

**Supporting Statement A for:**

**The Population Assessment of  
Tobacco and Health (PATH) Study (NIDA)**

-

**Fourth Wave of Data Collection**

**OMB No. 0925-0664, Expiration Date:  
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This is a revision request (OMB number 0925-0664, expiration date 8/31/2018) for the Population Assessment of Tobacco and Health (PATH) Study to conduct the fourth wave of data collection. The PATH Study is collecting behavioral data and biospecimens among a national longitudinal cohort to assess within-person changes and between-person differences in tobacco-product use behaviors and related health conditions over time. Its longitudinal, population-based data will help to enhance the evidence base that informs FDA's regulatory actions under the Family Smoking Prevention and Tobacco Control Act (TCA) to protect the Nation's public health and reduce its burden of tobacco-related morbidity and mortality.

## **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 number 0925-0664, expiration date 8/31/2018) for the Population Assessment of Tobacco and Health (PATH) Study to conduct the fourth wave (Wave 4) of data and biospecimen collection.

Under data collection authorization of Title 42 USC 285o (Attach1.NIDA's Data Collection Authority), NIDA is partnering with FDA to conduct the PATH Study through Westat, the prime contractor. The PATH Study uses computer-assisted interviews and the collection of biospecimens to examine 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 a national cohort of 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 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 (see 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. Pending available funding, the PATH Study will follow the Wave 1 cohort every year or every other year over the next 9 years. Each wave will be conducted over a 12-month period starting on December 1 and ending a year later on November 30; Wave 4 is scheduled to begin on December 1, 2016.

The Wave 1 or baseline sample size was 45,971 (32,320 adults and 13,651 youth); and the Wave 2 sample size was 40,558 (28,386 adults and 12,172 youth). The target sample size of the current wave, Wave 3, is 38,772 (27,224 adults and 11,548 youth). This revision request is for the next wave, Wave 4. After sample replenishment, the target Wave 4 sample size is 49,210 (34,151 adults and 15,059 youth).

This revision request seeks OMB approval of the PATH Study for 14 months to cover Wave 4. This includes 12 months for the sample replenishment and the collection of interview data and biospecimens scheduled to begin in early December 2016, plus approximately 1 month to allow for possible rescheduling of interview appointments and approximately 1 additional month to close out lagged appointments for the collection of biospecimens (i.e., biospecimen collections can occur up to 3 weeks after interviews).

Next year, NIDA will submit a subsequent revision request for three years of data collection beginning in 2017. That request will be for OMB approval to submit nonsubstantive change requests for additional data collection waves that are within scope of the new revision request (i.e., do not require major change in the instruments or protocols); that are annual with subgroups of the cohort and biennial with the entire cohort; and/or that involve small-scale research studies with subsamples of the cohort, as described in Objective 8 (see Section A.2a). Attachments describing these activities will be included

as part of the new revision request to OMB. NIDA, in partnership with FDA, will submit a 30-day Federal Register Notice (FRN) with any such nonsubstantive change request, to give the public proper notice of the planned activities, pending approval by OMB.

In addition, under the two existing generic clearances for the PATH Study, one for cognitive interviews and focus groups, and one for methodological studies, NIDA will submit requests to OMB to conduct cognitive interviews, focus groups, and methodological substudies to help inform and improve the PATH Study's data collection instruments and protocols.

This revision request addresses the terms of clearance of OMB's approval of the Wave 3 PATH Study (OMB number 0925-0664, expiration date 8/31/2018), which require a full revision request for the next wave of data and biospecimen collection, Wave 4. Prior to submitting the revision request for Wave 4, the terms of clearance stipulate that NIDA and FDA should report to OMB on the: (1) response rates associated with the full baseline wave [and full Wave 2], including screening, interview completion, and biospecimen response; (2) Wave 3 retention and recruitment rates for the youth who age up to the adult cohort and for the shadow youth who age up to the youth cohort; (3) the results of nonresponse analysis and statistical approach for addressing non-response, as well as implications for the study going forward; and (4) the statistical approach to be applied to the biospecimen data to address potential nonresponse bias from lower consent and cooperation rates with this aspect of the study. NIDA and FDA submitted this report (Attach20.PATH Study Interim Report) to OMB on June 9, 2016 for its review and consideration. (For additional information on this report, see Supporting Statement B, Section B.4.)

### **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 deaths in the U.S. each year are from cigarette use and second hand smoke exposure, and an estimated 16 million people alive today have at least one

serious illness caused by smoking. The 2014 National Youth Tobacco Survey (NYTS) found nearly one out of four high school students (24.6%) and approximately one out of thirteen middle school students (7.7%) were tobacco users in 2014, and 49 percent of youth tobacco users report past use of more than one tobacco product (Arrazola et al., 2015). The 2014 National Survey on Drug Use and Health (NSDUH) reported "an estimated 66.9 million people aged 12 or older were current users of a tobacco product. These 2014 numbers correspond to 25.2 percent of the population being current users of tobacco products." Also, 55.2 million persons (20.8% of the population) were current cigarette smokers; 12.0 million (4.5%) smoked cigars; 8.7 million (3.3%) used smokeless tobacco; and 2.2 million (0.8%) smoked tobacco in pipes (Center for Behavioral Health Statistics and Quality, 2015, p. 15). According to the Monitoring the Future survey, daily cigarette smoking among 8<sup>th</sup>, 10<sup>th</sup>, and 12<sup>th</sup> graders has continued to decline. In 2014, daily cigarette smoking dropped to 1.4 percent (95% CI, 1.0-1.9%) among 8<sup>th</sup> graders, compared to 2.7 percent five years ago (95% CI, 2.2-3.4%); among 10<sup>th</sup> graders, it dropped to 3.2 percent (95% CI, 2.5-4.0%), compared to 6.3 percent five years ago (95% CI, 5.4-7.2%); and among 12<sup>th</sup> graders, it dropped to 6.7 percent (95% CI, 5.8-7.8%), compared to 11.2 percent five years ago (95% CI, 10.0-12.5%) (Johnston et al., 2010, 2015; Miech et al., 2015; L.D. Johnston, personal communication, September 2016). In addition, past 30-day e-cigarette use was more prevalent than cigarette smoking. In 2015, past 30-day use was 9.5 percent for e-cigarettes (95% CI, 8.3-10.6%) among 8<sup>th</sup> graders, compared to 3.6 percent for cigarettes (95% CI, 3.0-4.1%); among 10<sup>th</sup> graders, it was 14.0 percent for e-cigarettes (95% CI, 12.2-15.8%), compared to 6.3 percent for cigarettes (95% CI, 5.5-7.1%); and among 12<sup>th</sup> graders, it was 16.2 percent for e-cigarettes (95% CI, 14.6-17.9%), compared to 11.4 percent for cigarettes (95% CI, 10.3-12.4%) (Johnston et al., 2016; L.D. Johnston, personal communication, September 2016).

On June 22, 2009, the Family Smoking Prevention and Tobacco Control Act (TCA) was signed into law. The TCA amended Section 201 of the Federal 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.

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 provides 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 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 between-person differences and within-person changes over time in tobacco-product use and potentially-related health conditions. Cumulative data from the PATH Study on tobacco use behaviors, attitudes, exposures, and health in the United States help to enrich the evidence base that informs FDA's regulatory actions under the TCA to reduce tobacco-related diseases, disabilities, and deaths.

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

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

The mission of the PATH Study is to gather and analyze national epidemiological and longitudinal data on tobacco use behaviors and health in the United States. The study involves computer-assisted interviews on tobacco-product use behaviors with the national longitudinal cohort, which at the end of Wave 3 is estimated to include 38,772 current, former, and never tobacco product users ages 12 years and older. For Wave 4, we will replenish

the sample, targeting a total sample size of 49,210 (that is 3,239 greater than Wave 1). In addition, the PATH Study collects biospecimens (urine only or both urine and blood) from respondents to assess biological indicators of tobacco-related exposures and changes over time in measures of tobacco use-related harm. For Wave 4, the PATH Study will request (a) urine from a subsample of approximately 11,000 adults who initially provided urine at a previous wave; (b) both urine and blood samples from aged-up 18 year olds and new adults added during the replenishment, thus for whom Wave 4 is the baseline; and (c) urine from all continuing, aged-up, and new youth.<sup>1</sup>

The longitudinal design of the PATH Study allows for the recurring and sequential achievement of its eight key objectives. That is, data from each wave partially address each objective and provide a basis for comparisons with data collected in the succeeding waves. Data collected from Wave 4 will help to inform future waves, to provide for comparisons with data from preceding waves, and to examine between-person differences and within-person changes over time. Thus, the PATH Study objectives are expected to 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,

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<sup>1</sup> Continuing participants are persons who participated in a previous wave in the same age cohort. Aged-up adults are persons who were previously interviewed as youth and are newly eligible for the adult cohort. Aged-up youth are persons who were previously tracked as “shadow youth” and are newly eligible for the youth cohort. New participants are persons who are identified and recruited from the Wave 4 replenishment sample.

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 with subsequent waves of data 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. Each wave 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 subgroups 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 behaviors, risk perceptions, and indicators of tobacco exposure and disease processes.
- **Objective 8:** Use the PATH Study comprehensive baseline (i.e., Wave 1 for most of the cohort) and 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 potential basis to screen respondents for participation in small-scale research studies. Such studies would be submitted for approval to OMB, for example, through one of the two generic clearances for the PATH Study for cognitive interviewing and focus groups or for methodological studies, or as an embedded study within a revision request, such as a

nonsubstantive change request to conduct a small-scale research study during a follow-up wave of data and biospecimen collection.

While the PATH Study's data are expected to produce cross-sectional prevalence estimates of health conditions by tobacco use subgroups, its focus is on the examination of within-person changes and between-person differences in tobacco use behaviors and related health conditions within the cohort over time. In addition, as is characteristic of longitudinal cohort studies, the PATH Study may lose its representativeness over time, especially in the absence of cohort refreshment. However, in keeping with OMB's terms of clearance for the previous waves, the PATH Study will always present its cross-sectional prevalence estimates relative to the prevalence estimates generated by HHS's ongoing, nationally-representative survey studies, such as the National Cancer Institute's (NCI) Tobacco Use Supplement to the Current Population Survey (TUS-CPS), the Substance Abuse and Mental Health Services Administration's (SAMHSA) National Survey on Drug Use and Health (NSDUH), the Centers for Disease Control and Prevention's (CDC) National Health Interview Survey (NHIS) and National Health and Nutrition Examination Survey (NHANES), the CDC and FDA's National Adult Tobacco Study (NATS), and the CDC and FDA's National Youth Tobacco Survey (NYTS).

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

For Wave 4 and thereafter, the PATH Study will conduct interviews every year or every other year with cohort participants 12 years of age and older, most of whom have been followed since Wave 1 began in 2013. Prior respondents will complete either the adult extended interview (adults 18 years of age and older), the youth extended interview (ages 12 to 17 years old), and the parent interview (parents of youth respondents). For the Wave 4 cohort replenishment, instruments will be tailored to include baseline information for those adults, youth, and parents of youth who are new to the PATH Study (see details in Supporting Statement B) or as "aged-up" youth and adults (for details on "aged-up," see footnote in Section A.2a).

The information to be collected in these instruments is described in detail below. Table A-1 provides a brief description of the purpose and content of each instrument that will be used by the PATH Study for Wave 4. Attach2.PATH Study Data Collection Instruments includes the instruments; Attach3.Crosswalk of PATH Study Objectives, Data Sources, Domains, and Analysis provides the data sources, domains/questionnaire components, and analysis plan for each PATH Study objective. Additional information on the instruments is summarized in Attach4.Summary of Changes to Instruments for Wave 4 and in the remainder of this section; the household screener, shadow youth only screener, and adult individual screener, which are intended to support sample replenishment, are discussed in Supporting Statement B, Section B.2b.

Table A-1. PATH Study Wave 4 instruments and data collected

<b>PATH Study instrument</b>	<b>Data collected</b>
Household Screener (for sample replenishment)	Number and names of people in household; sex, age, active duty military status, ethnicity, race for each household member; tobacco use status for all adults; relationships among all sampled household members; residential tenure; contact information for household respondent; initial contact information for sampled adults and parents of sampled youth and shadow sample youth. Data are reported in computer-assisted personal interviewing (CAPI) mode by one household respondent about other household members.
Shadow Youth Only Screener (for sample replenishment)	Age categories for persons living in the household. First name of the screener respondent is requested. Additional “engaging” questions are included to encourage respondents to complete and return the questionnaire (see further details under the description of this instrument). Data are reported on a hardcopy form by one household respondent about other household members.
Adult – Individual Screener (for sample replenishment)	Sex, age, ethnicity, race; main tobacco use status (the basis for final adult sample selection). Data are reported in ACASI mode by each adult respondent for him or herself.
Adult – Extended Interview (for returning participants)	Detailed 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; tobacco susceptibility (non-users); notice of/reactions to tobacco product packaging and health warnings; perceived risk and harm of tobacco products; media awareness and use; secondhand smoke exposure; social norms, peer and family influences; health effects; family history; exposure to advertising and promotion of tobacco; exposure to health promotion campaigns; other substance use; additional

<b>PATH Study instrument</b>	<b>Data collected</b>
	demographics; contact information.
Adult - Baseline Interview) (for newly recruited and aged-up participants)	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, or adults who are new to the PATH Study as part of the replenishment sample.
Adult and Youth - 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 and Youth - Tobacco Use Form	Specific time of use and quantity used for 9 different tobacco products, nicotine replacement therapies, or prescription drugs for tobacco cessation.
Parent - Extended Interview (for returning participants)	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 - Baseline Interview (for newly recruited and aged-up youth)	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, or parents of youth who are new to the PATH Study as part of the replenishment sample.
Youth - Extended Interview (for returning participants)	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 and harm of tobacco products; accessibility of tobacco; media awareness and use; secondhand smoke exposure; social norms, peer and family influences; health effects; exposure to advertising and promotion of tobacco; exposure to health promotion campaigns; other substance use; additional demographics.
Youth - Baseline Interview (for newly recruited and aged-up youth)	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, or youth who are new to the PATH Study as part of the replenishment sample.
Adult - Verification Interview	Whether one or all of the participants still live at the most current home address, identification of another parent if the baseline parent is no longer living with a youth participant, and updated contact information on adult participants and parents.
Adult - Validation Interview	For adults who complete extended interviews, information that can be used to confirm the information recorded by field interviewers, and information on other aspects of interviewer performance.

<b>PATH Study instrument</b>	<b>Data collected</b>
Adult and 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 who will be followed until age 12 when they will be invited to participate in the PATH Study. Forms for youth and shadow sample youth are completed by parents.

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

The core content of the adult and youth instruments is based on conceptual models of how and why tobacco regulations exert an influence on proximal and distal behavioral and health outcomes (see Attach5.Sample Conceptual Models). The PATH Study adult and youth instruments include questions related to tobacco use history; tobacco warning labels; exposure to health promotion messaging and National campaigns by FDA, CDC, and others; 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.

The PATH Study’s instruments for Waves 1, 2 and 3 were developed to ensure they maximize the utility of the data collected while minimizing burden on respondents, avoiding duplication with existing Federal surveys, and complying with data standards of the U.S. Department of Health and Human Services (HHS). For Wave 4, the PATH Study uses an iterative, comprehensive approach to identify candidate items of interest to add to or delete from its instruments, to inform the development of new related items, or to modify items already adapted and used by the PATH Study in previous waves. When making decisions about instrument changes, the PATH Study weighs whether such changes impact the established trend line from

previous waves' data or lead to a net increase on respondent burden relative to prior waves.

The PATH Study's assessment of whether changes are required to the instruments is informed by several factors, including changes in the tobacco marketplace (e.g., the evolving e-cigarette marketplace, or new tobacco product images and terminology), regulatory actions and activities, and findings from previous waves of the PATH Study. These types of changes may necessitate questions being added (new or cycled in) or removed (deleted or cycled out); for any added item, the PATH Study identifies a corresponding item for deletion, thus assuring there will be no net increase in burden from one wave to the next. New questions added to the PATH Study's instruments are assessed to ensure they align with one or more of the PATH Study's eight primary objectives; that, as appropriate, they are consistent with tobacco surveillance systems; that they are not duplicative of other tobacco-related studies; and above all, that they are designed to inform the overarching purpose and objectives of the PATH Study to provide national epidemiological and longitudinal data on tobacco use behaviors and health in the United States over time.

The remainder of this section describes the PATH Study's process of adding questions from existing surveys, developing new questions, and deleting and cycling out questions; the section ends with a summary of changes to the Wave 4 instruments, including how new or cycled in questions align with the PATH Study objectives (see Table A-2).

**Adding Questions from Existing Surveys.** When assessing for questions to add to the instruments, the PATH Study reviews other existing Federal surveys for potential items of interest. When items in these existing surveys (e.g., NHIS, NHANES, TUS-CPS, NYTS, NSDUH) have been revised, the PATH Study must weigh the pros and cons of whether the same changes should be made in its items relative to the impact such changes might have on the aforementioned trend line. Finally, in an effort to harmonize and reduce potential overlap or redundancy among tobacco-related data-collection efforts, the PATH Study invites program leads on tobacco-related studies within NIH (e.g., NCI) and at HHS sister agencies (e.g., CDC, SAMHSA) to

review and provide comments on its proposed Wave 4 instruments (see “Efforts to Identify Duplication and Use of Similar Information” for further information). The PATH Study draws from several existing surveys to inform the tobacco- and health-related questions on the adult and youth instrument, described below.

- **Tobacco-related questions from existing Federal surveys--**  
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 TUS-CPS, in the NYTS, and in the 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. The PATH Study questionnaires also include items from other international, state, and privately funded tobacco surveillance systems, such as questions about tobacco regulation that are based on International Tobacco Consortium 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. For Wave 4, for example, the PATH Study included items to assess how often respondents read, looked closely at, or thought about warning labels on ENDS, traditional cigars, cigarillos, filtered cigars, and hookah (ITC).
- **Health-related questions from existing Federal surveys--**  
Questions in the PATH Study instruments about physical health endpoints were drawn and adapted from the NHANES, a national cross-sectional survey that includes tobacco-use questions in its instruments and collects biospecimens. Other health-related items in the PATH Study questionnaire are drawn and adapted from standard screeners (i.e., the Global Appraisal of Individual Needs (GAIN) and the Patient-Oriented Outcomes Measurement Information System (PROMIS) and from health-related studies (e.g., the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)). Health-related items added in Wave 4 include those to assess the frequency of tooth brushing (NHANES) and a diagnosis of schizophrenia and psychosis (NESARC).

Table A-2. Alignment of new and cycled in Wave 4 questions with PATH Study objectives

Topic of new or cycled in question	P r i m a r y P A T H  S t u d y o b j e c t i v e ( s )
Respondent's sex, race, ethnicity, active duty military status, and residency in the U.S. during 2014	D e m o g r a p h i c s
Whether respondent has heard of a given product (not including cigarettes), and whether respondent has ever used a given product (including blunts)	1 , 4
Likelihood of smoking a cigarette of hookah, or using smokeless tobacco soon among non-users	1
Age first smoked/used a cigarette, cigar, pipe, hookah, snus, smokeless tobacco, or ENDS and on the amount smoked 12 months ago	1 , 4
Whether favorite cigarette to smoke is the first one in the morning, if they smoke more frequently in the first hours after waking, and if they smoke	3

Topic of new or cycled in question	P r i m a r y P A T H  S t u d y o b j e c t i v e ( s )
when they are ill	
Frequency of flavored cigars (including blunts), hookah, snus, smokeless tobacco, and ENDS used in the past 30 days	1 , 4
Dual use of cigarettes and ENDS	1 , 4
Frequency of using ENDS to smoke marijuana or marijuana derivatives	1 , 4
Number of times ENDS used on average day and number of puffs taken each time	1 , 4
Use of pouched or loose snus or smokeless tobacco	1 , 4
Reasons for using nicotine replacement therapy (NRT)	1 , 2
Whether respondent noticed health warnings on packages of ENDS, cigars, pipe tobacco, and hookah tobacco	2
Health warning labels on ENDS, cigars, hookah packages, including how often a respondent	2

Topic of new or cycled in question	P r i m a r y P A T H  S t u d y o b j e c t i v e ( s )
looked closely at them and how they make a respondent feel about the health risks associated with use	
Perceived harmfulness of the nicotine in cigarettes, ENDS, and NRT	2
Perceived addictiveness of reduced nicotine cigarettes	2
Perceived harm of using flavored ENDS compared to tobacco-flavored or unflavored ENDS	2
Perceived harm of using e-cigarettes/ENDS compared to NRT	2 , 3
Frequency of tooth brushing	4
Diagnosis of schizophrenia, schizoaffective disorder or psychosis, or psychotic illness or episode and age of diagnosis/onset	4 , 6
Pregnancy history	4 , 6
Substance history of alcohol, marijuana, prescription drugs of abuse, and illicit/street drugs	4
Branch of respondent's favorite advertisement for ENDS and other tobacco	2
Use of cigarettes, ENDS, pipes, cigars, blunts,	4

Topic of new or cycled in question	P r i m a r y P A T H  S t u d y o b j e c t i v e ( s )
hookah, snus, and smokeless tobacco, and/or NRTs in the past 3 days and identifying last brand smoked	
Quantity contained in a package of pouched smokeless tobacco and length of time taken to consume it	1 , 4
Perceived harm of intermittent versus daily use of cigarettes, cigars, snus, and smokeless tobacco	2
Length of time product can be used before harm occurs from use of cigarettes, cigars, hookah, snus, or smokeless tobacco	2
Use of inflammatory medications	4
Exposure to anti-tobacco messaging	2
Serving active duty in the military and branch in which respondent served	D e m o g r a p h i c

Topic of new or cycled in question	P r i m a r y P A T H  S t u d y o b j e c t i v e ( s )
	s
Interest in completing web-based PATH Study survey	D a t a c o l l e c t i o n

**Developing New Questions.** In some instances, existing surveys do not contain questions that the PATH Study can draw from in order to address the study objectives, leading the PATH Study to develop and add new items. For Wave 4, this was accomplished through formative research through the PATH Study’s Generic Clearance for Cognitive Interviews and Focus Groups (OMB number 0925-0663; formerly titled “Cognitive Testing of

Instrumentation and Materials for the PATH Study”). Cognitive interviews were conducted with separate samples of adults and youth to evaluate potential problems with existing questions and develop new questions with regard to use of electronic nicotine devices and products, smokeless tobacco products, and snus. Focus groups were also conducted with separate samples under the PATH Study’s Generic Clearance for Methodological Studies (OMB number 0925-0675) to help inform changes in existing questions and the development of new questions on such topics as dual use and polyuse of tobacco products, use of social media, and perceptions of harm associated with the use of tobacco products.

In other instances, existing surveys might contain questions of interest but require refinements or modifications, such as when the PATH Study adapts a question about cigarettes from other tobacco surveys to be asked about non-cigarette products. In addition, the PATH Study regularly reviews the performance of questions from previous waves to detect potential anomalies in item responses and response patterns. If potential anomalies are detected, the PATH Study explores the issue further before including the question on the Wave 4 instrument.

**Deleting and Cycling out Questions.** Once potential additions and refinements to items are identified and/or developed, the PATH Study uses a deliberate, methodical approach for assuring that respondent burden is kept to a minimum while ensuring the accuracy of its burden estimates for the adult and youth instruments. To do this, the PATH Study selectively deletes or cycles out questions to make room for new questions that, for a pending data collection wave, are determined to have higher priority for the PATH Study. The context of the evolving tobacco marketplace and the performance of questions from previous waves, mentioned above, help inform this decision-making process, as does the constant need to ensure that any added question has a corollary offset (i.e., a deleted or cycled out question) to minimize if not to maintain stability in burden from one wave to the next.

The PATH Study routinely assesses whether to cycle in or restore questions that have been cycled out or deleted on an alternating basis in future waves.

This rotational approach for cycling items is most commonly used for questions that capture respondents’ perceptions about changes in health warning labels on packaging for tobacco products not previously regulated by FDA. This rotational approach is also used for questions about brand of favorite advertisement for adults and exposure to movies depicting tobacco use for youth. However, respondents who join the PATH Study in the replenishment sample or age into a new cohort at Wave 4 (e.g., shadow youth who age into the youth cohort [12 year olds] and youth who age up to the adult cohort [18 year olds]) will receive the study-entry baseline questions in order to capture responses from the same questions initially asked of all participants in that age group in Wave 1.

**Summary of Changes to Instruments.** Questions that have been added, cycled in, deleted or cycled out of the PATH Study’s Wave 4 adult and youth instruments are outlined in Tables A-3 and A-4. As shown in the tables, the deletions offset an increase in respondent burden resulting from the additions of questions in Wave 4, resulting in no net change in estimated burden across instruments. See Attach4.Summary of Changes to Instruments for Wave 4 for more detailed information on these changes from Wave 3 to Wave 4, including a description of the importance of each change to the PATH Study.

Table A-3. Summary of questions added to or cycled into the Wave 4 adult and youth instruments

Adult	Youth	Sample impacted	Description of question(s)
X		Replenishment sample respondents*	Added study-entry baseline questions that are asked once of PATH Study respondents to establish an individual baseline measure. An example of a study-entry baseline question is “Have you ever smoked a cigarette?”
X	X	All respondents	Added items on: - How often health warnings are read, look closely at, or thought about on packages of ENDS, traditional cigars, cigarillos, filtered cigars, and hookah tobacco; - Perceived harmfulness of nicotine in cigarettes, ENDS, and NRT; - Exposure to anti-tobacco messaging; and - Interest in completing the PATH Study surveys online.
X		All respondents	Added items on:

Adult	Youth	Sample impacted	Description of question(s)
			- Diagnoses of schizophrenia and psychosis; - Frequency of brushing teeth; and - Perceived harm of ENDS versus NRT use.  Cycled in items on how often health warnings are noticed on packages of ENDS, traditional cigars, cigarillos, filtered cigars, pipe tobacco and hookah tobacco.
	X	All respondents	Added items on: - Use of anti-inflammatory medications; - Nicotine exposure to inform biospecimen collection; - Assessments of harm for cigarettes, traditional cigars, cigarillos, filtered cigars, snus, and smokeless tobacco; and - Likelihood of becoming addicted to cigarillos and filtered cigars
X	X	Tobacco users	Added item on frequency of flavored tobacco product use in the past 30 days.
X		Cigarette smokers	Added items from the Fagerstrom Test for Nicotine Dependence.
X	X	ENDS users	Added items on: - Perceived harm of using flavored versus unflavored ENDS or e-liquid; - Frequency of using ENDS to consume marijuana derivatives; - Dual use of cigarettes and ENDS; and - Daily average number of times an ENDS device is used and the number of puffs taken each time.
X	X	Snus users	Added item on the snus product form used (loose or pouched snus).
X	X	Smokeless tobacco users	Added item on the smokeless tobacco product form used (loose or pouched).
X		NRT users	Added item on reasons for using NRT.
	X	17 year old respondents	Added item on active military status.

\* For existing “continuing” PATH Study respondents, these items were asked in Wave 1 and are not asked again in subsequent PATH waves. In Wave 4, they are reinstated for only the new adult respondents in the replenishment sample to establish their individual baselines. This differs for youth respondents in the replenishment sample, however, because study-entry baseline questions are already in the Wave 4 Youth instrument for youth who age up (i.e., turn age 12) and join the youth cohort.

Table A-4. Summary of questions deleted or cycled out from the Wave 4 adult and youth instruments

Adult	Youth	Sample impacted	Description of question(s)
X	X	All respondents	Deleted items on: - Exposure to FDA and other national media campaigns; - Whether he/she owns a smartphone,

Adult	Youth	Sample impacted	Description of question(s)
			tablet or other media device; and - Use of apps on smartphones or tablet devices related to tobacco products or ENDS.
	X	All respondents	Deleted items on noticing health warning labels on packages of bidis and kreteks, including whether he/she tried to avoid looking at warning labels, found the warnings to be believable, never wanted to use the product again (among ever users), or felt less likely to start using (among never users).  Cycled out items on: - Noticing health warning labels on packages of snus and smokeless tobacco; - How frequently he/she has seen a list of chemicals contained in tobacco products; - Perceived ease of use between flavored and unflavored products for: ENDS, traditional cigars, cigarillos, filtered cigars, hookah, snus and smokeless tobacco; - Exposure to movies that depict tobacco use; - Rules inside the home for using combusted and non-combusted tobacco products (note: these questions are asked of the youth's parent); and - How many of the respondent's best friends smoke traditional cigars and filtered cigars.
X	X	Cigar smokers	Deleted item on frequency of coupon use when purchasing cigarettes.
X	X	ENDS users	Deleted items on: - Frequency of coupon use when purchasing ENDS or e-liquid; and - Use behaviors of secondary ENDS devices.  Cycled out item on whether user changes the voltage on ENDS devices.
X		ENDS users	Deleted item on using ENDS as an alternative to quitting tobacco (note: measure is already assessed in the PATH Study and was deleted to avoid redundancy).
	X	ENDS users	Deleted items on the number of milliliters of e-liquid an ENDS tank system holds.
X	X	Cigar smokers	Deleted items on frequency of coupon use when purchasing traditional cigars, cigarillos or filtered cigars.
X		Cigar smokers	Deleted items on smoking traditional cigars, cigarillos or filtered cigars as an alternative to quitting tobacco (note: this measure is assessed by other questions in the PATH Study and was deleted to avoid

Adult	Youth	Sample impacted	Description of question(s)
			redundancy).
X	X	Pipe smokers	Deleted item on frequency of coupon use when purchasing pipe tobacco.
X		Pipe smokers	Deleted item on smoking pipes as an alternative to quitting tobacco (note: measure is already assessed in the PATH Study and was deleted to avoid redundancy.)
X	X	Snus users	Deleted items on: - Frequency of coupon use when purchasing snus; and - Use of Skoal Bandits.
X		Snus users	Deleted item on using snus as an alternative to quitting tobacco (note: measure is already assessed in the PATH Study and was deleted to avoid redundancy).
X	X	Smokeless tobacco users	Deleted items on: - Frequency of coupon use when purchasing smokeless tobacco; and - Use of Skoal Bandits.
X		Smokeless tobacco users	Deleted item on using smokeless tobacco as an alternative to quitting tobacco (note: measure is already assessed in the PATH Study and was deleted to avoid redundancy).
X	X	Hookah smokers	Deleted item on the price paid for shisha or hookah tobacco.
X		Hookah smokers	Deleted item on smoking hookah as an alternative to quitting tobacco (note: measure is already assessed in the PATH Study and was deleted to avoid redundancy).
X		Users of at least 1 tobacco product	Deleted item on whether tobacco users paid more for health insurance premiums compared to non-tobacco users.
	X	Users of at least 1 tobacco product	Deleted item on whether he/she has bought a tobacco product because of a promotion.
X		Respondents aged 18-24 who have never smoked cigars and/or pipe tobacco	Deleted items on non-user's susceptibility to becoming a user of traditional cigars, cigarillos, filtered cigars or pipe tobacco, including curiosity about using, likelihood of using in the next year or using soon, and whether the he/she might use if offered the product by his/her best friend.
X		Respondents aged 25+ who have never used snus, smokeless tobacco, ENDS, cigarettes and/or hookah	Deleted items on: - Non-user's curiosity about using snus, likelihood of using snus in the next year, and whether he/she might use snus if it were offered by best friend; - Likelihood of smoking a cigarette or hookah, or using smokeless tobacco soon among non-users; and - Non-user's susceptibility to becoming an ENDS user, including curiosity about using, likelihood of using in the next year or using soon, and whether the he/she

Adult	Youth	Sample impacted	Description of question(s)
			might use ENDS if offered by his/her best friend.
X		Deleted items on:  Respondents who have not seen a doctor in the past 12 months	- Whether a medical doctor has told the respondent that he/she has COPD, chronic bronchitis, emphysema, asthma, lung or respiratory conditions; gum disease, bone loss around teeth; ulcer and gastrointestinal bleeding; cataract, glaucoma or rapid vision loss; cancer or precancerous oral lesions; osteoporosis or fragile bones; heart conditions such as high blood pressure, high cholesterol, congestive heart failure, stroke, heart attack or bypass surgery; - Treatment for gum disease; and - Whether a doctor has advised him/her to stop using ENDS.
X		Deleted item on whether he/she has a favorite aged 25+	Deleted item on whether he/she has a favorite tobacco advertisement.
X	X	Continuing respondents	Deleted items on: - US citizenship if already reported in a previous wave; - Military branch served for those who have ever been on active duty; and - His/her in-utero exposure to tobacco products (used by his/her mother during pregnancy).

### ***Parent Interview***

The parent instrument 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 instrument 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-up to the youth cohort will be asked to complete the Parent - Aged-up Interview, which collects information about youth who have aged into the youth cohort. This instrument includes new items (e.g., parental risk perceptions) and items from the original Wave 1 interview. See

Attach4.Summary of Changes to Instruments for Wave 4 for details regarding content changes to the instrument from Wave 3 to Wave 4. In summary, these changes include adding questions to capture youth diagnoses of schizophrenia and parent language proficiency. In addition, the PATH Study continually checks to ensure that any added questions are balanced by the deletion or cycling off of questions so there is no net increase in burden from one wave to the next.

### ***Biospecimens***

The PATH Study plans to collect biospecimens from consenting adult and youth respondents (age 12 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 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.

For Wave 4, urine will be requested from a subsample of approximately 11,000 adults who initially provided urine at a previous wave; from new adult respondents and adult respondents who age up to the adult cohort (i.e., completed a youth interview at Wave 3 but are 18 years old at Wave 4; and from an estimated 10,000 youth respondents age 12 to 17, pending parental consent and youth assent. New adult respondents and adult respondents who age up to the adult cohort at Wave 4 will also be asked to provide a blood sample. 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 - Assurances of Confidentiality Provided to Respondents). PATH Study respondents will be able to withdraw their biospecimen samples from the PATH Study, if they choose to do so, before the end of the study.

The biospecimens collected by the PATH Study among both youth and adult respondents in Wave 4 will allow the PATH Study to assess tobacco use exposure and potential susceptibility to disease associated with the use of tobacco products in a large, nationally representative sample, ages 12 years and older. 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. Examples include C-reactive protein (CRP) and interleukin 6 (IL-6) biomarkers of harm that 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. (Attach6.Additional Information on Biospecimens 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 or youth interview is administered during the visit or the biospecimen collection occurs less than four hours after the completion of the interview. (The adult and youth interviews incorporate 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 uses data collected by the PATH Study, in conjunction with the existing scientific literature, to enrich the knowledge base on the epidemiology and associated consequences of tobacco use in the United States.

The FDA uses PATH Study data to help inform its regulatory actions under the TCA. Cumulative longitudinal data from the first three waves of the PATH Study, combined with data expected from this revision request's Wave 4, pending OMB approval, are contemporaneous with FDA's regulatory decisions and actions under the TCA. Consequently, uses of information from the PATH Study by FDA 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 to assessing how these transitions are associated with tobacco use-related health conditions, the implementation of specific tobacco-related policies and programs, and changes in the tobacco product marketplace.

NIDA and FDA use the data generated by the PATH Study to elucidate factors associated with: tobacco use behaviors among youth and adults; use patterns, attitudes, and beliefs regarding emerging tobacco products (e.g., snus and ENDS); and tobacco use-related health outcomes among key population subgroups, such as young adults. In addition, NIDA and FDA will examine the PATH Study data on biomarkers of exposure to tobacco products and of tobacco use-related disease processes to understand the physiological changes associated with tobacco use and the natural course of nicotine dependence.

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

The PATH Study's nationally representative longitudinal cohort design provide epidemiological, population-based data on tobacco use behaviors,

attitudes, exposures, and health will be used 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. Through an inter-agency agreement between the FDA and the Centers for Disease Control and Prevention (CDC), CDC's Division of Laboratory Sciences is analyzing biospecimens collected by the PATH Study. NIDA and FDA may also arrange with other Federal, as well as non-Federal, laboratories for biospecimen analyses. Examples of specific analytes that biospecimens collected in the study are tested for are included in Attach6.Additional Information on Biospecimens.

To maximize their research value, NIDA and FDA intend to release the PATH Study's data for use by the scientific community as well as by other agencies whose missions are in service to the Nation's health, such as the CDC. To this end, a public use dataset from each wave's data will be released to the public on-line, consistent with OMB's Memorandum 13-13 (March 2013). The public use file (PUF) on the first wave of PATH Study data is now available for download from the Inter-university Consortium for Political and Social Research (ICPSR) at <http://doi.org/10.3886/ICPSR36498>. 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 and Biospecimen Access Committee and obtain a Data Use Certification. 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 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 also 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 Attach7.PATH Study Privacy Impact Assessments). 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 audio computer-assisted self-interviewing (ACASI) extended instruments (separate instruments for youth and adults) and a computer-assisted personal interviewing (CAPI) parent instrument to collect PATH Study data;
- Use of 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 make sense to respondents and facilitate the efficient flow of administration from one topic area to another;
- Elimination of questions that only need to be answered at the respondent's baseline and use of responses from earlier waves, to efficiently route the respondent through an interview;
- 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 not the respondent's preferred language for the interview.

Most 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 at Waves 1 and 2 of the PATH Study, and in the National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC) Study (OMB number 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 program leads on tobacco-related studies within NIH (e.g., NCI) and at HHS sister agencies (e.g., CDC, SAMHSA) to harmonize existing questions and reduce potential overlap or redundancy among tobacco-related data-collection efforts. Requirements of the TCA inform priorities for the PATH Study to ensure that 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 meet the data-collection needs of other HHS agencies, such as the CDC, by including questionnaire items and priority measures of shared interest. In

their review of the draft revision request documents, the HHS program leads suggested minor changes to Supporting Statements A and B, which are reflected in the current documents; overall, their comments indicated support for the proposed Wave 4 data and biospecimen collection for the PATH Study.

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.

The PATH Study's data complement data from existing national surveillance surveys (e.g., TUS-CPS, NYTS) and other federally-funded tobacco-related studies. This section describes key features of the PATH Study and distinguishes it from tobacco-related surveillance surveys and studies. (Attach8.Key Design Features of National Tobacco Surveys provides additional information.)

### ***Tobacco Surveillance Surveys and the PATH Study***

In contrast with such sentinel tobacco surveillance surveys as the TUS-CPS and NYTS, the PATH Study is a longitudinal cohort study, designed for research purposes rather than to provide cross-sectional prevalence estimates. Its population-based behavioral and biospecimen data collection 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 provides a rich source of contemporary research data that, in conjunction with data from existing surveillance surveys, 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 Attach8.Key Design Features of National Tobacco Surveys.

As noted in Section 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; one of the priority objectives of the PATH Study is 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.

### ***Tobacco-Related Studies and the PATH Study***

NIDA and FDA acknowledge the potential for duplication between the PATH Study and information collection requests that OMB has recently approved for FDA's CTP. They will work together with OMB to ensure there is no duplication in the type of information generated by the PATH Study and these and future CTP collections. Brief descriptions of recently approved tobacco-related studies and how the PATH Study will ensure it does not duplicate their information collections follow below.

Experimental studies, such as the FDA's **Experimental Study on Consumer Perceptions of Modified Risk Tobacco Products (MRTP) (OMB number 0910-0819)**, complement the PATH Study. For example, this experimental study provides information on how exposure to *specific* risk modification claims can influence consumer beliefs and intentions to use a tobacco product, and on how a consumer's tobacco use or brand loyalty might affect those outcomes.

FDA's **National Panel of Tobacco Consumer Studies (TCS) (OMB number 0910-0815)** is a set of sub-studies on consumers' responses to tobacco product-related communications. Data collected by the TCS among an estimated 4,000 adult tobacco users are expected to inform FDA's regulatory authority over tobacco products. The purpose of these sub-studies is to collect information from a national sample of tobacco users to provide data that may be used to develop and support FDA's policies related to tobacco products, including their labels, labeling, and advertising. The PATH Study will not duplicate the information collection of 0910-0815 on specific labels, labeling, and advertising campaigns. As has been done for Wave 4 in this Revision Request, the PATH Study will measure responses to tobacco product-related communications more broadly through one question.

**FDA's campaign outcome evaluation studies (OMB numbers 0910-0788, 0910-0753, and 0910-0808)** are designed to assess the effectiveness of public education campaigns that target specific youth subpopulations through such media as the television, internet, and various social media. These studies are not population-based, but are specific to the campaign and target audience; therefore, their data cannot be used to make statistical inferences about the U.S. youth population. The PATH Study will not duplicate the information collections of 0910-0788, 910-0753, and 0910-0808. Rather, as has been done for Wave 4 in this Revision Request, the PATH Study will add a new question to assess exposure to anti-tobacco messages in the past year, whether at the local, regional, or national level, in the past year.

### ***Longitudinal Design***

The longitudinal design of the PATH Study 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 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 probability-based Wave 1 sample ( $n=45,971$ ) 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). However, as a longitudinal study, the PATH Study could become less representative over time; for this reason, the study is planning to refresh the cohort at Wave 4 to achieve at least the same sample size as Wave 1. Cohort refreshment at Wave 4 will help to assure that the PATH Study achieves its objectives as a resource 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 follows youth as they age into young adulthood. This positions the PATH Study 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 marketplace, in marketing techniques, in messages on different types and brands of tobacco products, and in FDA’s regulatory decisions and activities.

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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).

## ***Focus on FDA Regulatory Issues***

The PATH Study takes 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 helps to enhance the evidence base that informs FDA's regulatory actions, such as those related to FDA's recent release of the deeming rule as well as regulations on misleading brand descriptors, marketing, and health promotion messaging and public education campaigns.

## ***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, 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, augment the specificity of the tobacco-use data, for example, by allowing the differentiation of traditional cigars, little filtered cigars, and cigarillos. In addition to respondent interview data, the PATH Study collected urine and blood samples from consenting adults during the entirety of Wave 1 to serve as the basis for examining and comparing biomarkers of exposure, including exposure to tobacco products, and tobacco brands and sub-brands. At Wave 4, a subsample of approximately 11,000 adults who initially provided urine at a previous wave will be asked to provide a urine sample. Also, adult respondents who aged up to the adult cohort at Wave 4 (i.e., completed a youth interview at Wave 1 but are 18 years old at Wave 4) will be asked to provide urine and blood. Finally, at Wave 4, all youth—continuing youth, aged-up youth, and new youth—will be asked to provide a urine sample. (At Waves 2 and 3, urine was collected from a subsample of adult respondents who provided a urine specimen at Wave 1, and urine and blood were collected from adult respondents who aged up to the adult cohort at Waves 2 and 3, respectively.) This multi-component data-collection protocol distinguishes the capacity of the PATH

Study to generate cumulative, contemporaneous data to inform FDA's regulatory actions under the TCA.

## **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 waves of data collection with the same study respondents. The PATH Study will use follow-up, retention, and tracking materials (Attach9.Follow-up, Retention, and Tracking Materials) to maintain contact with each respondent and to schedule regular appointments with each respondent for his/her follow-up interviews. Less frequent data collection could impact the ability to retain cohort respondents and achieve its annual and overall target response rates for the PATH Study. This would potentially impact the scientific quality and utility of study data, particularly data that would inform the development of new TCA-related policies and programs.

A longitudinal study is optimal for studying the dynamic environment of ever-changing policies and tobacco industry products. For example, the PATH Study will subsample adults who initially provided urine at an earlier wave to provide a urine sample again at Wave 4. 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 four points in time; urine collection at Wave 4 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 the Wave 1 data collection.

## **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 was published on April 15, 2016 in the Federal Register (Vol. 81, No. 73, pgs. 22290 – 22291). No comments were received.

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

Individuals from within NIH, FDA, and other units within HHS and numerous outside agencies, institutions, and universities were consulted from October 2011 to the present, and these consultations are ongoing. NIDA and FDA include time within the project schedule for reviews and feedback by program leads on tobacco-related studies at NCI, SAMHSA, and CDC on the PATH Study questionnaires and materials. Other individuals with expertise in the fields of tobacco research, epidemiology, and longitudinal studies contribute on an ongoing basis as members of the PATH Study Biological Workgroup, Questionnaire Workgroup, *Ad Hoc* Study Workgroup, and Sampling Workgroup, including researchers and methodologists from Roswell Park Cancer Institute, Truth Initiative, University of California San Diego Moores Cancer Center, University of Waterloo, Dartmouth College, The Medical University of South Carolina, SRI International, and Westat. The names, affiliations, and phone numbers of non-Federal individual consultants are presented in Attach10.List of Consultants.

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

The PATH Study requests respondents to give their time for interviews and the collection of biospecimens, both of which may require multiple visits to complete. To thank participants for giving their time to the PATH Study, to assist the study in meeting its response rate goals, and to retain participants in the study over time, incentives have been offered to respondents during the first three waves of data collection. Similar incentives are planned for use during Wave 4 (see Table A-5). Additional information on incentives in the PATH Study follows below.

- An incentive of \$2 will be included in the advance mailing to replenishment sample addresses. This incentive is intended as a thank you to households for reviewing the enclosed materials on the PATH Study; it also serves as an “attention grabber.”
- An incentive of \$35 will be offered to adult respondents who complete the adult extended interview at the Wave 4 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 4 home visit, an incentive of \$25 will be offered to new participants (i.e., adults who were identified and recruited from the replenishment sample) and newly aged-up adult respondents (i.e., youth from Wave 1 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 initially provided urine at a previous wave, and also provides urine at Wave 4. Collecting the urine sample is contingent on the adult completing the Wave 4 extended interview.
- An incentive of \$25 will be offered to new participants (i.e., adults who were identified and recruited from the replenishment sample) and newly aged-up adult respondents (i.e., youth from Wave 1 who have turned 18 years old and have consented to participate in the PATH Study as an adult) and 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.
- At the Wave 4 home visit, an incentive of \$25 will be offered to all youth participants (continuing youth, new youth, and aged-up youth) who consent to provide a urine sample.
- An incentive of up to \$10 is planned for participants who have changed and then updated their contact information.<sup>3</sup>

Table A-5. PATH Study - planned incentives for Wave 4

	<b>Activity</b>	<b>Incentive</b>
	Advance mailing to replenishment sample addresses	\$2
Adult	Adult Interview and Biospecimen Collection	
Extended	Extended Interview	\$35
Biospecimen	Biospecimen collection Visit 1 (urine - conducted by interviewer) <ul style="list-style-type: none"> <li>• Youth aging up to adult cohort</li> <li>• Subsample of eligible adults</li> </ul>	\$25
	Biospecimen collection Visit 2 (blood - conducted by health professional) <ul style="list-style-type: none"> <li>• New adults</li> <li>• Youth aging up to adult cohort</li> </ul>	\$25
Youth	Youth Interview and Biospecimen Collection	
Extended	Extended Interview	\$35
Biospecimen	Biospecimen collection (urine - conducted by interviewer) <ul style="list-style-type: none"> <li>• Continuing youth</li> <li>• New youth</li> <li>• Aged-up youth</li> </ul>	\$25

<sup>3</sup> Like the FDA's National Panel of Tobacco Consumer Studies (TCS) (OMB number 0910-0815), the PATH Study does not provide an incentive to participants for follow-up/tracking activities or for confirming contact information that is unchanged. However, unlike the TCS, the PATH Study provides an incentive if/when a respondent has updated his/her contact information after it has changed to stay in touch with the study, such as by a move, a new phone number, or a change of name (e.g., due to a change in marital status).

<b>Activity</b>	<b>Incentive</b>
Youth Interview	\$25
Parent Interview*	\$10
Contact Information Update	\$10 maximum

\* 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.

Use of separate incentives for completion of different components of a study was used in the previous three waves of the PATH Study, and has been used by other studies approved by OMB, such as NHANES (OMB number 0920-0950, expiration date 12/31/2017).

To assist the study in meeting its response rate goals by improving information on the location of participants, an incentive is offered to respondents who have changed their contact information and then updated it with the PATH Study. Adults who change their contact information will receive \$5 each time they update it with the PATH Study, up to a total of \$10 per calendar year; youth respondents whose contact information has changed will receive \$5 each time their parent provides their updated contact information to the study, up to a total of \$10 per calendar year. One year after the Wave 4 interview, a between waves reminder letter and Participant Information Form (PIF) will be sent to all participants in subgroups of the cohort that will be excluded from the next annual wave of data collection, to encourage the participants to update their contact information if it has changed. Three months prior to the household anniversary date, the reminder letter (notifying the adult participant or parent of a youth participant the next wave is about to begin) and PIF will be sent, to ensure the next data collection wave will start with a correct address. Respondents can return the PIF, go to the PATH Study website, or call the PATH Support Desk to update their contact information. Research supports the use of such incentives to help improve response rates by maintaining contact with cohort respondents and ensuring their locator information is current and accurate (Mercer et al., 2015; Singer & Ye, 2013).

Incentives are 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 Attach11.Consent Materials). These materials clearly state that incentives are 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, separately, for consenting to and providing biospecimens; and for providing contact information for future follow-up by the PATH Study). Biospecimens will only be collected from adults and youth who complete the PATH Study extended interview.

A new adult respondent at Wave 4 may receive up to \$95 as a thank you for participating in the PATH Study: \$35 for the Wave 4 extended interview, \$25 for urine collection at the first Wave 4 home visit, \$25 for blood collection at the second Wave 4 home visit, and an annual maximum of \$10 for updating contact information. An adult who participated at Wave 1, including providing urine, may receive up to \$70 as a thank you: \$35 for the extended Wave 4 interview at the home visit, \$25 if included in the core sample or supplement that provides another urine sample, and an annual maximum of \$10 for respondents who have updated their 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>4</sup> A youth respondent may receive up to \$60 for participating in the PATH Study: \$25 for completing the youth extended interview, \$25 for urine collection, and a maximum of \$10 for having a parent update his or her contact information.

The PATH Study proposes to pay some of the incentives by means of cash 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 \$5 in cash (up to two times between data collection waves) to the youth's parent 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 amount, depending

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

on the eligible activity. 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. In addition to the monetary incentives, the study plans to provide certificates of appreciation to youth, to acknowledge their participation in the study; additional information on the certificates is provided in Supporting Statement B.

## **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 HHS to NIH, of which NIDA is a part. Any person engaged in the research to which this section applies, and 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 are collected and some questions may be of a sensitive nature, the CoC helps the PATH Study 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 and August 17, 2016, is included in Attach12.Certificate of Confidentiality.

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 are 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 uses a range of procedures to protect respondents' Personally Identifiable Information (PII) and the confidentiality of all data. All data collection staff are proficient in data security, confidentiality, and privacy issues and procedures. PATH Study field interviewers are required to sign a pledge of confidentiality (see Attach13.Assurance of Confidentiality) 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 is protected through field procedures that ensure interviews are not overheard by others in the home, and the use of ACASI, which uses headphones to increase comfort levels and encourage honesty in answering sensitive questions. In the field, data are collected on laptop computers that use advanced data encryption to protect confidentiality of data. Data from the laptops are 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 are identified by unique identification (ID) numbers assigned to each respondent. The ID numbers link the respondent's extended interview responses with his or her own biospecimens. Crosswalks that match these numbers to PII are stored in secure, encrypted files accessible only to authorized staff whose roles on the study necessitate access. NIDA does not have access to identifying information, and personal identifiers are not included in the data received by NIDA. The prime contractor transfers all data for the PATH Study and associated products and documents to NIDA at the time of compiling final data files and does 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.

Prior to Wave 4 data collection, each PATH Study respondent will be informed of the study sponsor, the purpose and uses of study data, legal authorities, and the voluntary nature of his or her participation. New respondents (i.e., respondents identified and recruited from the replenishment sample) and aged-up respondents (i.e., respondents who have “aged up” to the youth or adult cohorts) will be informed in writing that their information 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.<sup>5</sup> Separate consent forms (see Attach11.Consent Materials) 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. Also, the study uses separate consent forms for collecting biospecimens from adults and youth. 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 Attach7.PATH Study Privacy Impact Assessments). The PATH Study also received approval from the prime contractor’s Institutional Review Board (IRB) (Attach14.IRB Approval Memo).

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<sup>5</sup> Oral or implied consent is obtained from household screener respondents, shadow youth only screener respondents, and parents of shadow youth.

## **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) (Attach15.NIH Privacy Act Systems of Record Notice). 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 are maintained in separate, encrypted tables, with password protection and access limited to authorized personnel. The PATH Study complies 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 are required to complete regular trainings on information security, including the NIH training on data security. Authorized users access research data that are free of PII behind a secure data firewall that does not permit downloading or printing of data. In addition, no individual names or other identifiers are ever reported to NIDA, FDA, or other government agency.

Study data are identified and retrieved by a study ID number only. Investigators cannot access PII. The majority of data collected in the study are captured electronically, avoiding concerns of hard-copy storage of materials that contain PII. Hard-copy data forms are identified only by a study ID number and stored in locked files at the contractor's facilities. Datasets collected by the study 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) are reviewed for FISMA compliance by the NIDA Chief Information Officer (CIO) and Information Systems Security Officer (ISSO), and cannot be operated in production mode until NIDA grants an Authority to Operate (ATO). FISMA moderate requirements govern the storage and maintenance of the PATH Study computerized data, none of which contain PII. Attach16.Procedures for Keeping Data Confidential lists the procedures that are followed by the contractor to protect the privacy of study data.

All contract staff members undergo background screening commensurate with their role on the study and their access to study data. Study staff are required to sign a pledge of confidentiality prior to beginning work (see Attach13.Assurance of Confidentiality) and to complete NIH Computer Security Awareness Training as well as Privacy Awareness Training. Access to PII is limited to a small number of immediate staff working on the study. All records, including hard copies of informed consent and other documentation, are 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 Attach15.NIH Privacy Act Systems of Record Notice).

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

NIDA, FDA, and the prime contractor intend to make PATH Study data available through a public use dataset 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 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).

As described in Section A.2d, NIDA and FDA develop restricted use files (RUFs) of the PATH Study data for deposit in the ICPSR’s NAHDAP, where data from other NIDA-funded research projects are routinely deposited for

public or restricted use. Researchers interested in accessing the PATH Study RUFs are required to apply to the NAHDAP. Upon receiving NAHDAP approval, researchers are required to submit a Data Use Agreement to the data repository (see example in Attach17.ICPSR Data Use Agreement) to gain access to the RUFs. These data files include PATH Study questionnaire data and will include data from biospecimens.

Qualified researchers interested in accessing PATH Study biospecimens to conduct analyses will be required to apply to the PATH Study Biospecimen Access Committee established by NIDA and the FDA. This committee manages the sharing of biospecimens, including reviewing applications from researchers requesting biospecimens; instructing the PATH Study biospecimen repository subcontractor to ship specimens to approved labs/researchers; tracking the progress of researchers; and, if necessary, recalling biospecimens.

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

As described in Section A.1, the cumulative data from the PATH Study on tobacco use behaviors, attitudes, exposures, and health in the United States enrich the evidence base that informs FDA's regulatory actions under the TCA to reduce tobacco-related diseases, disabilities, and deaths. To meet this purpose, the PATH Study asks questions about tobacco use. Additionally, to meet its eight objectives (see Section A.2), the PATH Study instruments include questions on other sensitive topics, ranging from psychological problems and conditions, substance abuse, and income to 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 FDA's CTP 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 supports this mission by collecting, analyzing, and reporting population-based data to enhance the evidence base that informs FDA's regulatory activities.

Tobacco use questions constitute the core of the PATH Study. Most of the tobacco use 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. Answers to these questions provide the depth and breadth of data the PATH Study produces to enhance understanding of risk factors for tobacco use initiation, motivations for product-switching, the use of multiple tobacco products, and behaviors associated with quitting and relapse. 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. 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, the PATH Study has implemented a range of procedures 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 CDC's NYTS (OMB number 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 questions provide context for the youth responses as well as for understanding youth's tobacco-use trajectories in future waves of data collection. Understanding trajectories and transitions among youth in tobacco use behaviors (e.g., onset, daily use, multiple product use, quitting attempts, relapse, and cessation) is 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 Disorders**

Tobacco use is associated with an array of psychological problems and conditions, including depression and anxiety. Persons with mental health disorders have been found to use tobacco at higher rates and have more difficulty quitting tobacco use (Glasheen et al, 2014). Research has also shown that some mental disorders, such as anxiety disorders, are more predictive of onset to daily nicotine use, while others, such as mood disorders, are associated more strongly with the development of nicotine dependence (Swendsen et al., 2010).

Epidemiologic and clinical studies indicate 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% versus 22.5%, respectively). Nearly half the cigarettes smoked in the United States (44-46%) are consumed by people with co-occurring psychiatric or addictive disorders.” Psychiatric disorders are associated with higher proportions of heavy smoking and lower likelihoods of cessation (Smith et al (2014). As noted by Hartz et al (2014), successful public health efforts to reduce smoking among persons 30 years of age and younger have been less effective among persons with psychiatric 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 facilitate understanding of how various program and policy changes may affect tobacco use behaviors in the population.

The PATH Study has developed a handout (see Attach18.Field Data Collection Materials) 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 5-minute Global Appraisal of Individual Needs Short Screener (GAIN SS). The GAIN SS includes a brief 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 (Dennis et al., 2006). At Wave 4, new questions have been added on schizophrenia and psychosis diagnoses. Items were adapted from the National Epidemiological Survey on Alcohol and Related Conditions-III (NESARC-III) and are asked of PATH Study adult respondents and parents of youth respondents.

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

Use of substances, including the use of alcohol and tobacco, frequently co-occurs. The PATH Study adult and youth interviews has questions on substance use, including alcohol. The adult interview asks questions on use of substances during pregnancy. The parent interview and the adult interview also ask three items on family history of tobacco use and substance use problems, which provide context for factors associated with the trajectory to nicotine dependence among tobacco users. These items were adapted from the Family History Assessment Module (FHAM), a semi-structured diagnostic instrument based on the DSM-III to assess psychiatric and substance use disorders in the relatives of a respondent (Rice et al., 1995).

### **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 questions 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**

Research has shown that the prevalence of use of any tobacco product is much higher among gay, lesbian, or bisexual (LGBT) adults, compared with heterosexual adults (Agaku et.al., 2014) and with the total population in the U.S. (King et al., 2012). This finding has been attributed to, in part, tobacco product marketing toward the LGBT community (HHS, 2014) as well as to the higher levels of psychosocial stress, victimization, and stigma that LGBT individuals may experience in their daily lives (Ryan, et al., 2001). 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.

To inform analysis of tobacco use behavior and related health conditions relative to gender identity and sexual orientation, the PATH Study adult interview includes two questions on each. The sexual orientation question is similar to the question asked at Wave 1 from the NHIS 2013 (Miller & Ryan, 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; Massachusetts Department of Public Health, 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 (R03\_AM0021 in the adult interview) and of youth ages 12 to 17 years (R03\_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**

The estimated annualized burden hours for the PATH Study Wave 4 data collection are 94,798. Burden estimates are based on the results from the previous waves of 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 validation interview.

An increase of 26,332 burden hours is estimated between Wave 3 (54,434) and Wave 4 (80,766). The factors accounting for this increase include the addition of: (1) household and shadow youth only screenings to support sample replenishment, (2) data collection for the new adults and new youth selected as part of sample replenishment, (3) urine and blood collection for the new adults selected as part of sample replenishment, and (4) urine collection for all youth. The household and shadow youth only screenings that are necessary for sample replenishment are responsible for a substantial portion of the increase in burden hours; similarly, much of the difference between Wave 1 and Wave 2 on burden hours was due to the Wave 1 household screening. Offsetting the increase in burden hours described here are decreases in the estimated burden hours for participant follow-up/tracking that result from using more accurate estimates of the number of respondents.

Table A-6 presents the estimated annualized burden hours for the PATH Study Wave 4 data collection.

Table A-6. Estimated annualized burden hours

<b>Form name</b>	<b>Type of respondent</b>	<b>Number of respondents</b>	<b>Number of responses per respondent</b>	<b>Average burden per response (in hours)</b>	<b>Total annual burden hours</b>
<b>1.</b> Household Screener	Households	48,018	1	14/60	11,204
<b>2.</b> Individual Screener	Adults - New adults	9,152	1	6/60	915
<b>3.</b> Extended Interview*	Adults - New adults and Wave 1 youth respondents who age up to adult cohort - Wave 4	10,737	1	68/60	12,169
<b>4.</b> Extended Interview*	Adults - Adult respondents - previous wave	23,414	1	1	23,414
<b>5.</b> Parent Interview	Adults - Parents of new youth and parents of shadow youth who age up to youth cohort - Wave 4	6,561	1	19/60	2,078
<b>6.</b> Parent Interview	Adults - Parents of youth respondents - previous wave	8,800	1	16/60	2,347
<b>7.</b> Extended Interview**	Youth - New youth and shadow youth who age up to youth cohort - Wave 4	6,432	1	45/60	4,824
<b>8.</b> Extended Interview**	Youth - Youth respondents - previous wave	8,627	1	35/60	5,032
<b>9.</b> Tobacco Use Form	Adults	23,133	1	5/60	1,928
<b>10.</b> Tobacco Use Form	Youth	10,239	1	5/60	853
<b>11.</b> Shadow Youth Only Screener	Households	41,207	1	5/60	3,434
<b>12.</b> Verification Interview	Adults	33,889	1	2/60	1,130

<b>Form name</b>	<b>Type of respondent</b>	<b>Number of respondents</b>	<b>Number of responses per respondent</b>	<b>Average burden per response (in hours)</b>	<b>Total annual burden hours</b>
<b>13.</b> Validation Interview	Adults	301	1	4/60	20
<b>14.</b> Biospecimen Collection: Blood	Adults - New adults and Wave 1 youth respondents who age up to adult cohort - Wave 4	4,832	1	18/60	1,450
<b>15.</b> Biospecimen Collection: Urine	Adults	18,301	1	10/60	3,050
<b>16.</b> Biospecimen Collection: Urine	Youth	10,239	1	10/60	1,707
<b>17.</b> Follow-up/ Tracking Participant Information Form	Adults	854	2	8/60	228
<b>18.</b> Follow-up/ Tracking Participant Information Form for Youth (completed by parents)	Adults - Parents of youth respondents	376	2	8/60	100
<b>19.</b> Follow-up/ Tracking Participant Information Form for sample shadow youth (completed by parents)	Adults - Parents of shadow youth	117	2	8/60	31
<b>20.</b> Consent for Extended Interview	Adults - New adults and Wave 1 youth respondents who age up to adult cohort - Wave 4	13,984	1	4/60	932
<b>21.</b> Parent Permission and Consent	Adults - Parents of new youth and parents of	7,657	1	5/60	638

Form name	Type of respondent	Number of respondents	Number of responses per respondent	Average burden per response (in hours)	Total annual burden hours
for Parent Interview	Shadow youth who age up to youth cohort - Wave 4				
22. Assent for Extended Interview	Youth - New youth and shadow youth who age up to youth cohort - Wave 4	7,657	1	3/60	383
23. Consent for Biological Samples	Adults - New adults and Wave 1 youth respondents who age up to adult cohort - Wave 4	10,737	1	5/60	895
24. Parent permission for urine collection	Adults - Parents of youth respondents - previous wave	15,360	1	3/60	768
25. Assent for urine collection	Youth	15,059	1	5/60	1,255
Total		335,389	336,736		80,766

\* Estimated total number of adult extended interview respondents is 23,414 + 10,737 = 34,151.

\*\* Estimated total number of youth extended interview respondents is 8,627 + 6,432 = 15,059.

Table A-7 presents the annualized cost to respondents associated with the PATH Study Wave 4 data collection.

Table A-7. Annualized cost to respondents

Form name	Type of respondent	Total annual burden hours	Hourly wage rate***	Respondent cost
1. Household Screener	Households	11,204	\$17	\$190,468
2. Individual Screener	Adults - New adults	915	\$17	\$15,555

Form name	Type of respondent	Total annual burden hours	Hourly wage rate***	Respondent cost
3. Extended Interview*	Adults - New adults and Wave 1 youth respondents who age up to adult cohort - Wave 4	12,169	\$17	\$206,873
4. Extended Interview*	Adults - Adult respondents - previous wave	23,414	\$17	\$398,038
5. Parent Interview	Adults - Parents of new youth and parents of shadow youth who age up to youth cohort - Wave 4	2,078	\$17	\$35,326
6. Parent Interview	Adults - Parents of youth respondents - previous wave	2,347	\$17	\$39,899
7. Extended Interview**	Youth - New youth and shadow youth who age up to youth cohort - Wave 4	4,824	\$4	\$19,296
8. Extended Interview**	Youth - Youth respondents - previous wave	5,032	\$4	\$20,128
9. Tobacco Use Form	Adults	1,928	\$17	\$32,776
10. Tobacco Use Form	Youth	853	\$4	\$3,412
11. Shadow Youth Only Screener	Households	3,434	\$17	\$58,378
12. Verification Interview	Adults	1,130	\$17	\$19,210
13. Validation Interview	Adults	20	\$17	\$340
14. Biospecimen Collection: Blood	Adults - New adults and Wave 1 youth respondents who age up to adult cohort - Wave 4	1,450	\$17	\$24,650
15. Biospecimen Collection: Urine	Adults	3,050	\$17	\$51,850

<b>Form name</b>	<b>Type of respondent</b>	<b>Total annual burden hours</b>	<b>Hourly wage rate***</b>	<b>Respondent cost</b>
<b>16.</b> Biospecimen Collection: Youth Urine	Youth	1,707	\$4	\$6,828
<b>17.</b> Follow-up/ Tracking Participant Information Form	Adults	228	\$17	\$3,897
<b>18.</b> Follow-up/ Tracking Participant Information Form for Youth (completed by parents)	Adults - Parents of youth respondents	100	\$17	\$1,709
<b>19.</b> Follow-up/ Tracking Participant Information Form for sample shadow youth (completed by parents)	Adults - Parents of shadow youth	31	\$17	\$530
<b>20.</b> Consent for Extended Interview	Adults - New adults and Wave 1 youth respondents who age up to adult cohort - Wave 4	932	\$17	\$15,844
<b>21.</b> Parent Permission and Consent for Parent Interview	Adults - Parents of new youth and parents of Shadow youth who age up to youth cohort - Wave 4	638	\$17	\$10,846
<b>22.</b> Assent for Extended Interview	Youth - New youth and shadow youth who age up to youth cohort - Wave 4	383	\$4	\$1,532
<b>23.</b> Consent for Biological Samples	Adults - New adults and Wave 1 youth respondents who age up to adult cohort - Wave 4	895	\$17	\$15,215

Form name	Type of respondent	Total annual burden hours	Hourly wage rate***	Respondent cost
24. Parent permission for urine collection	Adults - Parents of youth respondents - previous wave	7,668	\$17	\$130,556
25. Assent for urine collection	Youth	1,255	\$4	\$5,020
Total		80,766		\$1,202,648

\* Estimated total number of adult extended interview respondents is 23,414 + 10,737 = 34,151.

\*\* Estimated total number of youth extended interview respondents is 8,627 + 6,432 = 15,059.

\*\*\* 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 2014 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>.

The annualized cost to respondents associated with the PATH Study Wave 4 data collection is \$1,202,648.

### 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

The annualized cost to the federal government for the PATH Study Wave 4 data collection is presented in Table A-8. 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) with NIH/NIDA using tobacco user fees assessed under the authority of the TCA (PL 111-31, June 22, 2009). The biospecimen-related expertise that CDC will provide to Wave

4 of the PATH Study is similarly funded by FDA through an IAA with CDC. Estimates in Table A-8 are presented as the annualized cost to the U.S. Government for Wave 4 of the PATH Study's information collection.

Table A-8. Annualized cost to the federal government

Staff/item	Grade/step	Salary	% Effort	Fringe, if applicable	Annualized cost
NIDA Federal Staff Oversight (5)	GS13/9	116,722	100.0		583,610
NIDA In-house Contractor Staff (11)		101,000	50.0		555,500
NIDA Travel					3,500
FDA Federal Staff Oversight (15)	GS13/9	116,722	100.0		1,750,830
FDA Travel					9,000
CDC Federal Staff - Biospecimen-Related Expertise (5)	GS13/10	114,802	39.0		223,864
Contractor Cost					
• On-Site Salaried Staff (124)		70,334	81.8	56.21	11,144,206
• Off-Site Salaried Staff (6)		72,562	72.8	48.73	471,401
• On-Site Hourly Staff (72)		29,443	48.6	53.79	1,584,451
• Field Managers/ Supervisors (80)		51,483	99.2	46.55	5,987,580
• Field Interviewers (980)		37,107	49.0	46.55	26,113,424
Subcontractors					8,702,038
Consultants					54,784
Travel					2,550,700
Field Expenses					5,125,075
Respondent Incentives					3,116,362
Other ODC: Printing, Supplies, Shipping, Computing, Telephone, etc.					6,162,904
Overhead (Excluding Fringe) plus G&A and Fee					20,632,217

The total annualized cost to the federal government for the PATH Study Wave 4 data collection is \$94,771,447.

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

This is a revision request (OMB number 0925-0664, expiration date 8/31/2018) for the Population Assessment of Tobacco and Health (PATH) Study to conduct Wave 4 of data collection. An increase of 26,332 burden hours is estimated between Wave 3 (54,434) and Wave 4 (80,766). The factors accounting for this increase include the addition of: (1) household and shadow youth only screenings to support sample replenishment, (2) data collection for the new adults and new youth selected as part of sample replenishment, (3) urine and blood collection for the new adults selected as part of sample replenishment, and (4) urine collection for all youth.

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

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

Wave 4 data will be used to inform the PATH Study 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 4 data collection will focus on characterizing change in various outcomes relative to Wave 1 and examining correlates of that change. A participant's "baseline" will vary by whether he/she first completed an interview at Wave 1 or in the first three follow-up waves as a result of aging up (whether as a shadow youth to youth or as a youth to adult); Wave 4 will be the "baseline" for participants who are newly recruited for cohort replenishment in that wave as well as for participants who age up in Wave 4. Of interest, for example, are rates of tobacco product uptake between waves 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 are the basis for many of these analyses, although the longitudinal nature of the combined Wave 1, 2, 3 and 4 data may also provide an opportunity for more in-depth analysis. (See Attach19.Sample Analysis Plans for detailed examples of some of the analyses planned after completion of the Wave 3 data collection.)

The PATH Study data are 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 are tested are presented in Attach6.Additional Information on Biospecimens. 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**

Table A-9 outlines the key activities and time schedules for the PATH Study Wave 4 data collection.

Table A-9. Wave 4 timeline

Activity	Time schedule
OMB approval of Wave 4 data collection	October 2016
Begin Wave 4 data collection	December 1, 2016
Process and clean Wave 4 questionnaire data	4 - 36 Months after OMB approval
Wave 4 data analyses	5 - 36 Months after OMB approval
Publish Wave 4 preliminary study results/release public use data files for questionnaire data	Within 18 Months after completion of data wave
Publish Wave 4 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**

The OMB control number and expiration date will be displayed.

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

None.

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