DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Centers for Disease Control
and Prevention (CDC)

Memorandum

Date: September 15, 2006

From: Patricia Richter

Subject: Human Smoking Behavior Study, Clearance Project
MASO ID: 0920-05BA

To: John Kraemer, Desk Officer, Office of Management and Budget

On November 2005, the Centers for Disease Control and Prevention (CDC) submitted an Information Collection (IC) request to the Office of Management and Budget (OMB). Previously, two (2) conference calls were conducted with CDC OMB Desk Officer, Mr. John Kraemer, to address concerns about the methodology and goals of the study. Several of the concerns were based on public comments jointly provided by the Campaign for Tobacco-Free Kids (CTFK) and the American Heart Association (AHA). Based on the outcome of the discussions with Mr. Kraemer, CDC voluntarily withdrew the IC request for further review.

Following CDC's extensive discussion, it was decided that a revised request would be submitted with a newly focused role on several issues; cigarette yield category on levels of biomarkers of exposure and cardiovascular effects. Comments and recommendations provided by CTFK, AHA, and OMB, were considered and incorporated into the goals and design of the revised information collection request. In addition, statistical guidance provided in a January 2006 memorandum from OMB, "Guidance on Agency Survey and Statistical Information Collections" was used as a reference while preparing the Analysis Plan for the Supporting Statement.

The attached Supporting Statement provided herein describes CDC's proposal to study how body burdens of selected carcinogens, other smoke-derived toxic chemicals, and measures of cardiovascular reactivity vary in proportion to machine-smoked yields of tar, nicotine, and carbon monoxide across a wide range of commercially available cigarettes (ultralight, light, and full-flavored cigarettes). The study hypotheses and the methodologies to test the hypotheses are clearly stated on page 3 of the revised supporting statement.

Below is a brief summary of concerns expressed by OMB and CDC's response to the concerns.

1. There was a significant disconnect between the laboratory study and the comments in the package suggesting that this study could lead to changes in smoking machine measures and methods.

Response: This inconsistency was a major consideration in the refocusing of the proposal. The study no longer attempts to define average or "composite" smoking patterns from the quantitative and observational data to establish human behavior-based smoking machine methods for laboratory studies that require cigarette smoke for chemical or toxicological testing. Rather, in the refocused proposal, cigarettes of varying machine-measured tar delivery are the independent variables and the body burdens of toxins that result from their consumption are the dependent variables.

2. The utility of the laboratory environment was questioned out of concern that it is "not inflective of actual behavior." Additional justification was requested for the laboratory portion of the study.

Response: Laboratory smoking is the gold standard for evaluating smoking patterns (PHS 1988; Pickworth W.B. et al. 2005). The design of the refocused study is such that information will be available from both an extended (30 hours) period of chronic habitual smoking under natural smoking conditions, as well as information that can only be obtained with a high level of accuracy in a laboratory environment (e.g., smoking behavior, changes in cardiovascular reactivity). In addition, another objective of the study with an integral laboratory component is an investigation of how solanesol levels (a surrogate chemical measure of total smoke exposure) vary in spent cigarette filters in proportion to machine-smoked yield of the cigarettes under both controlled (laboratory) and naturalistic (home) conditions.

3. There was concern that the original sampling plan would not produce a sample of smokers that was representative or generalizable.

Response: The refocused project no longer uses cigarette smokers, but rather cigarette yield category (ultralight, light, or full-flavor), as the unit of comparison or "independent" variable. Specifically, the smoking machine determined yield category predictor variables and smoking behavior variables (e.g. total puff volume) will be entered in a multiple regression model, controlling for potential confounder variables (e.g., age, gender, ethnicity, cigarettes per day). The dependent variable for the analysis will be the levels of specific biomarkers.

4. The state of science may not support that any differences would be observed. Provide additional information on the biomarkers proposed for study and relevant power calculations.

Response: Section A.4, Efforts to Identify Duplication and Use of Similar Information, provides a literature review that describes recent efforts to determine the body-burden of carcinogens and other smoke toxins in smokers of several varieties of cigarettes. Limitations of previous studies are identified and strategies for overcoming or avoiding the limitations are also described in section A.4. A detailed list of proposed measurements and their use as either biomarkers of exposure or biomarkers of potential effect is provided in Appendix I. Power calculations are provided in detail in section B.1, Respondent Universe and Sampling Methods.

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5. Additional information was requested on how biomarkers are related to naturalistic smoking.

Response: The approach of the refocused study is to study how levels of long- and short-lived biomarkers of exposure or effect change in response to cigarette yield category. Urine and saliva samples will be collected from participants upon their arrival at the clinic and stored for later determination of levels of long-lived (i.e., long half-lives) biomarkers of exposure (carcinogens, nicotine metabolites, heavy metals). Their levels reflect subjects' usual smoking behavior under every day, naturalistic conditions. Other biomarkers that are short-lived (expired air carbon monoxide boost - the

difference between CO levels before and after smoking a cigarette, and markers of cardiovascular reactivity such as blood pressure, heart rate and arterial oxygen saturation) change quickly in response to smoking and must be measured in a laboratory setting.

As evidenced in the summary above and the enclosed Supporting Statement, the proposal has been refocused to answer critical questions in the public health and broader scientific communities regarding the implications of machine smoked yields on actual exposure to carcinogens and toxins in tobacco smoke. Within the Supporting Statement, modifications are in bold and can be found in sections A.1, A.2, A.4, B.1, B.2, B.4 (reference added) and Attachments were expanded and renumbered.

We welcome the opportunity to discussed the refocused proposal with OMB should there be any questions or need for additional information.

References

Pickworth W.B., Houlgate, P, Schorp, M, Dixon, M, Borgerding, MF, Zaatari, G. A review of human smoking behavior data and recommendations for a new ISO standard for the machine smoking of cigarettes. Report of the *AD HOC* WG9 Smoking Behaviour Review Team to ISO/TC 126 WG9. 8-10-2005.

PHS. 1988. *The Health Consequences of Smoking. Nicotine Addiction: A Report of the Surgeon General*. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.pp. 145-239.