

**Supporting Statement A**  
**for**  
**Population Assessment of**  
**Tobacco and Health (PATH) Study (NIDA)**  
**=**  
**Second Wave of Data Collection**

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**Submitted by:**

Kevin P. Conway, Ph.D.

Deputy Director

Division of Epidemiology, Services, and Prevention Research

National Institute on Drug Abuse

6001 Executive Blvd., Room 5185

Rockville, MD 20852

Phone: 301-443-8755

Email: [PATHprojectofficer@mail.nih.gov](mailto:PATHprojectofficer@mail.nih.gov)

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## **A. Justification**

### **A.1 Circumstances Making Collection of Information Necessary**

#### **A.1a Overview**

The National Institutes of Health (NIH), through the National Institute on Drug Abuse (NIDA) and in partnership with the Food and Drug Administration (FDA), requests Office of Management and Budget (OMB) approval of a revision (OMB 0925-0664, expires 11/30/2015) for the Population Assessment of Tobacco and Health (PATH) Study to conduct the second wave of data collection.

Under data collection authorization of Title 42 USC 285o (Attachment 1), NIDA is partnering with FDA to conduct the PATH Study through Westat, the prime contractor. Using computer-assisted interviews and collection of biospecimens, the PATH Study will collect baseline and follow-up information on tobacco-use patterns; trends in risk perceptions and attitudes regarding harmful constituents, and new and emerging tobacco products; tobacco initiation, cessation and relapse behaviors among youth aged 12 to 17 and adults aged 18 and older. These longitudinal data will allow the PATH Study to generate research hypotheses regarding relationships between tobacco exposure and use, health conditions, and the onset and progression of disease processes. The target baseline sample size is approximately 45,675 (31,625 adults and 14,050 youth), and the target Wave 2 sample size is 41,745 (29,103 adults and 12,642 youth). The population for this study is the civilian non-institutionalized population in the United States (U.S.). The PATH Study oversamples tobacco users, young adults, and African American adults; and it uses a “wide net” definition (as described in detail in Supporting Statement B) of a tobacco user to capture adults who have had experience with a range of different tobacco products and who may be at risk of progressing to more frequent use.

This revision request is for OMB approval of the PATH Study's second wave (Wave 2) of data and biospecimen collection. The current plan is to follow the baseline cohort for three years, which is over the duration of the current PATH Study contract. Additional follow-up waves are under consideration pending the availability of funding. Each follow-up wave is planned for 12 to 13 months, with the possibility of 1 or more months of overlap between the waves. Wave 2 data and biospecimen collection is scheduled to begin in the fall of 2014. NIDA will submit revision requests to OMB for each of the PATH Study's waves of data collection. In addition, NIDA will submit requests to conduct sub-studies of potential changes to the PATH Study's protocol using one of its currently approved generic clearances, such as cognitive testing or methodological studies.

This revision request addresses the terms of clearance of OMB's approval of the PATH Study's baseline (OMB 0925-0664, expires 11/30/2015). The terms of clearance require a full revision for OMB approval of the PATH Study's second wave of data collection. In addition, prior to submitting the revision request to OMB, the terms of clearance stipulate that NIDA and FDA report to OMB the response rates associated with the baseline (screening, interview completion, and bio-specimen response), the results of non-response analysis and the statistical approach to address non-response, and the implications of these analyses for the main study going forward. (For additional information on the interim report, see Supporting Statement B, Section B.4 and Attachment 21.)

### **A.1b Critical Need for the PATH Study Data**

According to the 2014 Surgeon General's report on smoking (U.S. Department of Health and Human Services, 2014), approximately 480,000 U.S. deaths each year are from cigarette use and second hand smoke exposure, and an estimated 16 million smokers have at least one serious illness due to smoking. The 2012 National Survey on Drug Use and Health (NSDUH) reported an estimated 69.5 million Americans (26.7% of the population ages 12 and older) were past month tobacco product users; among current users, approximately 57.5 million persons (22.1% of the

population) were cigarette smokers; 13.4 million (5.2%) smoked cigars; 9.0 million (3.5%) used smokeless tobacco; and 2.5 million (1.0%) smoked tobacco in pipes (Substance Abuse and Mental Health Services Administration, 2012). The NSDUH also estimated that about 6,400 persons became new cigarette smokers in the U.S. every day in 2012, and that about half (51.4%) of new smokers in 2012 initiated prior to age 18. According to the 2013 Monitoring the Future, current smoking rates (i.e., any cigarette smoking in the prior 30 days) among 8th, 10th, and 12th graders were 4.5 percent, 9.1 percent, and 16.3 percent, respectively (Johnston et al., 2014).

On June 22, 2009, the Family Smoking Prevention and Tobacco Control Act (referred to herein by TCA) was signed into law. The TCA amended Section 201 of the Food, Drug, and Cosmetic Act (FD&C) (21 U.S.C. 321) by inserting Chapter 9 (“Tobacco Products”), Section 901, which authorizes FDA to regulate tobacco-product standards; tobacco-product manufacturing practices, distribution, and marketing; the labeling of tobacco products, including health warnings on tobacco-product packages and in ads; tobacco-product constituents, ingredients, and additives, including requirements for testing and reporting of harmful or potentially harmful constituents (HPHC) by brand and sub-brand; and restrictions on access to tobacco products, advertising, and promotions among youth. To fulfill the mandates of the TCA, the FDA requires a solid evidence base to inform its regulatory decisions, their implementation, and subsequent assessments of their effectiveness, as well as to support its future regulatory decisions and actions.

The NIH, through NIDA, is partnering with FDA’s Center for Tobacco Products (CTP) in a large-scale collaboration to conduct the PATH Study. This national longitudinal study of tobacco use and health will enhance the evidence base available to the FDA by providing in-depth epidemiological, population-based data on the use of existing and emerging tobacco products; on attitudes and perceptions related to the use of different existing and emerging tobacco products; on knowledge of the contents of tobacco products and of the consequences of their use; on tobacco-use cessation attempts, rates of relapse, and product switching, such as from one product to another perceived to be less risky; on biomarkers of tobacco exposure; and on indicators of tobacco-use related health conditions and disease processes.

By virtue of its longitudinal cohort design, the PATH Study provides a unique opportunity to monitor and assess behavioral and biological between-person differences and within-person changes over time in tobacco-product use and potentially related health conditions. Its cumulative data will provide population-based evidence on tobacco use behaviors, attitudes, exposures, and health in the United States to help inform the evidence base the FDA uses to fulfill its regulatory authorities under the TCA and to reduce the Nation's burden of tobacco-related diseases, disabilities, and deaths.

## **A.2 Purpose and Use of the Information Collection**

### **A.2a Objectives and Purposes/Uses**

In broad terms, the PATH Study's overarching mission is to gather and analyze epidemiological and longitudinal data on the use of the full range of tobacco products available now and in the future to enhance the scientific basis for FDA's regulatory decisions and actions, as well as the missions of NIH and other agencies within HHS in service to the Nation's public health. Components of the study include conducting annual computer-assisted interviews on tobacco-product use behaviors from a national longitudinal baseline cohort of 45,675 current, former, and never tobacco product users ages 12 years and older. In addition, in Wave 2, biospecimens (urine and blood) are collected from two subgroups of PATH Study respondents to assess biological indicators of tobacco-related exposures and to monitor between-person differences and within-person changes over time in measures of tobacco use-related harm.<sup>1</sup> First, urine specimens will be collected in Wave 2 from a subgroup of 10,000 "core respondents," adults who completed the Wave 2 interview and provided urine and blood specimens in the baseline wave. The PATH Study plans to collect urine specimens again in Wave 3 from this subgroup of 10,000 respondents and, in the event that respondents from the group leave the study, to replenish the sample to maintain a target of 10,000 continuing adult respondents who

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<sup>1</sup> During the baseline wave, buccal cells also were collected from adult participants, but this collection was discontinued before the end of the wave. No buccal cell collection is planned for Wave 2 or subsequent waves.



provide an annual urine specimen. Second, biospecimens will be collected in Wave 2 from the subgroup of aging-in adults, that is, youth from the baseline wave who turn 18 and continue into the adult cohort. The PATH Study plans to collect urine and blood specimens from these “new baseline” adult respondents.

The PATH Study has eight overarching objectives rooted in the scientific partnership between NIDA and FDA to enhance the evidence base available to FDA to inform its regulatory decisions and development of regulatory actions under the TCA. Its longitudinal design allows for the recurring and sequential achievement of each objective, i.e., data from the baseline wave will partially address each objective and provide a basis for comparisons with data collected in the follow-up waves. Similarly, data collected from Wave 2 will be helpful for informing Wave 3 (and potential future waves), for comparing data between waves, and for examining between-person differences and within-person changes over time. Thus, the PATH Study’s objectives will be achieved iteratively and cumulatively over time; they are numbered here for convenience purposes only. The objectives are:

- **Objective 1:** Identify and explain between-person differences and within-person changes in tobacco-use patterns, including the rate and length of use by specific product type and brand, product/brand switching over time, uptake of new products, and dual- and poly-use of tobacco products (i.e., use of multiple products within the same time period, and switching between multiple products).
- **Objective 2:** Identify between-person differences and within-person changes in risk perceptions regarding harmful and potentially harmful constituents, new and emerging tobacco products, filters and other design features of tobacco products, packaging, and labeling; and, identify other factors that may affect use, such as social influences and individual preferences.
- **Objective 3:** Characterize the natural history of tobacco dependence, cessation, and relapse including readiness and self-efficacy to quit, motivations for quitting, the number and length of quit attempts, and the length of abstinence related to various tobacco products.
- **Objective 4:** Update the comprehensive baseline on tobacco-use behaviors and related health conditions (including markers of exposure and tobacco-related disease processes identified from the collection

and analysis of biospecimens) to assess between-person differences and within-person changes over time in health conditions potentially related to tobacco use, particularly with use of new and different tobacco products, including modified-risk tobacco products. This comprehensive baseline may also facilitate the selection of individuals by disease status, biomarker levels, or tobacco use status for participation in small-scale research studies (see Objective 8).

- **Objective 5:** Assess associations between TCA-specific actions and tobacco-product use, risk perceptions and attitudes, use patterns, cessation outcomes, and tobacco-related intermediate endpoints (e.g., exposure and disease biomarker levels). Analyses will attempt to account for other potential factors, such as demographics, local tobacco-control policies, and social, familial, and economic factors, that may influence the observed patterns.
- **Objective 6:** Assess between-person differences and within-person changes over time in attitudes, behaviors, exposures to tobacco products, and related biomarkers among and within population sub-groups defined by racial-ethnic, gender, age, and risk factors (e.g., pregnancy or co-occurring substance use or mental health disorders).
- **Objective 7:** To the extent to which sample sizes are sufficient, assess and compare samples of former and never users of tobacco products for between-person differences and within-person changes in relapse and uptake, risk perceptions, and indicators of tobacco exposure and disease processes.
- **Objective 8:** Use the PATH Study's comprehensive baseline and first follow-up wave data on tobacco-use behaviors, attitudes, related health conditions (including markers of exposure, tobacco use-related disease processes identified from the collection and analysis of biospecimens) as a basis for screening respondents for participation in small-scale research studies. Such studies would be submitted for approval to OMB, for example, through one of the PATH Study's two generic clearances for cognitive testing or for methodological studies, or as an embedded study within a revision request, such as a request to conduct a small-scale research study during a follow-up wave of data and biospecimen collection.

## **A.2b Information to Be Collected**

The PATH Study will obtain completed interviews annually from a nationally representative sample of respondents 12 years of age and older. An adult extended interview will be administered to adults age 18 and older, a youth extended interview will be administered to youth ages 12 to 17 years, and a parent interview will be administered to parents of youth respondents. These instruments will also be tailored for those adults, youth, and parents of youth who age into the PATH Study cohorts (i.e., a youth who turns 18, a shadow sample youth who turns 12 years old, and the parent of a shadow sample youth who turns 12). Biospecimen collection at follow-up will include the collection of approximately 10,000 urines from a subsample of adults who provided a urine sample at baseline; and urine and blood from adults who enrolled as youth at baseline but have subsequently aged into the adult cohort and given consent for collections at Wave 2.

Table A-1 lists the PATH Study Wave 2 instruments and briefly describes the purpose and content of each. Attachment 2 includes the instruments; Attachment 3 provides the data sources, domains/questionnaire components, and analysis plan for each PATH Study Objective. Additional information on the instruments is summarized in the remainder of this section.

Table A-1. PATH Study Wave 2 instruments and data collected

PATH Study instrument	Data collected
Adult - Extended Interview	Tobacco use history for each tobacco product respondent uses; reasons for using each tobacco product; dependence on nicotine and tobacco products; interest in/experience with quitting; notice of/reactions to tobacco product packaging and health warnings; perceived risk of tobacco products; media awareness and use; secondhand smoke exposure; peer and family influences; health effects; advertising and promotion of tobacco; health promotion campaigns; other substance use; additional demographics; contact information.
Adult - Age-in Interview	Same as Adult - Extended Interview with additional questions that were removed for rotation from the re-contacted follow-up interview with adults who provided responses to those questions in a previous wave.
Adult - Biospecimen Collection Forms	Chemotherapy status, hemophilia or blood-clotting problems, time of last urination, time of last food intake, and time of last fluid intake.
Adult - Tobacco Use Form	Specific time of use and quantity used for 10 different tobacco products, nicotine replacement therapies, or prescription drugs for tobacco cessation.
Parent Interview - Parent of Youth	Respondent's relationship to the child, education, and tobacco use status (if not ascertained elsewhere); household rules about tobacco; perception of child's tobacco use; child's curfew, school performance, school missed due to illness, health (height, weight, health effects, medications, emergency room visits); parents who live elsewhere; tobacco availability at home; detailed contact information if not ascertained elsewhere.
Parent - Age-in Interview	Same as Parent - Parent of Youth with additional questions that were removed for rotation from the re-contacted follow-up interview with the parent who provided responses to those questions about their youth participant in a previous wave.
Youth - Extended Interview	Tobacco use characteristics; tobacco use history for each tobacco product the respondent may use; tobacco susceptibility (non-users); reasons for using tobacco and specific tobacco products; dependence on nicotine and tobacco products; interest in/experience with quitting; notice of/reactions to tobacco product packaging and health warnings; perceived risk of tobacco products; accessibility of tobacco; media awareness and use; secondhand smoke exposure; peer and family influences; health effects; advertising and promotion of tobacco; health promotion campaigns; other substance use; additional demographics.
Youth - Age-in Interview	Same as Youth - Extended Interview with additional questions that were removed for rotation from the re-contacted follow-up interview with youth who provided responses to those questions in a previous wave.
Adult, Youth - Follow-up/Tracking Participant Information Forms	For adult and youth participants, detailed contact information for those who have moved between waves. For shadow sample youth, detailed contact information for youth ages 9-11 who will be followed until age 12 when they will be invited to participate

### ***Parent Interview***

The parent interview collects personal information about the parent of a sampled youth, some general characteristics of the youth's household, information about the youth that can be obtained more accurately and reliably from the parent than from the youth, and contact information to support future data collection activities. This interview includes information about the youth respondent's life that may be associated with tobacco use, such as parental supervision, parental risk perceptions of tobacco use, school performance, and tobacco use by youth. Additionally, parents of youth who age-in to the youth cohort will be asked to complete the Parent - Age-in Interview, which collects information about youth who have aged into the youth cohort. These interviews include new items (e.g., parental risk perceptions) and items from the original baseline interview.

### ***Adult and Youth Extended Interviews***

The core content of the adult and youth extended interviews is based on conceptual models of how and why tobacco regulations exert an influence on proximal and distal behavioral and health outcomes (see Attachment 4). The PATH Study's adult and youth instruments include questions related to tobacco use history; tobacco warning labels; exposure to health promotion messaging and FDA and other National campaigns; product regulation; product characteristics (e.g., flavors, packaging, design); advertising and promotion; and tobacco product standards. Questions are included on the potential impacts of tobacco regulations on tobacco use behaviors, attitudes, biomarkers, and health, including tobacco product use, cessation, relapse, and initiation patterns and knowledge, attitudes, beliefs, and risk perceptions toward the use of tobacco products. Others are included to characterize the general population, including demographics; environmental factors and

family and peer influences; general health; and health effects that may be associated with the use of tobacco products.

Existing national, cross-sectional surveillance surveys helped inform the contents of the PATH Study instruments. For example, many of the tobacco-related questions in the Tobacco Use Supplement to the Current Population Survey (TUS-CPS), in the National Youth Tobacco Survey (NYTS), and in the National Health Interview Survey (NHIS) were adapted to assess the full array of tobacco products of interest to the PATH Study, including the use of electronic nicotine delivery systems (ENDS), such as e-cigarettes; and dissolvable tobacco. For example, the TUS-CPS question, “Have you ever smoked a cigarette, even one or two puffs?” was the basis for the PATH Study question “Have you ever used an e-cigarette, such as NJOY, Blu, or Smoking Everywhere, even one or two times?”

Nicotine dependence items in the PATH Study instrument were derived in part from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) survey.

Questions in the PATH Study about physical health endpoints were drawn from the National Health and Nutrition Examination Survey (NHANES), a national cross-sectional survey that includes tobacco-use questions in its instruments and collects biospecimens. Some of these items have been tailored to assess PATH Study-specific tobacco-related health conditions. For example, the NHANES item “In the past 12 months, have you been told by a doctor or other health professional that you had cancer?” has been modified for the PATH Study to “Have you ever been told by a doctor, dentist, or other health professional that you have pre-cancerous oral lesions?” Other health-related items in the PATH Study questionnaire are from standard screeners (i.e., the Global Appraisal of Individual Needs (GAIN) and the Patient-Oriented Outcomes Measurement Information System (PROMIS). For Wave 2, the PATH Study added some new questions; for example, questions on respiratory health conditions that were adapted from Phase 3 of the International Study of Asthma and Allergies in Childhood (Ellwood et al., 2005) for the youth questionnaire and the Asthma Control Test (Nathan et al., 2004) for both the youth and adult questionnaires.

The PATH Study questionnaires include items from other international, state, and privately funded tobacco surveillance surveys, such as questions about tobacco regulation which are based on International Tobacco Consortium surveys; the advertising items drawn from the Visual Media Influences on Adolescent and Young Adult Smoking Behavior surveys; the cessation and nicotine replacement items from the Minnesota Adult Tobacco Survey; and the items on secondhand exposure from the Global Adult Tobacco Survey and Massachusetts Tobacco Survey.

The PATH Study baseline instruments were reviewed to ensure that they maximize the utility of the data collected by capturing changing use patterns and practices in the context of the changing tobacco-product marketplace and regulatory environment while also minimizing burden on respondents, avoiding duplication with existing Federal surveys, and complying with HHS data standards. This review resulted in decisions to add, delete, and rotate various questions. For example, questions have been added to ask about awareness and use of ENDS other than e-cigarettes, such as e-cigars or e-hookah. See Attachment 5 for more details regarding content changes to the instruments from Baseline to Wave 2.

Over time, PATH Study longitudinal cohort data will be used to develop and refine taxonomies of tobacco user subgroups, such as those who begin tobacco use by first using smokeless tobacco; those who switch among types of products, including new and emerging products such as snus; those who use multiple types of tobacco products (e.g., combustible and smokeless); and those who seek to reduce their health risks while continuing to use tobacco by, for example, switching to products perceived to be less risky (e.g., e-cigarettes). The PATH Study includes items on perceptions of health risks from smoking and use of other tobacco products. It also has items in the health outcomes section to assess current and former tobacco-product use among women reporting to be pregnant.

Some questions in the baseline questionnaire have been deleted from the Wave 2 instruments because they refer to experiences that are unlikely to change from wave to wave. These items will be asked in alternating year

waves (e.g., at baseline, at Wave 3, and so on). This rotational approach is also used for items such as warning labels on cigarette packs (given that policies on warning labels have been stable in recent years and are unlikely to change between waves). Should these policies change, items will be added to questionnaires in future waves to capture respondents' perceptions about the changes. However, respondents who age into a new cohort (e.g., shadow youth who age into the youth cohort (12 year olds) and youth who age into the adult cohort (18 year olds) will receive the baseline version of the questionnaire in order to capture responses from the same questions initially asked of all participants in that age group. Respondents who completed their respective (youth or adult) questionnaire at baseline will complete the Wave 2 instruments at their next follow-up visit.

While it is expected that PATH Study data will allow the generation of cross-sectional prevalence estimates of health conditions by tobacco use sub-groups, this study is not specifically designed to provide such nationally-representative estimates of prevalence. In general, longitudinal studies tend to lose some of their representativeness over time, especially in the absence of cohort refreshment. As such, FDA and NIDA will present such cross-sectional prevalence estimates in conjunction with estimates from HHS' signature nationally-representative studies, including the National Cancer Institute's (NCI) TUS-CPS, the Substance Abuse and Mental Health Services Administration's (SAMHSA) NSDUH, the Centers for Disease Control and Prevention's (CDC) NHIS, and the CDC and FDA's National Adult Tobacco Study (NATS). These studies serve as the Nation's primary sources of nationally-representative prevalence estimates that are used in generating analyses on associations between tobacco use and physical and mental health outcomes.

### ***Biospecimens***

The PATH Study is planning to collect biospecimens from consenting adult respondents (age 18 and older) over multiple waves of data collection to assess between-person differences and within-person changes in markers of tobacco exposure, and to detect and compare indicators of health status and



disease processes associated with the use of tobacco products. These data will allow the PATH Study to identify and assess changes in the biomarkers that potentially correspond to changes in tobacco products by manufacturers, including changes resulting from a manufacturer's response to new product standards or regulations enacted by FDA. The PATH Study's longitudinal research design, combined with its detailed questionnaire and collection of biospecimens, is thus positioned to identify and assess changes in tobacco-use patterns, risk perceptions, attitudes, and exposures that inform, and potentially reflect, the tobacco-regulatory decisions and actions of the FDA under the TCA.

The rotational approach used for items in the PATH Study questionnaire is similarly applied to biospecimen collection. This approach allows the PATH Study to contain costs and minimize participant burden. Specifically, a subsample of the adult respondents who provided urine at baseline will be asked to provide a urine sample at Wave 2. Also, adult respondents who aged into the adult cohort (i.e., completed a youth interview at baseline but are 18 years old at Wave 2) will be asked to provide urine and blood at Wave 2. Biospecimens will be coded, de-identified, shipped, preserved, analyzed, and shared in accordance with rigorous provisions promulgated by the NIH on data access and security within the context of the privacy laws under which it operates (see Section A.10).

Both types of biologic samples collected by the PATH Study yields information that other sample media cannot. Collectively, they constitute a panel of biomarkers of exposure and susceptibility to disease associated with the use of tobacco products. Urine provides the matrix by which many tobacco-exposure biomarkers are measured, including nicotine and nicotine metabolites, tobacco specific nitrosamines, metals, and volatile organic compounds (VOCs). Blood collection will allow for the measurement of biomarkers that cannot be detected (or accurately measured) in urine samples. For example, the gold standard for measurement of cotinine in tobacco users and non-users is in serum. Serum provides a matrix in which low levels of cotinine (i.e., outside the limits of detection in urine) can be accurately measured. This lower limit of detection may also be important for assessing nicotine exposure related to use of smokeless tobacco, new and

emerging tobacco products, and comparison of products that may claim modified risk compared to traditional combustible tobacco products. Biomarkers of harm such as C-reactive protein (CRP) and interleukin 6 (IL-6) will be measured in serum and plasma (respectively) isolated from blood samples. In addition to serum and plasma, blood samples will allow for nucleic acid isolations (DNA and RNA) for genetic and epigenetic analysis from the buffy coat and hemoglobin adducts (4-ABP hemoglobin) from red blood cells. (Attachment 6 provides a list of specific analytes and their preferred matrix.)

### ***Tobacco Use Form***

The Tobacco Use Form is administered at each follow-up visit in which biospecimens are collected, unless the adult extended interview is administered during the visit or the biospecimen collection occurs more than four hours after the completion of the adult extended interview. (The adult extended interview incorporates all of the questions from the Tobacco Use Form.) This form collects the time that the respondent last used any type of tobacco products, including other sources of nicotine, such as pharmaceutical smoking cessation medications. Its purpose is to inform and qualify the laboratory analyses of the biospecimens, which are sensitive to recent use of various tobacco and nicotine-containing products.

### **A.2c Uses of Information by NIDA**

NIDA will use data collected by the PATH Study in conjunction with the existing scientific literature, to enhance the evidence base available to the U.S. government.

As a research study, the PATH Study will collect and analyze population-based data over time to enhance the evidence-based framework that FDA uses in meeting its regulatory mandates under the TCA. The PATH Study's baseline and Wave 2 data support this framework, first through the analyses of between-person differences in tobacco use behaviors and health and, over

time, by analyzing within-person changes, both in parallel with FDA's regulatory decisions and actions. Analyses include but are not limited to identifying key transitions in the course of nicotine dependence (from the earliest experiences of initiation, to daily use, poly-tobacco use, cessation attempts, and relapse) and assessing how these transitions are associated with tobacco use-related health conditions, the implementation of specific tobacco-related policies and programs, or changes in the tobacco product marketplace.

NIDA and FDA will also use data from the PATH Study to help elucidate factors that influence tobacco use behaviors among youth and adults; that shape beliefs, attitudes, and perceptions regarding new tobacco products (e.g., dissolvable tobacco products; snus; and ENDS, including e-cigarettes); that impact tobacco use-related health outcomes among key population subgroups; and that enhance knowledge of physiological changes associated with tobacco use and the natural course of nicotine dependence by examining biomarkers of exposure to tobacco products and of tobacco-use related disease processes.

#### **A.2d Use of Information by Other Agencies and Organizations**

As NIDA's principal partner in conducting the PATH Study, FDA plans to use the data to help inform its regulatory decisions and actions under the TCA. The TCA authorizes FDA to regulate tobacco-product advertising, labeling, marketing, constituents, ingredients and additives. The TCA mandates the regulation of tobacco products using a population health standard including users and non-users of tobacco products. FDA's Center for Tobacco Products (CTP) aims to prevent Americans from starting to use tobacco, to encourage current users to quit, and to decrease the harms of tobacco product use. Information from the PATH Study is critical to facilitating this mission. Its nationally representative longitudinal cohort design will provide epidemiological, population-based data on tobacco use behaviors, attitudes, exposures, and health to help inform FDA's regulatory decisions and actions under the TCA.

An important component of the PATH Study is the collection of biospecimens from respondents. NIDA supports FDA's approach for analyzing some of the biospecimens, which is through an inter-agency agreement with the Centers for Disease Control and Prevention (CDC). Through this agreement, CDC's Division of Laboratory Sciences will analyze a subset of the biospecimens collected in the PATH Study. NIH and FDA may consider making arrangements with other Federal as well as non-Federal laboratories for other biospecimen analyses. Examples of specific analytes that biospecimens collected in the study will be tested for are included in Attachment 6.

Because the PATH Study data are an invaluable research resource, they will be shared with the scientific community as well as with other agencies within HHS whose missions are in service to the Nation's health, such as the CDC. NIDA and FDA will create a public use dataset from each wave's data, making it available to the public on-line, consistent with OMB's Memorandum 13-13 (March 2013). The time period from completion of a wave to availability of a public use dataset is anticipated to be within 18 months. Data underlying all government-funded scientific publications will be made available to the public at the time of publication, to the greatest extent feasible and consistent with applicable laws. Such transparency is particularly important in the regulatory context (see the Office of Science and Technology's Scientific Integrity Guidance, December 2010).

Restricted use datasets not suitable as public use files will be deposited into a repository for data sharing purposes with qualified researchers who apply to the PATH Study Data Access Committee and obtain a Data Use Certification (DUC). NIDA and FDA will collaborate in developing plans for the repository for the PATH Study data and biospecimens, as well as plans for data disclosure, sharing, and confidentiality for qualified researchers with interests in analyzing the PATH Study data.

Data sharing plans promulgated by the NIH dictate dissemination of appropriately de-identified data. After PATH Study data are stripped of personally identifiable information (PII) and subjected to disclosure limitation procedures, the data sets will be deposited in a repository, such as the

National Addiction and HIV Data Archive Program (NAHDAP) at the University of Michigan's Inter-University Consortium for Political and Social Research (ICPSR). Data from other NIDA-funded research projects, including research studies and surveys, are routinely deposited in NAHDAP for public or restricted use.

### **A.3 Use of Information Technology and Burden Reduction**

The Privacy Impact Assessments (PIA) for the PATH Study Management System were promoted on July 6, 2012 (see Attachment 7). Appropriate technology will be used to keep respondent burden to a minimum.

Examples of information technology approaches to be used to minimize burden during the PATH Study data collection include:

- Use of automated audio computer-assisted self-interviewing (ACASI) extended instruments (separate instruments for youth and adults) and an automated CAPI parent instrument to collect PATH Study data;
- Use of flashcards or on-screen displays of lists and images to aid respondents with multiple response categories;
- Arrangement of sections and questions in the PATH Study extended interviews that will make sense to the respondents and will facilitate the flow of administration from one topic area to another;
- Use of data collectors who are bilingual in English and Spanish; and
- Use of all instruments, consent forms, and other study documents in Spanish where English is not spoken or it is the respondent's preferred language for the interview.

The majority of the PATH Study data will be gathered via computer-assisted questionnaires (i.e., CAPI or ACASI). The adult and youth questionnaires are designed with separate modules, and all but a few sections have lead-in questions that respondents can check for relevance in order to quickly skip out of non-relevant modules. This design was successfully used in the National Epidemiologic Survey on Alcohol and Related Conditions-III

(NESARC) study (OMB # 0925-0628, expiration date 4/30/2014). Brief tests of the PATH Study instruments with fewer than 9 individuals indicated that the average adult or youth respondent answered questions in about one-third of the total number of sections in the adult or youth instrument, respectively. Further, within each instrument, about one-third of the associated questions were applicable to any particular respondent, leaving two-thirds inapplicable and, therefore, requiring no answer from either the adult or youth respondent taking the respective interview.

#### **A.4 Efforts to Identify Duplication and Use of Similar Information**

Tobacco-related data collections supported by the Federal government and reviewed by OMB seek to harmonize their efforts to assure they maximize the utility of data collected, minimize burden on participants, and comply with HHS standards. NIH and FDA coordinate with the Assistant Secretary for Planning and Evaluation (ASPE) at HHS in an effort to facilitate the harmonization of existing questions and the reduction of any redundancy that may exist across tobacco-related data-collection efforts. From a feasibility perspective, requirements of the TCA give priority to the PATH Study for ensuring its collected research data are relevant to FDA's regulatory mission regarding the manufacture, marketing, and distribution of tobacco products. Consequently, within the limits and authorities of the TCA, the PATH Study has flexibility to integrate the data-collection needs of other HHS agencies, such as the CDC, by including questionnaire items and priority measures of shared interest.

The PATH Study design is intended for examining between-person differences and within-person changes in tobacco use behavior, exposure, and disease processes for a full range of new and emerging tobacco products. Its nationally representative prospective-cohort design was chosen for this purpose because it is the gold standard for generating epidemiological data on population trends and within-person changes in tobacco-use behaviors and tobacco-related knowledge, attitudes,

perceptions, biomarkers of exposure and harm, and tobacco-related health conditions.

There are national surveillance surveys on tobacco use in the U.S. (see Attachment 8). Key features of the PATH Study distinguish it from tobacco-specific surveillance surveys, as described below.

**Tobacco Surveys and the PATH Study.** The PATH Study's unique features distinguish it from tobacco surveillance surveys, such as the TUS-CPS, NYTS, and NATS. For example, the PATH Study, as a longitudinal cohort study, is designed for research purposes rather than to provide cross-sectional prevalence and incidence estimates. Its population-based behavioral and biospecimen data collection will support the generation and testing of research hypotheses over time, such as relationships between tobacco use-related risk perceptions, attitudes, behaviors, and associated markers of tobacco exposure and potential disease processes. As such, the PATH Study will provide a rich source of contemporary research data that, in conjunction with data from existing surveillance surveys, will help inform FDA's regulatory decision making and actions. For additional information on the PATH Study and on cross-sectional surveillance surveys on tobacco use, see Attachment 8.

In addition, as pointed out in A.2b, some items in the PATH Study questionnaires were selected because they harmonize with items in national surveys of tobacco use. For example, items for commonly-used tobacco products in the PATH Study have been adapted from the TUS-CPS. Some items in the PATH Study Youth Questionnaire have been adapted from the NYTS. A major difference between these studies and the PATH Study, however, is the PATH Study's capacity to replace questionnaire items between data waves to collect time-sensitive data about new and emerging product-use behaviors; this is one of the priority objectives of the PATH Study, i.e., to identify and examine between-person differences and within-person changes over time relative to the use of new and emerging types and brands of tobacco products.

**Longitudinal Design.** The PATH Study’s longitudinal design gives it the capacity to generate data on between-person differences and within-person changes in tobacco-use behaviors, attitudes and risk perceptions, biomarkers of harm associated with tobacco use, and related health outcomes over the lifespan. This is important for understanding factors associated with the uptake of new products, in product switching, in poly tobacco use, and in cessation and relapse among the same individuals followed over time. By contrast, cross-sectional surveillance surveys such as NYTS, NATS, and TUS-CPS are primarily designed to generate representative “snapshots” of the prevalence of given behaviors or conditions in the U.S. population at a specific point in time.

The PATH Study’s probability-based baseline sample ( $n=45,675$ ) is sufficiently large to generate data on between-person differences and within-person changes in use of the full-range of tobacco products (especially of emerging products). Although as a longitudinal study the PATH Study may become less representative with time, especially in the absence of cohort refreshment, its data will provide an important resources for understanding attitudes and risk perceptions, biomarkers of exposure and harm associated with tobacco use, tobacco dependence, and tobacco use-related health outcomes over the lifespan of the cohort. It will also permit estimates for given subgroups, such as non-cigarette tobacco users, or by subgroup characteristics, such as by race, ethnicity, gender, pregnancy status, or co-occurring health disorder. Additionally, the PATH Study will oversample Blacks/African Americans to increase the sample size of menthol smokers<sup>2</sup> for statistical analyses.

As a longitudinal cohort study, the PATH Study has the capability to follow youth as they age into young adulthood. This places the PATH Study in a position to assess between-person differences and within-person changes over the life course, from youth to adolescence, young adulthood, and adulthood, to understand contemporary trends in tobacco-use patterns, including onset and progression, cessation efforts and relapse, and successful cessation, all in the context of changes in the tobacco product

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<sup>2</sup> The 2010 rate of menthol cigarette use among Blacks/African Americans was approximately triple the rate among whites and five times the rate among Asians (SAMHSA, 2011).



marketplace, in marketing techniques and messages on different types and brands of tobacco products, and in FDA's regulatory decisions and activities.

**Focus on FDA Regulatory Issues.** The PATH Study will take place in parallel with the rollout of tobacco product regulations by FDA as authorized by the TCA. Timely population-based data on between-person differences and within-person changes in tobacco-product use behaviors and health from the PATH Study will help to inform FDA's regulatory decisions and actions, such as those related to requirements for warning labels, regulations on misleading brand descriptors, marketing, health promotion messaging and public education campaigns, and tobacco product standards.

**Scope of Data Collection.** The PATH Study is distinguished by the breadth and depth of its coverage of tobacco use, tobacco products (e.g., cigarettes; cigars; pipes; smokeless; and new and emerging products such as snus, hookah, and ENDS), and tobacco product brands and sub-brands. Data-collection methods, which include an image database of tobacco products, brands, and sub-brands, will enhance the specificity of the tobacco-use data, for example, by allowing the differentiation of traditional cigars, little filtered cigars, and cigarillos. It also provides for the assessment of respondents' recognition, exposure, and receptivity to tobacco marketing. In addition to respondent interview data, the PATH Study is collecting two biospecimens from consenting adults (i.e., urine and blood) at baseline to serve as the basis for examining and comparing biomarkers of exposure, including exposure to tobacco products, tobacco brands and sub-brands. For Wave 2, a subsample of adult respondents who provided a urine specimen at baseline will be asked to provide a urine sample at Wave 2. Also, adult respondents who aged into the adult cohort (i.e., completed a youth interview at baseline but are 18 years old at Wave 2) will be asked to provide urine and blood at Wave 2. This multi-component data-collection protocol distinguishes the PATH Study's capacity to enhance the evidence base FDA needs for its tobacco-related regulatory activities with timely, specific, population-based data.

## **A.5 Impact on Small Businesses or Other Small Entities**

No small businesses or other small entities will be involved in the PATH Study.

## **A.6 Consequences of Collecting the Information Less Frequently**

The longitudinal design of the PATH Study underscores the importance of maintaining its schedule of regular, annual waves of data collection with the same study respondents. The PATH Study will use follow-up, retention, and tracking materials (Attachment 9) to maintain contact with each respondent and to schedule regular, annual appointments with each respondent for their annual follow-up interviews. Less frequent data collection would impact the study's ability to retain cohort respondents and achieve its annual and overall target response rates. This would have implications for the scientific quality and utility of study data, particularly data that would inform the development of new TCA-related policies and programs.

Not conducting the PATH Study as scheduled (or delaying its annual follow-up interviews of each cohort respondent) would significantly reduce FDA's ability to capitalize on the strengths of the cohort study design to examine associations between enacted policies and tobacco use uptake, cessation, and relapse in the population. The dynamic environment of ever-changing policies and tobacco industry efforts requires annual data and biospecimen collection. For example, the PATH Study will subsample adults who gave a urine sample at baseline to provide a urine sample again at Wave 2. This will allow the PATH Study to characterize and compare within-person changes and between-person differences in the urine analyte signatures of tobacco users and non-users at two points in time. Urine collection at Wave 2 will also allow for the examination of tobacco exposure biomarkers in new and emerging products that may not have been on the market at the time of baseline data collection. Data collected less frequently would be considerably less precise, and would significantly decrease the capacity of

the study to meet the scientific needs of NIDA and FDA to establish a science framework that informs FDA's efforts to protect the Nation's public health.

## **A.7 Special Circumstances Relating to the Guidelines of 5 CFR 1320.5**

This project fully complies with the guidelines of 5 CFR 1320.5.

## **A.8 Comments in Response to the Federal Register Notice and Efforts to Consult Outside Agency**

### **A.8a Federal Register Notice**

The 60-day Federal Register Notice, required by 5 CFR 1320.8 (d) to solicit comments on the information collection prior to submission to the OMB, was published on February 6, 2014 in the Federal Register (Vol. 79, No. 25, pgs. 7206 – 7207). One comment was received, which was a letter in support of the collection of data for the PATH Study. The comment and NIDA's response to it are included in Attachment 10. The 30-day Federal Register Notice, submitted through the NIH Office of Management Assessment, was published on July 2, 2014.

### **A.8b Efforts to Consult Outside Agency**

Individuals from within NIH, FDA, and other units within DHHS and numerous outside agencies, institutions, and universities were consulted from October 2011 to the present, and these consultations are ongoing. The individuals consulted include the PATH Study biological workgroup, the questionnaire workgroup, the ad hoc study workgroup, and the sampling workgroup, which include individuals from Roswell Park Cancer Institute, Legacy/The Schroeder Institute for Tobacco, University of California San Diego Moores Cancer Center, University of Waterloo, Dartmouth College, The Medical University of South Carolina, Westat, CDC, and FDA. These workgroup members represent

experts in the fields of tobacco research and survey methodology, and provide significant input on questionnaire content, sampling design, and methodology. Numerous other individuals also contribute their expertise regarding sample design and methodology, questionnaire content, and related issues. The names, affiliations, and phone numbers of all individual consultants are presented in Attachment 11. During the aforementioned consultations, all issues raised were satisfactorily resolved.

## **A.9 Explanation of Any Payment or Gift to Respondents**

The design of the PATH study involves significant burden to respondents, both in terms of interview time, multiple visits, and the provision of biospecimens. To assist in meeting the response rate goals of the PATH Study, multiple incentives were offered to respondents during baseline data collection. Similar incentives are proposed to be offered as compensation for time and effort during Wave 2 (see Table A-2). Additional information on incentives in the PATH Study follows below.

- An incentive of \$35 will be offered to adult respondents who complete the adult extended interview at the Wave 2 home visit. This \$35 incentive payment is solely tied to a respondent's participation in the extended interview, regardless of whether he or she consents to provide biospecimens.
- At the Wave 2 home visit, an incentive of \$25 will be offered to newly aged-in adult respondents (i.e., youth from the baseline who have turned 18 years old and have consented to participate in the PATH Study as an adult) who consent to provide a urine sample.
- An incentive of \$25 will be offered to an adult respondent who provided a urine sample at the baseline and who, after completing the Wave 2 extended interview, is subsampled by an algorithm to provide another urine sample at Wave 2.
- An incentive of \$25 will be offered to newly aged-in adult respondents (i.e., youth from the baseline who have turned 18 years old and have consented to participate in the PATH Study as an adult) who consent to provide a blood sample.

- An incentive of \$10 is planned for parents who complete a parent interview.
- An incentive of \$25 is planned for youth who complete the youth extended interview.

Table A-2. PATH planned incentives for Wave 2

Activity	I n c e n t i v e
Adult Interview and Biospecimen Collection	
Adult Extended Interview	\$35
Biospecimen collection Visit #1 (urine - conducted by interviewer)	\$25
<ul style="list-style-type: none"> <li>• Youth aging into adult cohort</li> <li>• Subsample of eligible adults</li> </ul>	
Biospecimen collection Visit #2 (blood - conducted by health professional)	\$25
<ul style="list-style-type: none"> <li>• Youth aging into adult cohort</li> </ul>	
Youth Interview	\$25
Parent Interview*	\$10
Contact Information Update**	\$10

\* Parents receive \$10 for each interview they complete for a youth, and may complete a total of 2 interviews for 2 youth to receive a maximum of \$20. In households with multiple births, parents may complete a total of 4 interviews for 4 youth to receive a maximum of \$40

\*\* An adult respondent will receive \$5 for updating his/her contact information up to two times between data collection waves, for a total of \$10. A youth respondent will receive \$5 each time, up to two times, their parent updates the youth's contact information, for a total of \$10.

Use of separate incentives for completion of different components of a study was used in the baseline wave of the PATH Study and has been used by other studies approved by OMB (e.g., National Children's Study OMB #s 0925-0661, expiration date 6/30/2015; and 0925-0647, expiration date 1/31/2015).

To encourage retention of PATH Study respondents over time, an incentive will be offered to adult respondents who provide updates to their contact information in between data collection waves. Adults will receive \$5 each time they update their contact information up to a total of \$10 per year. Youth respondents will receive \$5 each time their parent updates their contact information up to a total of \$10 per year. Research supports the use of incentives such as this (i.e., between data collection waves), as they help to increase response rates and the amount of updated locator information received from respondents (McGonagle et al., 2011; Castiglioni et al., 2008).

Incentives will be described in PATH Study materials, including the study consent document provided to each “new” respondent prior to the start of the PATH Study extended interview (see Attachment 12). These materials will clearly state that incentives will be offered as a thank you for completing each visit and associated tasks (the first adult visit for completing the adult extended interview and separately, for consenting to and providing biospecimens; a second adult visit for consenting to and providing additional biospecimens; the parent interview; the extended youth interview; and for providing contact information for future follow-up by the PATH Study). Biospecimens will only be collected from adults who complete the PATH Study extended interview.

Thus, a new adult respondent at Wave 2 may receive up to \$95 as a thank you for participating in the PATH Study: \$35 for the Wave 2 extended interview, \$25 for urine collection at the first Wave 2 home visit, \$25 for blood collection at the second Wave 2 home visit, and an annual maximum of \$10 for updating contact information. An adult who participated at baseline, including providing urine, may receive up to \$70 as a thank you: \$35 for the extended Wave 2 interview at the home visit, \$25 if selected by algorithm to provide another urine sample, and an annual maximum of \$10 for updating contact information. Parents may receive up to \$20 for completing parent interviews for a maximum of two youth (\$10 as a thank you for completing each parent interview).<sup>3</sup> A youth respondent may receive up to \$35 for participating in the PATH Study: \$25 for completing the youth extended interview, and a maximum of \$10 for having their parent provide updated contact information.

The PATH Study proposes to pay some of the incentives by means of cash or check, and others by means of debit cards. For the group of identified 9 to 11 year olds, who are not yet enrolled in the PATH Study, the study will send cash when contact information is updated. Once an adult or youth participant is enrolled in the PATH Study, he/she receives a debit card. This debit card is then electronically loaded with the appropriate incentive

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<sup>3</sup> In households with multiple births, parents may complete a total of 4 interviews for 4 youth to receive a maximum of \$40.

amount, depending on the eligible activity. So, each time the respondent completes an eligible activity (e.g., updates contact information) the PATH Study will transfer the correct funds to the debit card within approximately 3 business days.

## **A.10 Assurances of Confidentiality Provided to Respondents**

### **A.10a Overview**

Concern for privacy plays a central role in the implementation of the PATH Study. Such protection is provided to respondents under the authority of 42 U.S.C. 241(d). The authority of 42 U.S.C. 241(d) has been delegated by the Secretary of Health and Human Services to NIH of which NIDA is a part. Any person engaged in the research to which this section applies, who desires authorization to withhold names and other identifying characteristics of individuals who are subject to such research from any person or authority not connected with the conduct of such research, may apply to the Office of the Director, NIDA for an authorization of confidentiality (also called a Certificate of Confidentiality or COC). Persons authorized by NIH to protect the privacy of research subjects may not be compelled in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings to identify them by name or other identifying characteristic. Because biospecimens will be collected and some questions may be of a sensitive nature, the COC will help researchers avoid involuntary disclosure that could expose participants or their families to adverse economic, legal, psychological, and social consequences. The COC issued to the PATH Study on August 31, 2012, and amended on June 6, 2013, is included in Attachment 13.

Law governing Federal employees conducting this research study, 18 U.S.C. 1905, (which prohibits disclosure of individuals' identifying information or confidential statistical data by Federal employees) is also relevant to the maintenance of confidentiality of data. In addition, all study activities under this contract will be conducted in compliance with 45 CFR Part 46, Protection



of Human Subjects, HHSAR 352.270-4(b) (January 2006), the Privacy Act of 1974, and the Systems of Records Notice 09-25-0200 (regulations pertaining to confidentiality of data).

The PATH Study will implement a range of procedures to protect respondents' Personally Identifiable Information (PII) and the confidentiality of all data. All data collection staff will be proficient in data security, confidentiality, and privacy issues and procedures. PATH Study field interviewers will be required to sign a pledge of confidentiality (see Attachment 14) and to complete training on standards and ethics in research, including detailed content on topics such as confidentiality and informed consent.

The privacy of study respondents will be protected through field procedures that ensure interviews are not overheard by others in the home, and the use of ACASI (Audio Computer-Assisted Self- Interviewing technology), which uses headphones to increase comfort levels and encourage honesty in answering sensitive questions. In the field, data will be collected on laptop computers that use advanced data encryption to protect confidentiality of data. Data from the laptops will be transmitted securely and directly to the research data warehouse maintained by the prime contractor, reducing risks associated with unsecured electronic data collected on laptops or transported on removable media.

Data will be identified by unique identification numbers assigned to each respondent. The ID numbers will link the respondent's extended interview responses with his or her own biospecimens. Crosswalks that match these numbers to PII will be stored in secure, encrypted files accessible only to authorized staff whose roles on the study necessitate access. NIDA will not have access to identifying information, and personal identifiers will not be included in the data received by NIDA. The prime contractor will transfer all data for the PATH Study and associated products and documents to NIDA at the time of compiling final data files, and will not retain any records of the data. Procedures for the storage and disposition of data collected as part of the PATH Study are described in Section A.10b.

All PATH Study respondents will be informed of the sponsor, the nature, purpose and uses of the study data, legal authorities, the voluntary nature of the PATH Study by data collectors prior to the collection of Wave 2 data. “New” respondents, (i.e., respondents who have aged into the youth or adult cohorts) will be informed in writing that the information they provide will be kept private to the extent permitted by law under the Privacy Act. Participation is voluntary; respondents may decline to answer particular questions without any consequence. An informed consent form, which includes descriptions of risks, benefits, and privacy protections, will be reviewed with each potential PATH Study respondent and will be signed by all those choosing to participate in the study. Separate consent forms (see Attachment 12) and procedures have been developed for adults and youth. For youth, parental permission will be obtained in writing prior to seeking youth assent to participate in the PATH Study. There is also a separate consent form for adult biospecimen collection. Information in the consent documents is presented in language that is easily understood and covers many topics, including the (1) voluntary nature of the data collection; (2) purposes and uses of the data; (3) storage and use of the biospecimen samples; (4) privacy of the information; (5) whether study results or information are available to the respondent; (6) benefits/risks; and (7) contact information regarding questions about the PATH Study.

As noted previously in A.3, two PIAs for the PATH Study were promoted on July 6, 2012 (see Attachment 7). The PATH Study also received approval from the prime contractor’s Institutional Review Board (IRB) (Attachment 15).

#### **A.10b Storage and Disposition of the Information**

Information collected in the PATH Study is covered by NIH Privacy Act SORN 09-25-0200, “Clinical, Basic, and Population-based Research Studies of the National Institutes of Health (NIH), HHS/NIH/OD” published in the Federal Register on September 26, 2002 (67 FR 60776) (Attachment 16). The NIH Privacy Act Officer has also reviewed the information contained herein and determined that the Privacy Act applies to the PATH Study data collection.

Compliance with the Privacy Act includes protections on identifying information residing in computer files. Data will be maintained in separate, encrypted tables, with password protection and access limited to authorized personnel. The PATH Study will comply with the Federal Information Processing Standards (FIPS PUB 41) and Computer Security Guidelines for Implementation of the Privacy Act of 1974, and FIPS PUB 73 (“Guidelines for Security of Computer Applications”). All staff members will complete regular trainings on information security, including the NIH training on data security. Authorized users will have access to research data free of PII only behind a secure data firewall that will not permit downloading or printing of data. In addition, no individual names or other identifiers will ever be reported to NIDA, FDA, or to any other government agency.

Study data will be identified and retrieved by a study number only. Investigators will not have access to PII. The majority of data collected in this study will be captured electronically, avoiding concerns of hard-copy storage of materials that contain PII. Hard-copy data forms will be identified only by a study identification number and will be stored in locked files at the contractor’s facilities. The datasets collected will be maintained until the completion of the study or until they are no longer required for research purposes.

The prime contractor for the PATH Study is responsible for storing identifiers in a secure, database environment in accordance with the security guidelines defined by the Federal Information Security Management Act (FISMA) and NIST Special Publication 800-53 for Moderate information system security. All systems and databases handling or storing PII and/or PHI (protected health information) will be reviewed for FISMA compliance by the NIDA Chief Information Officer (CIO) and Information Systems Security Officer (ISSO), and will not be operated in production mode until granted an Authority To Operate (ATO) by NIDA. All computerized data will be maintained in a manner that is consistent with the FISMA Moderate requirements. No reports or analysis files will contain PII. A complete list of the procedures the contractor will take to keep the study data private is found in Attachment 17.

Access to the PII is limited to a small number of immediate staff working on the study, and all staff members will sign a pledge of confidentiality prior to beginning work (see Attachment 14). In addition, all contract staff members are required to undergo background screening commensurate with their role on the project and their access to study data, and are required to complete NIH Computer Security Awareness Training as well as Privacy Awareness Training.

The prime contractor will share PII only with a single subcontractor responsible for collecting blood biospecimens from consenting adult respondents. This subcontractor's staff phlebotomists will receive PII because they will need to visit adult respondents who consent to provide biospecimens to obtain samples of their blood. As with the prime contractor, this subcontractor will not receive any PII until their secure database environment is in accordance with the security guidelines for FISMA Moderate information system security, and is reviewed for FISMA compliance by the NIDA CIO and ISSO and given ATO by NIDA.

A detailed inventory of all files, including hard copy consent forms, which include respondent names, and all other PII, will be secured separately from research data and accessible only to authorized staff. All records, including hard copies of informed consent and other documentation, will be retained and disposed of under authority of the NIH Records Control Schedule contained in NIH Manual Chapter 1743, Appendix 1B "Keeping and Destroying Records" (HHS Records Management Manual, Appendix B-361) (see Attachment 16).

### **A.10c Plans for Data Sharing**

NIDA will work with FDA and the prime contractor to create a public use dataset from each wave's data and make it available to the public online, consistent with OMB's Memorandum 13-13 (March 2013). The time period from completion of a wave to availability of a public use dataset is anticipated to be within 18 months. Data underlying all government-funded scientific publication will be made available to the public at the time of

publication, to the greatest extent feasible and consistent with applicable laws. Such transparency is particularly important in the regulatory context (see the Office of Science and Technology's Scientific Integrity Guidance, December 2010).

Another version of the PATH Study data, unsuitable for a public use file, will be stored in a repository. NIDA and FDA will develop plans for a repository for the PATH Study data, including plans for data disclosure, sharing of data between NIDA and FDA and with researchers, and confidentiality requirements for qualified researchers interested in working directly with NIDA and FDA to analyze the PATH Study data and biospecimens. Data sharing plans promulgated by the NIH dictate dissemination of appropriately de-identified data; and, as explained in Section A.2d, PATH Study data that have been stripped of PII and subjected to disclosure limitation procedures may be deposited in a repository such as the ICPSR's NAHDAP, where data from NIDA-funded research projects are routinely deposited for public or restricted use.

Researchers interested in accessing PATH Study data will be required to apply to the PATH Study Data Access Committee (DAC), to be established by NIDA and the FDA. This committee will work with the data repository, such as ICPSR's NAHDAP, to manage access to the data repository and track the progress of researchers who receive approval.

Upon receiving DAC approval, researchers will be required to submit a Data Use Agreement to the data repository, such as NAHDAP/ICPSR (see Attachment 18), to gain access to the restricted data files. These data files will include PATH Study questionnaire data and may include data from biospecimens; however, qualified researchers interested in accessing PATH Study biospecimens to conduct analyses will be required to apply to the PATH Study Biospecimen Access Committee (BAC). This committee will manage the sharing of biospecimens; instruct the PATH Study biospecimen repository subcontractor to ship specimens to approved labs/researchers; track the progress of researchers; and if necessary recall biospecimens.

## **A.11 Justification for Sensitive Questions**

As mentioned in Section A.1, data from the PATH Study will serve as a scientific framework to help inform Federal programs that aim to improve public health and reduce tobacco-related diseases, disabilities, and deaths in the U.S. population. To meet this purpose, the PATH Study asks questions about tobacco use. Additionally, as described in Section A.2, the PATH Study has eight objectives rooted in the shared scientific needs of NIDA, in service to its research mission, and of FDA to its mandate under the TCA. To meet these objectives, the PATH Study instruments include questions on other sensitive topics including: psychological problems and conditions; substance abuse; income; and sexual identity, orientation, and attraction. These questions relate directly to key outcomes or major correlates of tobacco use and health and are included in both the adult and youth instruments.

### **A.11a Tobacco**

The mission of CTP at FDA is to protect Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products; and by educating the public, especially young people, about tobacco products and the dangers their use pose to themselves and others. The PATH Study is central to this mission and will provide population-based scientific evidence to inform FDA's regulatory activities. Tobacco use questions are the critical core of the PATH Study. Without these questions, FDA's ability to achieve its mandated mission under the TCA would be significantly impaired.

The PATH Study's focus is on tobacco use. Most of the items in its instruments are similar to or slight variations of items common to widely-used surveys on tobacco that have been approved by OMB. The PATH Study adult instrument contains questions that assess tobacco use in great detail and breadth. Answers to these questions will provide a resource to NIDA and FDA to understand risk factors associated with tobacco use initiation, as well

as motivations for product-switching, use of multiple tobacco products, and quitting. Such questions are not generally considered sensitive when administered to adults.

Similar to the adult interview, the PATH Study youth interview contains questions that assess attitudes toward tobacco, and tobacco use in great detail and breadth. These questions, especially when asked of underage children, may be considered sensitive by at least a portion of parents or youth. (As described in Section A.10 several procedures will be implemented in the field to protect youth's privacy and ensure that he/she feels comfortable in answering the questions). The youth tobacco use questions are modeled on the Centers for Disease Control and Prevention's NYTS (OMB # 0920-0621, expiration date 1/31/2015); however, they have been expanded to cover a more diverse and specific array of tobacco products.

The PATH Study parent interview includes questions about the youth's tobacco use and future tobacco use. These are intended to provide context for the youth responses, and will be critical for future waves of data collection, particularly data on the youth's tobacco-use trajectory. Understanding the trajectories and transitions in tobacco use behaviors (e.g., onset, daily use, multiple product use, quitting attempts, relapse, and cessation) are essential to communicate effectively about tobacco products and the consequences of their use, as FDA is mandated by the TCA to do by educating young people.

### **A.11b Psychological Problems and Conditions**

Tobacco use is highly associated with an array of psychological problems and conditions, including depression and anxiety. Adults (John et al., 2004) and youth (Udaphyaya et al., 2002) with mental health concerns use tobacco at higher rates and find it more difficult to quit tobacco use (Snyder, 2006). Epidemiologic and clinical studies have shown that psychiatric disorders are important moderators of nicotine dependency severity (as measured by Fagerstrom Test of Nicotine Dependency or FTND scores, for example), withdrawal, craving, quitting, and responses to changes in cigarette pricing.

As reported by Legacy (2012), “People with mental illnesses smoke at rates almost twice as high as the general population (41 percent versus 22.5 percent, respectively). Nearly half the cigarettes smoked in the United States (44-46 percent) are consumed by people with co-occurring psychiatric or addictive disorders.” Moreover, remission from nicotine was moderated by comorbid psychiatric disorders and substance use disorders, findings that have been replicated in cross-sectional and longitudinal analyses. In summary, including these constructs in PATH Study instruments will facilitate understanding of how various program and policy changes may affect tobacco use behaviors in the population.

Questions dealing with depression, anxiety and personality traits and disorders have appeared frequently in national surveys of the general population since the early 1980s. These include the National Institute of Mental Health’s Epidemiological Catchment Area Survey (ECA), fielded between 1981 and 1985 and its 1990-1992 and 2001-2002 National Comorbidity Surveys (NCSs); supplements to the NCHS NHIS in 1983, 1988, and 1991; CDC’s Behavioral Risk Factor Surveillance System since 1980; and in 15 National Institute on Alcohol Abuse and Alcoholism (NIAAA) supported national surveys conducted by the Alcohol Research Group since 1991. An analysis of all these surveys indicates that questions about psychological problems and conditions were not considered sensitive by respondents. Nonresponse for these questions was extremely low (i.e., less than 4.0 percent), comparable to questions not normally regarded as sensitive.

The PATH Study has developed a handout (see Attachment 19) that provides respondents with national help lines for problems with tobacco, alcohol, drug, and mental health issues. This handout will be provided to all interviewed persons who express an interest in getting help with one of these problems.

To assess potential associations between tobacco use and psychological problems and conditions, the PATH Study adult and youth interviews include items from the GAIN SS. These are a series of questions designed to identify respondents who have one or more behavior health disorders, including



internalizing or externalizing psychiatric disorders and substance use disorders.

### **A.11c Substance Use**

Use of substances, including the use of alcohol and tobacco, frequently co-occurs; substance abuse and substance use disorders are often found to be comorbid conditions. In numerous household surveys conducted since 1960 in the U.S., results indicate that questions on substance use are not considered to be sensitive by respondents. Item nonresponse for such questions tend to be low (generally below 5.0 percent), and interview break-offs and refusals to these questions are generally negligible (below 1.0 percent). Examples of these surveys, all of which obtained OMB approval, include: SAMHSA's NSDUH, conducted since the early 1980s (OMB # 0930-0110, expiration date 8/31/2014); the Bureau of Labor Statistics' National Longitudinal Survey of Youth (NLSY), conducted periodically since 1973 (OMB # 1220-0109, expiration date 12/31/2013); and CDC's NHANES (OMB # 0920-0950, expiration date 11/30/15). The PATH Study adult and youth interviews include questions on substance use, including alcohol. The adult interview includes questions on use of substances during pregnancy.

### **A.11d Income**

The PATH Study does not ask questions about salary, which is considered by many people to be sensitive. Instead, the adult and parent interviews include one item about household income. Collecting information about household income is important for analysis of nonresponse and potential cofactors. The wording of this item was adapted from NHANES so that it could be a self-administered item (rather than an interviewer-administered item); it includes household income categories that a respondent selects.

### **A.11e Gender Identity, Orientation, and Attraction**

A growing research base indicates that the prevalence of tobacco use among gay, lesbian and bisexual and transgender (LGBT) individuals in the U.S. is higher compared with persons who are heterosexual (King et al., 2012). Pollard et al. (2011) found that, for females, a change from self-reported heterosexual attraction to lesbian or bisexual attraction was more predictive of higher smoking trajectories and differences in smoking patterns when compared with females who reported no change in sexual attraction. These differences point to the need for careful analyses of the PATH Study to account for these potential co-factors.

The PATH Study adult interview includes two questions that ask about gender identity/sexual orientation. The sexual orientation question is similar to the question asked in the baseline from the NHIS 2013 (Miller, et al, 2011), except it omits a follow-up question to the “something else” response option. The gender identity question is based on the Massachusetts State Optional Module for the 2014 Behavioral Risk Factor Surveillance System (MA-BRFSS, 2014); it includes a follow up question for respondents who identify as transgender. The PATH Study youth interview includes the same two questions for youth ages 14 to 17 years of age. Items similar to these have been tested and used in the 2001 to 2009 school-based survey, the Youth Risk Behavior Surveillance System (YRBS), conducted among students in the same age group (14 to 17 years) in grades 9 to 12 (CDC, 2011).

The PATH Study includes one item on the respondent’s level of attraction to both sexes, asked of adults (#AM0021 in the adult interview) and of youth ages 12 to 17 years (#YM0021 in the youth interview). This item is from the National STD and Behavior Measurement Experiment (NSBME), as modified from the National Survey of Sexual Attitudes and Lifestyles (NATSAL); (Villarroel et al., 2008). It was selected and recommended for inclusion in the PhenX Toolkit by an NIH panel of experts for use in all studies that measure sexual attraction (Hamilton et al., 2011).

## **A.12 Estimates of Annualized Burden Hours and Costs**

Table A-3 presents the estimated annualized burden hours for the Wave 2 data collection, the total of which is 56,939. Annualized cost to respondents associated with the PATH Study for the Wave 2 data collection is presented in Table A-4. Burden estimates are based on the results from the baseline data collection. These estimates include the time needed to read introductory text; provide consent (as appropriate); complete the entire interview and biospecimen collection (as appropriate); and, potentially, respond to the data quality verification interview. The reduction of 79,950 estimated burden hours between the first wave (136,889) and the second wave (56,939) is attributed to the following: (1) Wave 2 does not have a screening phase; (2) as indicated in Supporting Statement B, an 86 percent response rate for adult interviews and a 90 percent response rate for youth interviews are projected for Wave 2; and (3) fewer biological samples will be collected in Wave 2.

The estimate for adult hourly wages is based on the national median hourly estimate for all occupations reported in the Bureau of Labor Statistics' Occupational Employment Statistics, May 2013 National Occupational Employment and Wage Estimates United States. See [http://www.bls.gov/oes/current/oes\\_nat.htm](http://www.bls.gov/oes/current/oes_nat.htm). The estimate for youth hourly wages is based on the federal minimum wage. See <http://www.dol.gov/dol/topic/wages/minimumwage.htm>.

Table A-3. PATH Study Wave 2 hour burden estimates

Type of respondent and instrument	Estimated number of respondents	Estimated number of responses per respondent	Average burden hours per response	Estimated total annual burden hours requested
Adults – Baseline adult respondents -Extended Interview	27,113*	1	1	27,113
Adults – Baseline youth respondents who age into adult cohort – Consent for Extended Interview	2,295	1	2/60	77
Adults – Baseline youth respondents who age into adult cohort – Extended Interview	1,990*	1	68/60	2,255
Adults – Baseline youth respondents who age into the adult cohort -- Consent for Biological Samples	1,990	1	4/60	133
Adults – Biospecimen Collection: Urine	11,373	1	10/60	1,896
Adults – Biospecimen Collection: Blood	896	1	18/60	269
Adults – Tobacco Use Form	12,269	1	4/60	818
Adults – Follow-up/Tracking Participant Information Form	33,615	2	8/60	8,964
Youth – Extended Interview	10,537**	1	32/60	5,620
Youth – Shadow youth who age into youth cohort -- Assent for Extended Interview	2,338	1	2/60	78
Youth – Shadow youth who age into youth cohort – Extended Interview	2,105**	1	42/60	1,474
Adult – Parent Interview	10,748	1	14/60	2,508
Adults – Parents of Shadow youth who age into youth cohort – Parent Permission and Consent for Parent Interview	2,338	1	2/60	78
Adults – Parents of Shadow youth who age into youth cohort -- Parent Interview	2,147	1	17/60	608
Adults – Follow-up/Tracking Participant Information Form for	14,165	2	8/60	3,777

Youth (completed by parents)						
Adults – Follow-up/Tracking Participant Information Form for sample Shadow youth (completed by parents)	4,772	2	8/60			1,273
Total						56,939

\* Estimated total number of adult extended interview respondents is 27,113 + 1,990 = 29,103.

\*\* Estimated total number of youth extended interview respondents is 10,537 + 2,105 = 12,642.

Table A-4. PATH Study Wave 2 annualized cost to respondents

Type of respondent and instrument	Number of respondents	Frequency of response	Average time per respondent	Annual hour burden	Hourly wage rate	Respondent cost
Adults – Baseline adult respondents - Extended Interview	27,113	1	1	27,113	\$16.87	\$457,396
Adults – Baseline youth respondents who age into adult cohort – Consent for Extended Interview	2,295	1	2/60	77	\$16.87	\$1,299
Adults – Baseline youth respondents who age into the adult cohort -- Extended interview	1,990	1	68/60	2,255	\$16.87	\$38,042
Adults – Baseline youth respondents who age into the adult cohort -- Consent for Biological Samples	1,990	1	4/60	133	\$16.87	\$2,244
Adults – Biospecimen Collection: Urine	11,373	1	10/60	1,896	\$16.87	\$31,986
Adults – Biospecimen Collection: Blood	896	1	18/60	269	\$16.87	\$4,538
Adults – Tobacco Use Form	12,269	1	4/60	818	\$16.87	\$13,800
Adults – Follow-up/Tracking Participant Information Form	33,615	2	8/60	8,964	\$16.87	\$151,223
Youth – Extended Interview	10,537	1	32/60	5,620	\$7.25	\$40,745
Youth – Shadow youth who age into youth cohort -- Assent for Extended Interview	2,338	1	2/60	78	\$7.25	\$566
Youth – Shadow youth who age into youth cohort-- youth Interview	2,105	1	42/60	1,474	\$7.25	\$10,687

Adult - Parent Interview	10,748	1	14/60	2,508	\$16.87	\$42,310
Adults - Parents of Shadow youth who age into youth cohort - Parent Permission and Consent for Parent Interview	2,338	1	2/60	78	\$16.87	\$1,316
Adults - Parents of Shadow youth who age into youth cohort - Parent Interview	2,147	1	17/60	608	\$16.87	\$10,257
Adults - Follow-up/Tracking Participant Information Form for Youth (completed by parents)	14,165	2	8/60	3,777	\$16.87	\$63,718
Adults - Follow-up/Tracking Participant Information Form for sample Shadow youth (completed by parents)	4,772	2	8/60	1,273	\$16.87	\$21,476
Total						\$891,600

\* Estimated total number of adult extended interview respondents is 27,113 + 1,990 = 29,103.

\*\* Estimated total number of youth extended interview respondents is 10,537 + 2,105 = 12,642.

### **A.13 Estimate of Other Total Annual Cost Burden to Respondents or Record Keepers**

The PATH Study has no other annual cost burden to respondents or Record Keepers. This study has no capital, operation or maintenance costs.

### **A.14 Annualized Cost to the Federal Government**

This project is a multi-year, continuous activity, with interviews, biospecimen collection, and data processing occurring simultaneously. It is conducted by a contractor with oversight, management, scientific direction, and analyses by federal and contractor staff at NIH/NIDA, FDA, and CDC. The PATH Study contract is funded by FDA through an Interagency Agreement (IAA) to NIH/NIDA using tobacco user fees assessed under the authority of the TCA (PL 111-31, June 22, 2009). CDC's laboratory oversight, management, and biospecimen analyses for the PATH Study are similarly funded by FDA through an IAA to CDC. Estimates in Table A-5 are presented as the annualized cost to the U.S. Government for this information collection.

Table A-5. Annualized cost to the Government for information collection

<b>Type of cost</b>	<b>Contract</b>	<b>Other</b>	<b>Total</b>
Study Implementation, Data Collection and Processing, Operations	\$61,000,000	--	\$61,000,000
NIH/NIDA and FDA Oversight, Monitoring, Scientific Direction, and Analyses	\$808,000	\$1,276,000	\$2,084,000
CDC Laboratory Oversight, Management, and Biospecimen Analyses	\$1,232,000	\$832,000	\$2,064,000
<b>Total</b>			<b>\$65,148,000</b>

### **A.15 Explanation for Program Changes or Adjustments**

This is a revision request (OMB 0925-0664, expires 11/30/2015) for the Population Assessment of Tobacco and Health (PATH) Study to conduct the second wave of data collection. There is a reduction of 79,950 estimated burden hours between the first wave (136,889) and the second wave (56,939). As noted in A.12, factors accounting for this reduction include the following: (1) the initial target sample size for the baseline (Wave 1) was reduced to a total of 45,675 respondents; (2) Wave 2 does not have a screening phase; (3) as indicated in Supporting Statement B, a 86 percent response rate for adult interviews and a 90 percent response rate for youth interviews are projected for Wave 2; and (4) fewer biological samples will be collected in Wave 2.

## **A.16 Plans for Tabulation and Publication and Project Time Schedule**

### **A.16a Plans for Tabulation and Publication**

Plans for tabulation, statistical analysis, and publication of the PATH Study data are driven by its research design and major objectives presented in Section A.2 and by FDA regulatory science priorities. As a longitudinal cohort study, the PATH Study involves repeated observations on the same individuals to examine between-person differences and within-person changes over the same period of time. Benefits of the longitudinal research design include observing changes more accurately over time because the same persons are observed at multiple points over the same temporal order of events. The PATH Study Wave 2 data will be used for comparison purposes with the baseline data. The baseline data provide a comprehensive assessment for the cohort that will serve as the “anchor” against which individuals will be compared to examine within-person changes over the follow-up waves. The Wave 2 data will also provide the PATH Study with the capability to screen respondents for participation in small-scale research studies, such as in cognitive testing or methodological studies under the PATH Study’s existing generic clearances, or in other types of research studies that focus on new and emerging tobacco-related issues and regulatory science priorities for FDA.

In addition, Wave 2 data will be used to inform the PATH Study’s major objectives, primarily by examining between-person differences in: (1) tobacco-use patterns, including specific product type and brand, product/brand switching over time, uptake of new products, and dual- and poly-use of tobacco products (i.e., use of multiple products within the same time period, and switching between multiple products) (Objective 1); (2) risk perceptions regarding HPHC, new and emerging tobacco products, filters and other design features of tobacco products, packaging, and labeling, and other factors that may affect use, such as social influences and individual preferences (Objective 2); (3) tobacco use dependence, cessation, and relapse, including readiness and self-efficacy to quit, motivations for quitting,



the number and length of quit attempts, and the length of abstinence related various tobacco products (Objective 3); and (4) potential early markers of tobacco use exposures and related disease processes (Objective 4).

Planned analyses after completion of the Wave 2 data collection will focus on characterizing change in various outcomes relative to the baseline and examining correlates of that change. Of interest, for example, are rates of tobacco product uptake between Wave 1 and Wave 2 and potential relationships between uptake and changes in risk perceptions. Additional interest focuses on inter-wave changes at the population level in tobacco use status (e.g., quitting, reducing consumption, or switching to one or more other products) relative to changes in health status indicators. Wave 1 data will be the basis for many of these analyses, although the longitudinal nature of the combined Wave 1 and Wave 2 data may also provide an opportunity for more in-depth analysis. (See Attachment 20 for detailed examples of some of the analyses planned after completion of the Wave 2 data collection.)

The PATH Study data will be used to assess and compare samples of former and never users of tobacco products for between-person differences and within-person changes in relapse and uptake, risk perceptions, and indicators of tobacco exposure and tobacco use-related disease processes. All such analyses will attempt to account for other potential factors that may influence these measures (e.g., demographics, local tobacco-control policies, and economic, social network, peer group, and family factors (Objectives 5 through 7). Major outcome variables represent dependent variables, while tobacco policy variables and major demographic and socioeconomic variables will serve as independent, confounding, mediating or moderator variables. Many of these analyses will include the use of logistic regression models, however, specific multivariate procedures will depend on: (1) basic characteristics of the outcome data (e.g., their continuous or discrete nature); (2) specific hypotheses or research questions being addressed; (3) whether the data meet underlying assumptions of the statistical model; and (4) sample size and power considerations for the specific multivariate analysis.

Additionally, as mentioned in Section A.2d, FDA has established a partnership with CDC to analyze a sub-set of PATH Study biospecimens. Examples of specific analytes for which some of the biospecimens will be tested are presented in Attachment 6. These analyses will allow the PATH Study to assess biomarkers of tobacco exposure as well as assess intermediate endpoints (i.e., markers of exposure and tobacco-related disease processes) and health outcomes.

### **A.16b Project Time Schedule**

The following table outlines the key activities and time schedules for the PATH Study Wave 2 data collection.

Table A-6. Wave 2 timeline

<b>Activity</b>	<b>Time schedule</b>
OMB approval of Wave 2 data collection	August, 2014
Begin Wave 2 data collection	2 Months after OMB approval
Process and clean questionnaire data	4 - 36 Months after OMB approval
Data Analyses	5 - 36 Months after OMB approval
Publish preliminary study results/release public use data files for questionnaire data	Within 18 Months after completion of data wave
Publish preliminary study results/release public use data files for biospecimen data	Within 18 months after completion of data wave

### **A.17 Reason(s) Display of OMB Expiration Date is Inappropriate**

There is no reason not to display the OMB expiration date for this data collection activity.

## **A.18 Exceptions to Certification for Paperwork Reduction Act Submissions**

This data collection activity does not seek any exception to the certification statement associated with 5 CFR.1320.9, Certification for Paperwork Reduction Act Submissions.

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