

Attachment D: Informed Consent Form

Cross-sectional epidemiologic study of carbon nanotube and nanofiber workers

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH)
CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)
U.S. PUBLIC HEALTH SERVICE

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

You have been asked to take part in a CDC/NIOSH research study. We explain here the nature of your participation, describe your rights, and tell you how NIOSH will treat your records.

I. DESCRIPTION

1. Study Title: Industrywide Exposure Assessment and Epidemiologic Studies of Workers at Facilities Manufacturing, Distributing, or Using Carbon Nanotubes or Carbon Nanofibers in the United States
2. Sponsor and Project Officer: This project is to be done by the National Institute for Occupational Safety and Health (NIOSH) of the Centers for Disease Control and Prevention, 4676 Columbia Parkway, Cincinnati, OH 45226. NIOSH project officers are Mary Schubauer-Berigan, PhD and Matthew Dahm, MPH
3. Purpose and Benefits: The overall purpose of this study is to find out whether U.S. workers exposed to carbon nanotubes (CNT) or carbon nanofibers (CNF) have early signs of health effects, such as lung disease, heart disease, or cancer. At this time, no certain tests exist to tell whether any health effects are occurring in workers exposed to CNT or CNF. But this study will measure markers of early health effects to see if they may be related to CNT or CNF exposure.

The purposes of this study are:

- (a) Measure Exposure: to measure exposure to CNT and CNF in the work place and in the personal breathing zone of the worker. We will also measure whether there are CNT or CNF particles on the worker's skin after a work shift.
- (b) Measure possible clinical health effects: to measure lung function using spirometry, and to measure blood pressure, heart rate, body mass index, waist circumference, and a complete blood count. We will interview you about your lung and heart health and past work. We will look at these health measures and interview responses together with the exposure measurements to see if CNT or CNF exposure is related to health status.

(c) Study Biomarkers: to look at proteins in some body tissues [sputum (phlegm), nasal cells or cheek swabs] and blood that may be biomarkers (early indicators) of health effects. These could include genetic changes, lung impairment, or oxidative stress and inflammation. These biomarkers may be related to early lung disease, heart disease or cancer. We will look at these biomarker results to see if they are related to your measured CNT or CNF exposure.

Answers to these questions will help NIOSH, companies, and workers understand whether exposure to CNT or CNF may be related to early health effects in U.S. workers. Similar studies are being done in workers exposed to CNT or CNF in other countries.

The benefits to you from being in the study include:

(a) You will receive the results of your lung function test, blood pressure and heart rate tests, complete blood count tests, and other tests using blood, sputum, cheek cells or nasal swipes, and of your exposure measurements to CNT and/or CNF.

You will receive a verbal summary of the results of the lung function, blood pressure and heart rate tests on the day these tests are done. NIOSH will send you written results and copies of these tests and of the complete blood count within one month of your exam. We will also send suggestions (if any) for follow-up care to be discussed with your personal physician

NIOSH will send you results of your personal air samples (or those of a co-worker performing the same job as you) within about 6 months of our site visit. NIOSH will send you all remaining test results done on your blood, sputum, nasal or cheek cells, within one month of us getting the results. It may take up to 18 months before we can share these results with you, because we must store these samples until all the workers are enrolled in our study. Study enrollment could take more than one year.

NIOSH will also send you the results of some research tests done on your samples, but the health importance of these tests is not known.

(b) Your being in the study may also help fellow workers and others exposed to CNT or CNF, as a result of what is learned from this study. NIOSH will provide you and your personal doctor (if you wish) with all findings. We will do this when the study is finished, or sooner, for some findings. You will also receive a copy of the study report along with a brief summary of the study results.

Besides the information about your exposure, health status, biomarker results, and the results of the study, which we will send to you, there are no other benefits to you of being the study.

II. CONDITIONS OF THE STUDY

1. All parts of this study will be done during your normal workday. You will not need to take time off from work to be in the study. Being in the study will involve:
 - i. Exposure measurements will be done at your workplace for two to three days. During this period, most of you will be asked to wear three small sampling pumps placed in the pockets of a fishing vest. The sampling pumps pull air through (1) a filter to measure amounts of elemental carbon (a marker for CNT or CNF) and (2) a filter used to count

the number of structures containing CNT and CNF in the air you are breathing. We ask you to wear the pumps so we can measure the amount of CNT or CNF in the air around you. Other than the inconvenience, there should be no discomfort from wearing the pumps. We will also look at whether CNT or CNF may be present on your skin after your work shift by placing and then removing a small piece of adhesive tape on the skin of your fingers, palms and wrists. Back in the lab, we will look at the adhesive under a microscope to see if CNT or CNF are present on the sample.

- ii. Once during the study, you will be asked to have an interview and medical examination, which will take about 90 minutes. The interview will take 30 minutes or less. The interview will be done in a private area near the NIOSH mobile study trailer or other private place. We will ask about your work history, medical history, lung and heart health, smoking, drinking, and other topics. We realize that some questions are sensitive. We need to ask them so we make sure that you are healthy enough to have the medical tests done. We also need them to interpret the results of your laboratory tests. Your answers to these and any other questions will remain private, as detailed in the Federal Privacy Act of 1974. You may decline to answer any question for any reason.
- iii. After completing the interview, you will undergo a clinical examination by a physician. This examination will take about 10 minutes. This will take place in a private area of the NIOSH mobile study trailer. First, a physician will take a pulse and blood pressure reading. Your height, weight and waist circumference will be measured. The health-care staff will also ask some questions about your medical history. You will remain clothed during the examination, except that your height and weight will be measured in stocking-feet.
- iv. After the clinical exam, you will have a spirometry test to measure lung function. This test will take about 15 minutes. This test measures the volume of air that you can blow out after taking a very deep breath. It also measures how fast you can blow out the air. The test will be repeated at least three times (but no more than eight times), in order to measure your lung function accurately. If you are feeling dizzy or faint at all while taking the test, you should stop and tell the spirometry technician.
- v. After having the lung function test, you will be asked to provide a blood sample of 44 milliliters, about 3 tablespoons. The sample will be drawn from your inside arm, opposite the elbow, by a trained phlebotomist. This will take about 15 minutes.

Measurements that will be done on your blood samples include: (1) tests to measure any changes to the chromosomes within your white blood cells; (2) levels of certain proteins in your blood, which may be early indicators of lung or heart disease; (3) complete blood count; and (4) levels of some proteins produced in your blood indicating a possible inflammatory response to exposure.

- vi. After collecting your blood sample, the technician will collect a sample of your sputum (phlegm), nasal or cheek cell. If you have a cold or asthma, you will not be able to give a sputum sample. If you are healthy enough for the sputum sample collection, you will breathe an aerosol of sterile saline solution through a mouthpiece. This will take about 30 minutes in total. Every two minutes, you will remove the mouthpiece, spit out saliva into

a cup, take a deep breath through the mouthpiece, and then cough phlegm into a collection cup. You will do this five or six times. After the first six minutes, we will check your lung function again using spirometry.

If you cannot or choose not to give a sputum sample, we will ask to collect a swab of the inside of your cheek or nose.

We will do three tests on these sputum, nasal or cheek cell samples. First, we will measure whether any CNT or CNF structures can be observed in them. Second, we will measure any changes to the chromosomes within these cells. Third, we will measure some of the same proteins as in your blood samples.

- vii. We will send you the results of each test after the analysis is completed. Some of the tests will be done after all the workers are enrolled in the study, so results may not be available for some time to come (a year or more). It may not be possible to do every test on every person in the study. Some of the tests are research tests and the significance of the results of these tests for indicating your health is not known. You will receive your test results for every test done on your blood, sputum, nasal or cheek samples, as well as information on the reference or group range found in the study. Reference ranges will be given for laboratory tests that have a known relationship to your health, and group ranges will be provided for tests that do not. If any of your test results fall outside the reference range, the findings will be reviewed by a doctor, who will explain the possible significance of the test result to you by letter or telephone. No tests for drugs or alcohol will be conducted on your blood, sputum, nasal or cheek samples.

Your blood, sputum, nasal and cheek samples will be split into different parts for the various measurements. Since there will be more than enough of some parts than is needed to run the tests, we would like your permission to use the extra for methods development or future research. These samples would be coded so that they cannot be linked back to your name. You will not receive any results of tests done on the samples. Any information that can be linked to the samples will be saved in broad categories (such as age 40-60) so that it cannot be used to identify you. If tests are developed using your samples that are clearly important to your health, we will notify all participants about this and offer you the chance to have the test done and the individual results reported to you. When you sign the consent form to be in the study, you will be asked for separate permission to store your samples for future research.

- 2. There is a slight risk of unintentional disclosure of your information in the questionnaire and medical examination, but we will take extensive steps to minimize this risk. Your questionnaire data will be kept only in electronic form on a password-protected, encrypted laptop or thumb drive while away from NIOSH. Your data will be stored in highly protected electronic systems at NIOSH, and will be accessible only to those with a need to use the data for the purposes of the study.

There should be no discomfort from the blood pressure or heart rate readings, or the collection of nasal or cheek samples. There should be no more than slight discomfort from the lung function (spirometry) and induced sputum tests. Each spirometry test involves taking a deep breath and blowing all the inhaled air out as fast as possible. Some people feel lightheaded during or after

the test. This is generally minor and goes away after sitting down. A small percentage (<3%) of people who have the induced sputum procedure may have temporary bronchial spasm. Bronchial spasm gives a sensation of tightness in the chest, difficulty breathing air out, or wheezing. Sometimes the only symptom is a drop in how well you can breathe out air quickly, measured by spirometry. We are minimizing the chance of this happening to you by using a less irritating form of saline solution. We will check your lung function with a spirometer midway through the sputum procedure to see if you may be having bronchial spasm. We will have a physician in the NIOSH mobile trailer to administer a bronchial dilator if this should happen to you. The bronchial dilator we will use is an emergency inhaler of albuterol (Proventil), which is often used by people with asthma. The other alternatives to using albuterol are (1) using a different type of beta-adrenergic receptor agonist that has a similar mode of action, or (2) doing nothing to reverse the bronchospasm. Doing nothing is not recommended as it may lead to further difficulties in breathing.

During the blood draw, you will feel a slight prick when the needle enters your arm; some people feel lightheaded or dizzy when their blood is drawn. Infrequently, an individual faints. You may also have swelling, bruising or discoloration in the area where the needle was inserted; this will disappear in about a week. Another disadvantage of all the clinical and biomarker tests is that a test result may be outside the range of "normal" even though nothing is wrong. This could result in a recommendation for further evaluation that, ultimately, may not have been necessary. If you have any reaction to or concerns about these procedures you should contact Mary Schubauer-Berigan, Ph.D., at (513) 841-4251.

3. There are no alternative procedures that would provide more information about your specific workplace exposures and possible associated health effects..
4. Injury or harm from this project is unlikely. But if it results, medical care is not provided, other than emergency treatment as described in item #2 above. If you are injured through negligence of a NIOSH employee you may be able to obtain compensation under Federal Law. If you want to file a claim against the Federal government your contact point is: General Law Division of the Office of General Counsel, request the Claims Office: (202) 233-0233. If an injury or harm should occur to you as the result of your participation, you also should contact:

Mary Schubauer-Berigan, Ph.D.
Epidemiologist
NIOSH
Division of Surveillance, Hazard Evaluations, and Field Studies
4676 Columbia Parkway R15
Cincinnati, OH 45226
(513) 841-4251

or

Mark A. Toraason, PhD
Chair
NIOSH Human Subjects Review Board
4676 Columbia Parkway
Cincinnati, OH 45226

(513) 533-8591

5. If you have questions about this research, contact Dr. Mary Schubauer-Berigan at the address and phone number above. If you have questions about your rights as a member of this study, contact Dr. Mark A. Toraason, Chair, Human Subjects Review Board, at 513-533-8591.
6. Your participation in this study is voluntary and you may withdraw your consent and your participation in this study at any time without penalty or loss of benefits to which you are otherwise entitled. By agreeing to be in the study, you should understand that the most important parts of this study are the interview, the spirometry and blood pressure tests, the blood tests, and the exposure measurements.
7. NIOSH will provide you and your doctor (if you wish) with your results in writing when the study is completed, or sooner, if they have clinical meaning. NIOSH will send you a copy of the final report, and a brief summary of the study results. This summary report will not contain any information that could identify people in the study.

III. USE OF INFORMATION

This study is being done by The National Institute for Occupational Safety and Health (NIOSH). NIOSH is part of the Centers for Disease Control and Prevention (CDC), a government agency in the Department of Health and Human Services. We collect this information in order to learn about various kinds of work hazards that may influence the health of the American worker.

NIOSH is allowed to collect and keep information about you, including your results from this study along with your social security number (SSN), because of two laws passed by Congress. These laws are:

1. The Public Service Act, Section 301 (42 U.S.C. 241);
2. The Occupational Safety and Health Act, Section 20 (29 U.S.C. 669).

The information you supply, including your SSN, is voluntary and there is no penalty for not providing it. You are free to choose not to be in this study. It is up to you. We collect your SSN so that we can link your information with your work history records, and so that we can find your updated mailing address so that we can notify you of your individual results and about overall study findings.

The data from this study will be used to evaluate associations between early lung and heart disease and other health effects and exposure to carbon nanotubes and carbon nanofibers. Data will become part of CDC Privacy Act system 09-20-0147, "Occupational Health Epidemiological Studies" and may be disclosed to private contractors assisting NIOSH; to collaborating researchers under certain limited circumstances to conduct further investigations; to the Department of Justice in the event of litigation; and to a congressional office assisting individuals in obtaining their records. An accounting of the disclosures that have been made by NIOSH will be made available to you upon request. Except for these and other permissible disclosures expressly authorized by the Federal Privacy Act, no other disclosure may be made without your written consent.

IV. SIGNATURES

I have read this consent form and I agree to participate in this study (Title: Industrywide Exposure Assessment and Epidemiologic Studies of Workers at Facilities Manufacturing, Distributing, or Using Carbon Nanotubes or Carbon Nanofibers in the United States)

PARTICIPANT _____ DATE _____
(signature)

I give permission for extra amounts of my blood, sputum, nasal or cheek specimens to be stored and used for future research in laboratory tests. I understand that my name and identification number will be taken off these stored specimens and that I will not receive the results of any of the research tests. I understand I will not be contacted again before these analyses are performed.

___ **GIVE PERMISSION** ___ **DO NOT GIVE PERMISSION**

PARTICIPANT _____ DATE _____
(signature)

PARTICIPANT'S NAME: _____
Address: _____
City: _____ State: _____ Zip: _____
Phone: (____) _____
Email address: _____
Participant Social Security number: _____
Participant ID number: _____

I, the NIOSH/CDC representative, have accurately described this study to the participant.

REPRESENTATIVE _____ DATE _____
(signature)

REQUEST AND AUTHORIZATION FOR RELEASE OF INFORMATION

I, _____ request and permit NIOSH/CDC to inform the doctors or health care facilities whose names and addresses I have entered below of any significant findings from this study that concern me. (Do not leave blank. Write "NO" where you do not wish to give a name and address).

1. My personal doctor(s):

Dr. _____

Street _____

City _____ State ____ Zip ____

2. Other doctors or health care providers:

Dr. _____

Street _____

City _____ State ____ Zip ____