.

Yes ____ No _____

Thank you for considering participation in this research.

Permission to Store Tissue and Health Information for Future Research Use:

Please sign this form if you wish your samples and information to be used for future research on the effects of air pollution.

If you do **not** wish for your samples and information to be used for future research, you may **not** participate in the study and should **not** sign this form.

_____

I agree to have my samples and information used for future research about air pollution.

SUBJECT:

Print Name: _____ Signature:_____ Date:_____

INVESTIGATOR/PERSON OBTAINING CONSENT:

Print Name: _____ Signature:_____