Revisions to the Supporting Statement, Cigarette Yield and Body Burden of Smoke Toxins

March 14, 2007, Conference call participants: CDC (Patricia Richter, Clifford Watson, Thelma Sims, Catina Connor), Battelle (Pam Clark, Deon Harvey, Wally Pickworth), and OMB (John Kraemer, Margo Schwab).

1. Where mentioned in the supporting statement, clarify that participants are smoking 1 cigarette during each appointment and bringing 4 cigarette butts to the first appointment.

Page 2-3, Section A.2.

This is an *ad lib* smoking and laboratory smoking study to determine the relationship between cigarette smoke yield (machine-smoked tar and nicotine levels) and actual body burden of selected carcinogens, other toxins, and biomarkers associated with cardiovascular risk (nicotine and its metabolites, urine cadmium, expired-air carbon monoxide, heart rate, blood pressure, oxygen saturation). Approximately 360 established smokers of cigarettes with a range of machine-smoked yields will provide urine and saliva samples for measurement of biomarkers of exposure under natural smoking conditions, and cigarette butts for determination of solanesol levels (another measure of exposure under natural smoking conditions). In addition, each will smoke **one cigarette of** their usual brand during **each of the** two laboratory visits while smoking topography behaviors are measured and recorded, with measurement of cardiovascular physiologic responses and expired-air carbon monoxide levels before and after smoking. Spent cigarette butts from the laboratory sessions will be collected so that solanesol levels can be compared with those of the *ad lib* smoked cigarettes. The design of the study is such that information will be available relative to both chronic habitual smoking under natural smoking conditions (e.g., biomarkers of exposure, collected cigarette butts), as well as information that must be generated within a laboratory environment (e.g., smoking topography behavior, changes in cardiovascular reactivity). Participants will be provided with a pack of their own brand of cigarettes at their first appointment to minimize the possibility that they will smoke a brand other than their current, usual brand during the study period. It has been our experience that participants will smoke whatever brand is immediately available if they run out of their regular brand; we want to reduce unnecessary complications in the data analysis and interpretation.

Page 9. Section A.6

A.6 Consequences of Collecting the Information Less Frequently

This is a one time study. The data collection activities for this study will involve collection of urine, saliva, breath carbon monoxide, smoking behavior **(one cigarette at each visit)**, ventilation hole blocking behavior and breath measurements at each of two

visits over a two-day period. The first visit will be in the morning of the first day, and the second visit will be in the afternoon of the consecutive day. This schedule is important because during the morning of day 1, biomarker levels should commonly be at their nadir, while during the afternoon of day 2, biomarker levels should commonly be at their peak. This will allow a realistic approximation of smoking behavior and biomarker levels in the same individual when nicotine (and other biomarker) levels are at their lowest (after awakening and relatively few cigarettes) and at their highest (during the day after several cigarettes). Deleting any data collection would lead to inadequate data.

Page 13. Section A.12A

The response burden was estimated based on the researchers' previous experience with similar types of data collections. The total burden for each respondent who completes screening, visit 1 and visit 2 will be two hours and five minutes. The CATI screening will take five minutes. Visit 1 will take one hour, which includes a short screening item, the informed consent process, biologic sample collection (urine, saliva, breath carbon monoxide), smoking behavior **of smoking one cigarette**, ventilation hole blocking procedure and breath measurements. Visit 2 will also take approximately one hour, which includes compensation, discussion of quit opportunities if requested, collection of cigarette butts, biologic sample collection (urine, saliva, breath carbon monoxide), smoking behavior **of smoking one cigarette**, ventilation hole blocking procedure and breath measurements. The clinic visits will occur on two consecutive days.

Page 39. (Computer-Assisted Telephone Interviewing Instrument)

*The study would involve your coming to our smoking research laboratory clinic 2 days in a row for about 1 hour each time. The first visit needs to be in the morning and the second visit needs to be in the afternoon, and you should come to the laboratory clinic feeling like you "really want" a cigarette. At each visit you will answer some questions and give urine, saliva and breath samples. You will smoke **one of your own cigarettes** through our smoking machine while wearing a special vest to measure your breathing. In addition, you will have some glow-in-the-dark lipstick applied to your lips and vitamin solution applied to your fingers to see how you hold your cigarette. Before we discuss the study further, I would like to ask you a few questions to see if you qualify for the study. It should take about 5 minutes, and everything you say will be treated in a confidential manner. Do you have time for this now or any questions?*

Page 42 (Computer-Assisted Telephone Interviewing Instrument)

*If you take part in the study, you will come to the laboratory clinic 2 times, with each visit about 30 hours apart. This means that you will come to your first visit in the morning and your second visit will be the next day in the afternoon. You will need to make sure that you arrive for each appointment really "wanting" a cigarette and be sure to bring some of your own cigarettes with you. We also ask that you bring **at least 4 cigarette butts of your own brand** that you have smoked at home to your first appointment. We*

will send you baggies in which to collect these butts. Bring these baggies with you for your first visit.

Page 49 (consent form)

> **First Visit.** At the first visit, you will be asked questions to make sure you are still eligible for the study. We also ask that you bring **at least 4 cigarette butts of your own brand** that you smoked at home before your first appointment. If you are no longer eligible, we will compensate you as if you were completing the first visit, and you will no longer be able to participate in the study. If you are still eligible, you will provide a urine sample. The sample will be sent to a laboratory at the CDC to find out what chemicals from cigarette smoke are in your urine. You will also be given a small piece of cotton to place in your mouth until it is soaked with your saliva. You will put this cotton into a special container. You will be given another piece of cotton for another saliva specimen. The two saliva specimens will also be sent to the CDC to determine the levels of chemicals from cigarette smoke you have in your saliva.

2. Where mentioned in the supporting statement, remove race and/or ethnicity as a basis for eligibility or ineligibility.

Removed on the following pages:

Page 12 Section A.11 Justification for Sensitive Questions: removed in one place

Page 17-19 Section B.1 Respondent Universe and Sampling Methods: removed in four places

Page 40 Computer-Assisted Telephone Interviewing Instrument: Eligible response to question "Please tell me which of these best describes your race and ethnic group:" changed to "Dependent upon cell availability."

Page 41 Computer-Assisted Telephone Interviewing Instrument instructions: removed in one place

Page 45 Eligibility Screener: Response to question "Please tell me which of these best describes your race and ethnic group:" changed to "Dependent upon cell availability."

3. Where mentioned in the supporting statement, replace racial/ethnic specific cigarettes smoked per day ranges with one overall range of cigarettes smoked per day.

Page 13 Section A.12A

A.12A This is a one-time study over two years. There will be no annual collections of data. The final completion goal will be 360 participants; 180 each year. Participants will be established smokers, defined as smoking daily for at least two years, smoking a

minimum number of **6 cigarettes per day, and a maximum number of 40 cigarettes per day,** and aged 18 or older.

Page 16 Section B1

Participants will be established smokers, defined as smoking daily for at least two years, smoking a **minimum of 6 and a maximum of 40 cigarettes per day**, and legal smokers aged 18 or older. In addition, participants must be current smokers of brands in the most popular U.S. cigarette categories (for at least 3 months) chosen based on recent United States market share. Recruitment is expected to yield a distribution of smokers of a wide range of cigarette yield categories, as determined by smoking machine tar levels. Enrollment will be targeted to ensure a wide range of machine-smoked tar levels.

Page 40 Computer-Assisted Telephone Interviewing Instrument: Eligible response to question "How many cigarettes do you smoke on a typical day?"changed to "min ≥ 6 max ≤ 40"

Page 45 Eligibility Screener: Response to question "How many cigarettes do you smoke on a typical day?"changed to "min ≥ 6 max ≤ 40"

4. Where mentioned in the supporting statement, indicate that a pack of cigarettes will be provided and explain why

Page 2. Section A.2.

This is an *ad lib* smoking and laboratory smoking study to determine the relationship between cigarette smoke yield (machine-smoked tar and nicotine levels) and actual body burden of selected carcinogens, other toxins, and biomarkers associated with cardiovascular risk (nicotine and its metabolites, urine cadmium, expired-air carbon monoxide, heart rate, blood pressure, oxygen saturation). Approximately 360 established smokers of cigarettes with a range of machine-smoked yields will provide urine and saliva samples for measurement of biomarkers of exposure under natural smoking conditions, and cigarette butts for determination of solanesol levels (another measure of exposure under natural smoking conditions). In addition, each will smoke **one cigarette of** their usual brand during **each of the** two laboratory visits while smoking topography behaviors are measured and recorded, with measurement of cardiovascular physiologic responses and expired-air carbon monoxide levels before and after smoking. Spent cigarette butts from the laboratory sessions will be collected so that solanesol levels can be compared with those of the *ad lib* smoked cigarettes. The design of the study is such that information will be available relative to both chronic habitual smoking under natural smoking conditions (e.g., biomarkers of exposure, collected cigarette butts), as well as information that must be generated within a laboratory environment (e.g., smoking topography behavior, changes in cardiovascular reactivity). **Participants will be provided with a pack of their own brand of cigarettes at their first appointment to minimize the possibility that they will smoke a brand other than their current, usual brand during the study period. It has been our experience that participants will**

smoke whatever brand is immediately available if they run out of their regular brand; we want to reduce unnecessary complications in the data analysis and interpretation.

5. On the consent form, remove any statement that indicates that cigarettes will be provided.

Page 49 consent form: text removed.

> Finally, we will show you how to collect your smoked cigarette butts for 2 days using the special containers that we will give you. You will place one butt in each small container and write down the time that you smoked it. ~~**We will also provide you a pack of your own brand to smoke so that there is no chance you will run out overnight.**~~ It will be very important that you smoke only your regular brand of cigarette. We may also give you a diary to fill out to record how you felt each time you smoked.

6. Where mentioned in the supporting statement and in the consent form indicate that participants will only be provided breath carbon monoxide and heart rate and how the information will be explained.

Page 4. Section A.2

Carbon monoxide levels and heart rates will be provided to participants if they are interested in knowing them. An average range for comparison will also be provided.

Page 51. consent form

POSSIBLE BENEFITS

> Participation in the study is not expected to benefit you directly. As you may know, smoking causes lung cancer, heart disease, emphysema and may complicate pregnancy. Quitting smoking now greatly reduces serious risks to your health.
>
> **If you are interested, after each visit we will give you your carbon monoxide levels and heart rates, and, for comparison, an average range of levels and rates for smokers and non-smokers.**

7. Include current IRB approval in supporting statement.

Page 66. Attachment G

From: Galusha, Pamela (CDC/OD/OCSO) On Behalf Of Human Subjects Review-OD (CDC)
Sent: Thursday, December 28, 2006 12:10 PM
To: Richter, Patricia (CDC/CCHP/NCCDPHP)
Cc: Redmond-Leonard, Joan A. (CDC/CCHP/NCCDPHP); Merritt, Robert (CDC/CCHP/NCCDPHP); Bonds, Constance (CDC/OD/OCSO); Bertrand, Jacquelyn (CDC/CCHP/NCBDDD); Lipman, Harvey (CDC/CCID/NCPDCID)
Subject: 4443: IRB Approval of Continuation

DATE: 12/28/2006

FROM: IRB Administrator
Human Research Protection Office
Office of Scientific Regulatory Services
Office of the Chief Science Officer, OD/CDC

SUBJECT: IRB Approval of Continuation of Protocol #4443, "Human Smoking Behavior Study" (Expedited)

TO: Patricia Richter, PhD [PIR1]
NCCDPHP/OSH

CDC's IRB G has reviewed and approved your request to continue protocol #4443 for the maximum allowable period of one year and it will expire on 12/8/2007. The protocol was reviewed in accordance with the expedited review process outlined in 45 CFR 46.110(b)(1), category (3).

If other institutions involved in this protocol are being awarded CDC funds through the CDC Procurement and Grants Office (PGO), you are required to send a copy of this IRB approval to the CDC PGO award specialist handling the award. You are also required to verify with the award specialist that the awardee has provided PGO with the required documentation and has approval to begin or continue research involving human subjects as described in this protocol.

As a reminder, the IRB must review and approve all human subjects research protocols at intervals appropriate to the degree of risk, but not less than once per year. There is no grace period beyond one year from the last IRB approval date. It is ultimately your responsibility to submit your research protocol for continuation review and approval by the IRB. Please keep this approval in your protocol file as proof of IRB approval and as a reminder of the expiration date. To avoid lapses in approval of your research and the

possible suspension of subject enrollment and/or termination of the protocol, please submit your continuation request at least six weeks before the protocol's expiration date of 12/8/2007.

Any problems of a serious nature should be brought to the immediate attention of the IRB, and any proposed changes to the protocol should be submitted as an amendment to the protocol for IRB approval before they are implemented.

If you have any questions, please contact the Human Research Protection Office at (404) 639-4721 or e-mail: huma@cdc.gov.

Pam Galusha

cc:
Joan Redmond-Leonard
Rob Merritt
Constance Bonds
Jacqui Bertrand
Harvey Lipman

8. Where mentioned in the supporting statement, indicate that free, voluntary pregnancy tests will be available to female participants that do not know if they are pregnant.

Page 11. Section A.10

While the database with identifying information will be kept separately from the database of questionnaire responses and other study data, identifying numbers will be used to connect the two databases; therefore, the contractor (Battelle) has the ability to link data to respondent. The determination that the Privacy Act is applicable, even though the contractor will only maintain the identifiable information for a limited amount of time, is based on the fact that sensitive information is being collected, and legal determinations by HHS attorneys in the past have upheld this view. The sensitive information includes medical history of heart or lung disease, smoking history, **and free, voluntary pregnancy testing if requested by the participant**.

Page 12. Section A.11

A.11 Justification for Sensitive Questions

The study will ask questions of a sensitive nature. During the screening interview questions will inquire whether the study subject has ever been told by a healthcare professional that they have/had lung or heart problems or have been diagnosed with cancer. Some people feel uncomfortable discussing medical conditions such as lung disease or heart problems. Smoking histories will also be obtained. In addition, women will be asked if they are pregnant, breastfeeding, or trying to become pregnant. These questions are necessary because we are not including people with cancer or heart or lung problems or un-established smokers (daily smoking for less than two years) in the study. These groups are not included because it is unethical to enroll participants with tobacco-related diseases, novice smokers, or pregnant or breastfeeding women into a smoking study. **If a woman does not know if she is pregnant, she will be offered a free, voluntary pregnancy test.** Smoking histories are necessary in order to have an accurate picture of the subject's baseline smoking levels. The smoking history information will also aid in analyzing the smoking behavior data. Basic demographic data such as age and sex also will be collected to establish the prospective respondent's eligibility to participate in the study.

Page 48 consent form

1. PURPOSE OF THIS RESEARCH STUDY

You are being asked to participate is a research study to look at how people smoke different brands of cigarette. You qualify for this study because you are an established smoker who smokes the brand of cigarettes we want to research. This study will also look at nicotine, cancer-causing and possible heart disease-causing chemicals from cigarette smoke that appear in your urine and saliva. It will also look at carbon monoxide in your breath, and changes in your heart rate and blood pressure.

Everyone in the study will smoke their own brand of cigarettes. Everyone will also come to two laboratory clinic visits in a row. If you are a woman and there is any chance that you may be pregnant, you cannot be in this study. **If you are a woman and do not know if you are pregnant, you will be offered a free, voluntary pregnancy test.** Approximately 360 people will participate in the study. The study is sponsored by the U.S. Centers for Disease Control and Prevention (CDC).

Page 54 consent form: Text deleted.

FEMALE VOLUNTEERS ONLY

I understand the risks of smoking tobacco while pregnant. To the best of my knowledge, I (am ❑ / am not ❒) currently pregnant. ~~I understand that I will be given a pregnancy test at the beginning of the study. A positive result will disqualify me from participating, but I will receive payment for attending the first visit.~~

9. Previous OMB requested changes to the consent form.

Page 51. consent form

2. INCENTIVES

~~You will be paid for your time and effort.~~ You will be paid $30 for completing your first laboratory session. This includes $10 for a brief eligibility questionnaire, carbon monoxide measurements and smoking one of your own cigarettes using the special holder; $10 for providing saliva and urine specimens; and $10 for being on time for your scheduled appointment. You will be paid $50 for completing your second laboratory visit. This includes $10 for carbon monoxide measurements and smoking one of your own cigarettes using the special holder; $10 for submitting saliva and urine specimens; $20 for collecting your cigarette butts; and $10 for being on time for your scheduled appointment. The maximum payment for completing this study is $80.