Supporting Statement A
for
Population Assessment of
Tobacco and Health (PATH) Study (NIDA)

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LIST OF ATTACHMENTS
(Appearance in Supporting Statement A)

A. Justification

A.1 Circumstances Making Collection of Information Necessary

A.1a Overview

This request is for Office of Management and Budget (OMB) approval for the Population Assessment of Tobacco and Health (PATH) Study, a longitudinal data collection scheduled to begin in the fall of 2013 by the National Institutes of Health (NIH), through the National Institute on Drug Abuse (NIDA), in partnership with the Food and Drug Administration (FDA). This is a nonsubstantive change request to a currently approved collection.

Under data collection authorization of Title 42 USC 285o (Attachment 1), NIDA is conducting the PATH Study through Westat, the prime contractor. Using computer-assisted interviews and collection of biospecimens, the PATH Study will collect baseline and follow-up information on tobacco-use patterns; trends in risk perceptions and attitudes regarding harmful constituents, and new and emerging tobacco products; tobacco initiation, cessation and relapse behaviors among youth aged 12 to 17 and adults aged 18 and older. Pending sufficient sample sizes over time, the PATH Study may also examine longitudinal relationships between health outcomes and tobacco exposure and tobacco use. Examination of data from interviews and the collection of biospecimens (buccal cells, urine, and blood) among adults will be used for hypothesis generation regarding disease processes. The target sample size is approximately 58,916 (42,730 adults and 16,186 youth). The population for this study is the civilian non-institutionalized population in the United States (U.S.).
The PATH Study oversamples tobacco users, young adults, and African American adults; and it uses a “wide net” definition (as described in detail in SSB) of a tobacco user to capture adults who have had experience with a range of different tobacco products and who may be at risk of progressing to more frequent use.

This nonsubstantive change request is for OMB approval of the first (baseline) wave of data and biospecimen collection of the PATH Study. The baseline wave is planned for 12 months; approximately half-way through the baseline wave NIDA will report recruitment rates to the Assistant Secretary for Planning and Evaluation in the U.S. Department of Health and Human Services (HHS) and OMB, and begin preparing an OMB package for the second wave. The current plan is to follow the cohort for three years over the duration of the current PATH Study contract. Additional follow-up waves are under consideration pending the availability of funding. NIDA will submit revisions of this package to OMB prior to each wave of data collection, including requests to pilot test substantive protocol changes using one of the PATH Study's approved generic clearances, such as for cognitive testing of methodological studies.

OMB previously approved a field test to examine the overall flow of methods, procedures, systems, and data to be collected at baseline (OMB # 0925-0664, expiration 11/30/2015). This field test was conducted from December 2012 – February 2013 with 1,170 household screener respondents, 480 adult interview respondents, 122 youth interview respondents, and 128 parent interview respondents. Results of the field test are summarized in section A.2c and are reflected in sections B.1, B.2, and B.3. The Field Test Report is provided in Attachment 2. Nonsubstantive changes described herein to the PATH Study data collection instruments, materials, and procedures are based on the field test; they are also responsive to the terms of clearance of OMB's approval for the PATH Study to conduct the field test.

A.1b Critical Need for the PATH Study Data

Approximately 443,000 U.S. deaths each year are from cigarette use and second hand smoke exposure (Hyland et. al., 2003), and an estimated 8.6 million smokers have at least one serious illness due to smoking (Adhikari, et al., 2008). According to the 2011 National Survey on Drug Use and Health (NSDUH), an estimated 68.2 million Americans (26.5% of the population ages 12 and older) were past month tobacco product users; among current users, approximately 56.8 million persons (22.1 percent of the population) were cigarette smokers; 12.9 million (5.0 percent) smoked cigars; 8.2 million

(3.2 percent) used smokeless tobacco; and 2.1 million (0.8 percent) smoked tobacco in pipes (SAMHSA, 2012). NSDUH also reported that approximately 6,600 Americans were new cigarette smokers every day. The majority of new cigarette smokers in 2011 initiated use before age 18 (55.7 percent) (*ibid*).

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

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

By virtue of its longitudinal cohort design, the PATH Study provides a unique opportunity to monitor and assess behavioral and biological between-person differences and within-person changes over time in tobacco-product use and

potentially related health conditions. Its cumulative data will provide population-based evidence on tobacco use behaviors, attitudes, and health in the United States to help inform the evidence base the FDA needs to fulfill its regulatory authorities under the TCA and to reduce the Nation's burden of tobacco-related diseases, disabilities, and deaths.

A.2 Purpose and Use of the Information Collection

A.2a Objectives and Purposes/Uses

In broad terms, the PATH Study's overarching mission is to gather and analyze epidemiological and longitudinal data on use of the full range of tobacco products available now and in the future to support and inform FDA's regulatory decisions and actions. Components of the study include conducting annual computer-assisted interviews on tobacco-product use behaviors from a national longitudinal cohort of 58,916 current, former, and never tobacco product users ages 12 years and older; in addition, biospecimens will be collected (urine, buccal cells, and blood) from adult participants to assess biological indicators of tobacco-related exposures and to monitor between-person differences and within-person changes over time in measures of tobacco use-related harm.

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

- **Objective 1:** Identify and explain between-person differences and within-person changes in tobacco-use patterns, including the rate and length of use by specific product type and brand, product/brand switching over time, uptake of new products, and dual- and poly-use of tobacco products (i.e., use of multiple products within the same time period, and switching between multiple products).

- **Objective 2:** Identify between-person differences and within-person changes in risk perceptions regarding harmful and potentially harmful constituents, new and emerging tobacco products, filters and other design features of tobacco products, packaging, and labeling; and, identify other factors that may affect use, such as social influences and individual preferences.

- **Objective 3:** Characterize the natural history of tobacco dependence, cessation, and relapse including readiness and self-efficacy to quit, motivations for quitting, the number and length of quit attempts, and the length of abstinence related to various tobacco products.

- **Objective 4:** Establish a comprehensive baseline on tobacco-use behaviors and related health conditions (including markers of exposure and tobacco-related disease processes identified from the collection and analysis of biospecimens) as a benchmark for assessing 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-use products, including modified risk tobacco products. This comprehensive baseline may also facilitate the selection of individuals by disease status, biomarker levels, or tobacco use status for participation in small-scale research studies (see Objective 8).

- **Objective 5:** Assess associations between TCA-specific actions and tobacco-product use, risk perceptions and other attitudes, use patterns, cessation outcomes, and tobacco-related intermediate endpoints (e.g., exposure and disease biomarker levels). All analyses will attempt to take into account other potential factors influencing the observed patterns (e.g., demographics, local tobacco-control policies, and economic, social network, peer group, and family factors).

- **Objective 6:** Assess between-person differences and within-person changes over time in attitudes, behaviors, exposures to tobacco products, and related biomarkers among and within population sub-groups defined by racial-ethnic, gender, age, and risk factors (e.g., pregnancy or co-occurring substance use or mental health disorders).

- **Objective 7:** To the extent to which sample sizes are sufficient, assess and compare samples of former and never users of tobacco products

for between-person differences and within-person changes in relapse and uptake, risk perceptions, and indicators of tobacco exposure and disease processes.

- **Objective 8:** Use the PATH Study's comprehensive baseline on tobacco-use behaviors, attitudes, and related health conditions (including markers of exposure and tobacco-related disease processes identified from the collection and analysis of biospecimens) as a basis for screening respondents for participation in small-scale research studies, such as in cognitive testing or methodological studies under the PATH Study's existing generic clearances, or in other topic-specific research studies that focus on new and emerging tobacco-related behavior, attitudes and health issues of interest to FDA.

A.2b Information to be Collected

The PATH Study will obtain completed interviews at baseline from a nationally representative sample of respondents 12 years of age and older. A household screener will be conducted in sampled households to select the PATH Study sample of adults and youth. For adults, a second-phase individual screener will be administered to adults selected from the household screener, to confirm or correct the household screener information. Responses to the second-phase screener will form the basis for applying the final adult sampling criteria, based on tobacco use status, age, and race. (See Section B.1 for details on the sampling design). Once selected, an adult extended interview will be administered to adults age 18 and older, a youth extended interview will be administered to youth ages 12 to 17 years, and a parent interview will be administered to parents of youth respondents. Additionally, biospecimens will be collected from adults who respond to the PATH Study adult extended interview. Table A-1 lists the PATH Study baseline wave instruments and briefly describes the purpose and content of each. The instruments are included in Attachment 3. Attachment 4 provides the data sources, domains/questionnaire component, and analysis plan for each PATH Study Objective.

Table A-1. PATH Study instruments and data collected

PATH Study Instrument	Data Collected
Household Screener – Adult Household Respondent	Number and names of people in household; Sex, age, active duty military status, ethnicity, race for each household member; Multiple-birth status for same-age youth; 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 CAPI mode by one household respondent about other household members.
Adult – Individual Screener	Demographics (sex, age, active duty military status, ethnicity, race); main tobacco use characteristics for various tobacco products (the basis for final adult sample selection). Data are reported in ACASI mode by each adult respondent about him or herself.
Adult – Extended Interview	Tobacco use history for each tobacco product respondent uses; Reasons for using each tobacco product; Dependence on nicotine and tobacco products; Interest in/experience with quitting; Notice of/reactions to tobacco product packaging and health warnings; Perceived risk of tobacco products; Media awareness and use; Secondhand smoke exposure; Peer and family influences; Health effects; Advertising and promotion of tobacco; Other substance use; Additional demographics; Contact information.
Adult – Biospecimen Collection Forms	Chemotherapy status, hemophilia or blood-clotting problems, oral health issues, last time of urination, time of last meal, fluid intake, and tooth brushing.
Adult – Tobacco Use Form	Specific time of use and quantity used for 10 different tobacco products, nicotine replacement therapies, or prescription drugs for tobacco cessation.
Adult – Follow-up/Tracking Participant Information Form	Detailed contact information for people who have moved between waves.
Parent Interview – Parent of Youth	Respondent's relationship to the child, education, and tobacco use status (if not ascertained elsewhere); Household rules about tobacco; Perception of child's tobacco use; Child's curfew, school performance, school missed due to illness, health (height, weight, health effects, medications, emergency room visits); Parents who live elsewhere; Tobacco availability at home; Detailed contact information if not ascertained elsewhere.

Youth – Extended Interview	Demographics (sex, age, ethnicity, race); Tobacco use characteristics; Tobacco use history for each tobacco product the respondent may use; Tobacco susceptibility (non-users); Reasons for using tobacco and specific tobacco products; Dependence on nicotine and tobacco products; Interest in/experience with quitting; Notice of/reactions to tobacco product packaging and health warnings; Perceived risk of tobacco products; Accessibility of tobacco; Media awareness and use; Secondhand smoke exposure; Peer and family influences; Health effects; Advertising and promotion of tobacco; Other substance use; Additional demographics.
Youth -- Follow-up/Tracking Participant Information Form for Youth (completed by parents)	Detailed contact information for people who moved since the last PATH interview.
Youth – Follow-up/Tracking Participant Information Form for Shadow Sample Youth (completed by parents)	Detailed contact information for youth ages 9-11 who will be followed until age 12 when they will be invited to participate in the PATH Study

Core information for the PATH Study will be collected in the adult extended interview, the youth extended interview, and the biospecimens (for the adults).

Adult and Youth Extended Interviews

The core content of the adult and youth extended interviews is based on conceptual models of how and why tobacco regulations exert an influence on proximal and distal behavioral and health outcomes (see Attachment 5). The PATH Study's adult and youth instruments include questions related to tobacco warning labels; product regulation; misleading brand descriptors, such as "light" and "mild"; advertising and promotion; and tobacco product standards. They include questions that address 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, as well as questions designed to characterize the general population, including demographics; environmental factors and family and peer influences, general health, and health effects that may be due to use of tobacco products.

Existing national, cross-sectional surveillance surveys have helped to inform the contents of the PATH Study instruments. For example, tobacco-related questions in the PATH Study instruments were adapted from the Current Population Survey – Tobacco Use Supplement (TUS-CPS). Tobacco-related questions in the National Health Interview Survey (NHIS) are also similar to those in TUS-CPS. TUS-CPS questions were adapted to assess the full array of other tobacco products of interest to the PATH Study, such as use of e-cigarettes and dissolvable tobacco (e.g., the TUS-CPS question "Have you ever smoked a cigarette, even one or two puffs?" was the basis for the PATH Study question "Have you ever used an e-cigarette, such as NJOY, Blu, or Smoking Everywhere, even one or two times?").

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

The baseline data collection will include detailed information about health status, which significantly increases the burden of this first wave. Such information is valuable to establish a comprehensive baseline for the cohort from which to compare data collected in future waves; to generate hypotheses, such as those related to biomarkers of tobacco exposure and tobacco use behaviors, and to screen individuals and sub-cohorts for further data collection, for example on the basis of biomarkers of disease progression. Although it is expected that these data will allow the generation of cross-sectional prevalence estimates of health conditions by tobacco use subgroups, this study is not specifically designed for the purpose of providing such nationally-representative estimates of prevalence. In general, longitudinal studies tend to lose some of their representativeness over time, especially in the absence of cohort refreshment. As such, FDA and NIDA will always present such cross-sectional prevalence estimates in conjunction with estimates from HHS' signature nationally- representative studies, including the National Cancer Institute's TUS-CPS, SAMHSA's NSDUH, the National Center for Health Statistics' NHIS, and the Center for Disease Control and Prevention's National Adult Tobacco Study (NATS), which are the Nation's primary sources of nationally-representative prevalence estimates used in

generating analyses on associations between tobacco use and physical and mental health outcomes.

Questions in the PATH Study on physical health endpoints were drawn from the National Health and Nutrition Examination Survey (NHANES), a national cross-sectional survey that includes tobacco-use questions in its instruments and collects biospecimens. Some of these items have been tailored to assess PATH Study-specific tobacco-related health conditions. For example, the NHANES item “Have you ever been told by a doctor or other health professional that you had cancer?” has been modified for the PATH Study to “Have you ever been told by a doctor, dentist, or other health professional that you have pre-cancerous oral lesions?” Other health-related items in the PATH Study questionnaire are from standard screeners (i.e., GAIN and PROMIS).

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

As a longitudinal cohort study, the PATH Study is collecting participants’ baseline health status as the anchor from which to assess between-person differences and within-person changes in tobacco use behaviors and health and in the context of FDA’s regulatory decisions and actions under the TCA. Over time, longitudinal data from the PATH Study will be used to inform the development of new taxonomies of tobacco user subgroups, such as initiates to tobacco product use by first using smokeless tobacco; users who switch among types of products, including new and emerging products such as snus; those who use multiple types of tobacco products (e.g., combustible and smokeless); users who seek to reduce their health risks while continuing to use, such as by switching to products perceived to be less risky (for example, e-cigarettes). The PATH Study includes a number of items on

perceptions of health risks from smoking and of changes in perceived harm associated with graphic warnings. It also has items in the health outcomes section to assess former and current tobacco-product use among women reporting to be pregnant.

Biospecimens

The PATH Study is planning to collect biospecimens from consenting adult respondents (age 18 and older) over multiple waves of data collection to assess between-person differences and within-person changes in markers of tobacco exposure, and to detect and compare indicators of premorbid conditions and related disease processes associated with the use of tobacco products. This will enable the PATH Study to focus, for example, on the biomarkers of users of tobacco products that have recently changed due to a manufacturer's response to new regulations enacted by FDA under the TCA. The PATH Study's longitudinal research design, combined with its detailed questionnaire and collection of biospecimens, are intended to help it achieve its main purpose of providing FDA with timely, population-based data to inform its regulatory decisions and actions under the TCA.

At baseline, adult respondents will be asked to provide buccal cells and urine and blood samples. 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).

Each of the three types of biologic samples to be collected by the PATH Study yields information that other sample media do not. Collectively, they constitute a panel of biomarkers of exposure and susceptibility to disease associated with the use of tobacco products. Urine provides the matrix by which many tobacco exposure biomarkers are measured, including nicotine and nicotine metabolites, tobacco specific nitrosamines, metals, and volatile organic compounds (VOCs). Blood collection will allow for the measurement of biomarkers that cannot be detected (or accurately measured) in urine samples. For example, the gold standard for measurement of cotinine in

passive users, non-users/second hand exposure to tobacco smoke is in serum. Serum provides a matrix in which low levels of cotinine (i.e., outside the limits of detection in urine) can be accurately measured. This lower limit of detection may also be important for assessing nicotine exposure related to use of smokeless tobacco, new and emerging tobacco products, and comparison of products that may claim modified risk compared to traditional combustible tobacco products. Biomarkers of harm such as C-reactive protein (CRP) and interleukin 6 (IL-6) will be measured in serum and plasma (respectively) isolated from blood samples. In addition to serum and plasma, blood samples will allow for nucleic acid isolations (DNA and RNA) for genetic and epigenetic analysis from the buffy coat and hemoglobin adducts (4-ABP hemoglobin) from red blood cells (see Attachment 6).
Collection of buccal cells will allow for a number of analyses. From buccal cells, researchers can examine genetic and epigenetic alterations of cells in the mouth that may come in direct contact with inhaled smoke (or vapor, in the case of electronic cigarettes) and/or smokeless tobacco products. (Attachment 6 provides a list of specific analytes and their preferred matrix.)

The remaining part of Section A.2.b elaborates on the need for and functions of other specialized instruments listed in Table A-1.

Household Screener/Adult Individual Screener

The household screener combines typical screener functions (e.g., enumerating the household, collecting basic demographic information about each member, collecting some household-level data, selecting subjects for the study) with a special purpose for the PATH Study, which is to collect minimum information on each adult's tobacco use in order to classify him/her with sufficient validity to select subjects according to the PATH Study's sampling strata on tobacco use crossed by other demographic characteristics.

The PATH Study sampling plan anticipates some amount of misclassification of household members' tobacco use status using this traditional household screening approach, which employs a single household informant as the

screener respondent to provide needed information about every household member. Such misclassification may include false positives (those identified as tobacco users who are not actually tobacco users by the PATH Study's criteria) and false negatives (those identified as not using tobacco but actually use, based on the PATH Study's criteria).

Reasons for such misclassification include:

1. Lack of awareness by the household informant of each of the other members' tobacco use;

2. Lack of awareness by the household informant that a household member has quit using tobacco;

3. Concealment of tobacco use from the household informant by other members (e.g., teenagers or young adults concealing their smoking from their parents);

4. Reticence by the household screener respondent to self-report tobacco use in the HH screening interview, which is administered aloud by an interviewer using a CAPI instrument;

5. A lack of awareness by the household informant that other members of the household are using less visible or salient forms of tobacco than smoking, such as new and emerging products that are consumed orally without combustion; and

6. A similar lack of knowledge about a member's occasional or low levels of use, which may just not be known by the proxy respondent.

Given the potential for such misclassifications, the adult individual screener was developed as a second-phase screener to administer to each individual adult selected as a likely sampled subject based on the information obtained from the first-phase household screener. It addresses the issues above by (1) providing privacy via the ACASI mode so that no one else in the household will know the person's answers about tobacco use; this can help to foster an important sense of comfort, privacy, and candor on the part of the respondent and (2) asking directed and detailed questions about many types of tobacco products to help capture all those who are tobacco users or non-

users as defined by the PATH Study's uniquely broad and intricate standard of tobacco use, one that may not be considered by the average person.

Further, the PATH Study seeks to obtain information from users and former users of all tobacco products, some of whom may have little or no experience in use of newly emerging products. Despite the various directed questions and illustrative show cards used in the household screener, false negatives (users incorrectly sampled as non-users) from the household screener are expected to include a disproportionate number of such product users. As a result, the PATH Study expects to sample more non-users in the first-phase household screening process than are needed to achieve the sampling plan target size for the non-user stratum. Upon completion of the second-phase individual adult screener, confirmed non-users will be subsampled at a rate needed to achieve the sampling plan target size for the non-user stratum; false negatives sampled from the first-phase household screener (i.e., sampled as non-users but subsequently classified as users in the second-phase screener) will be retained at a high rate.

Overall, the two screeners are designed to provide the means for efficiently identifying and oversampling the rare population of tobacco users (estimated at ~25% of all adults) by covering users of all forms of tobacco with high validity, as based on the PATH Study's definitions. The first-phase household screener also collects information needed to select youth and shadow samples, which are based solely on age eligibility and a probability of selection set to obtain the desired sample sizes.

See Section B.1 for further details on the within-household sample design.

Tobacco Use Form

The Tobacco Use Form is administered immediately before collecting any biospecimens at follow-up visits, such as when a respondent is unable to provide buccal cells or a urine sample at the time of the interview and schedules a separate follow-up appointment, or for second visits that are scheduled for blood collection by a health professional. This form collects the time of immediate recent use of various types of tobacco products and

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. The Tobacco Use Form is administered at each follow-up visit in which biospecimens are collected, unless the adult extended interview is administered during the visit. (The adult extended interview incorporates all of the questions from the Tobacco Use Form.)

Parent Interview

Once youths are selected for the PATH Study sample, the parent interview collects personal information about the parent of a sampled youth, some general characteristics of the household as a whole, information about the youth that can be obtained more accurately and reliably from a parent, and contact information to support reaching the parent and youth for future data collection activities. The parent interview focuses on gaining information about the youth respondent's life that may be associated with tobacco use, and includes questions on parental supervision, school performance, and tobacco use by youth. Demographic information will also be verified in the parent interview; this is necessary because the household screener respondent may have been incorrect, or the youth may have had a birthday since the screener was conducted, which may place him or her in the adult sample stratum (18 years and older) rather than the youth sample stratum.

A.2c Results of Field Test

Upon receipt of OMB approval (OMB # 0925-0664, expiration 11/30/2015), the PATH Study conducted a field test. Objectives of the field test were to examine: (1) administration and performance of the data collection instruments; (2) biospecimen collection procedures (buccal cells, urine, and blood specimens were collected, packaged, shipped, and analyzed); (3) field interviewer training procedures and materials; (4) data processing and the interface between the biorepository and the prime contractor; (5) systems and security architectures; (6) alternative incentive levels for completing the household screener ($0 vs. $5 vs. $10) and incentive procedure; and (7) a

short and long version of the household screener. The field test included 1,170 household screener respondents, 480 adult interview respondents, 122 youth interview respondents, and 128 parent interview respondents. Due to the short field period (December 6, 2012 to February 17, 2013) and the emphasis given to its objectives, the field test is not a useful test of sample yield or response rates. (For additional information on the field test methods, see Section B.4.)

When compared against relevant performance standards, the field test findings indicated that several aspects of the protocol and procedures performed well overall and require only minor modification for the baseline wave, but that other aspects fell short of expectations and need more extensive modification. For example, whereas the interview lengths were acceptable, the screening rate was about 40 percent, and the biospecimen consent and response rates were lower than expected, resulting in several changes to the protocol and procedures to increase the biospecimen consent rates (see below).

Table A-2 presents selected field test findings, as well as key measures, standards for assessing performance, and comments on proposed changes for the baseline wave. An expanded version of this table and a version of the field test report are included in Attachment 2. Informed by the field test results, proposed changes for the baseline wave are now reflected in Supporting Statement B.

The proposed changes designed to maximize the data and biospecimen response rates in the baseline wave, which are summarized in Table A-2 and Supporting Statement B, are a result of a process that considered and rejected other changes to the protocol and procedures Possibilities considered included increasing incentive amounts; combining the consents for the adult interview and biospecimen collection; having health professionals join interviewers on home visits; and reducing the length of the extended interviews. The PATH Study decided against these options, mainly because they would have substantially increased costs or interfered with the timely achievement of the PATH Study’s objectives.

Table A-2. Selected field test findings

Study Component	Measure	Performance Standard	Field Test Result(s)	Comments
Methods, Procedures, and Systems				
Screener Response	Household Screener Response rate	No design assumption was made for field test. Original design assumption for baseline wave: 87%, based on findings from the 2011 National Survey of Drug Use and Health (NSDUH)	40 percent	Purpose of field test was to assess the data collection protocol and operations. This, in addition to an abbreviated follow-up period, provide context for the field test sample yields and response rates. Proposed protocol changes for baseline include: emphasizing importance of study in advance materials, improving contact and consent procedures, and enhancing interviewer training.
Comparison of Screener lengths	Interview length—Household screener (adults)	Projected time: 17 minutes	12.7 minutes for short version, 14.0 minutes for long version	Length is acceptable, use strongest items from each version.
Incentive Experiment: Household Screener Incentive ($0 vs. $5 vs. $10)	Difference in Household screener response rate	Household screener response rate is associated with incentive amount	Marginally significant difference in screener response rates: $0: 36.7% $5: 40.3% $10: 43.0%	Results suggested a positive effect of incentive amounts on the household-level screener response rates.

Study Component	Measure	Performance Standard	Field Test Result(s)	Comments
Biospecimen Collection	Consent rate for blood, urine, and buccal cell samples	Experience from other studies varies, depending on factors such as incentives and number of visits. Range observed: Urine – 60-95% Blood – 55-83%	Consent rates among those who completed visit 1 interviews: Buccal cell – 74.0% Urine – 59.6% Blood – 46.9%	Modifications have been implemented to improve consent rates, including: modifying the structure of incentives, providing additional information in consent materials on the importance of biological specimens to the study, providing interviewers with specific information to address common respondent concerns, and enhancing interviewer recruitment and training. The field test was not intended as a test of response rates.
Processing at the Repository	Success in obtaining the expected number of aliquots from each collected biospecimen	Number of aliquots specified by the processing protocol	All urine aliquots were obtained when an adequate volume of urine was collected. Fewer than expected small volume plasma and serum aliquots were obtained.	The processing protocols for plasma and serum have been modified for baseline to ensure an adequate number of small volume aliquots will be obtained.
Flow of Scientific Information				

Study Component	Measure	Performance Standard	Field Test Result(s)	Comments
Questionnaire Performance	Computer-assisted recorded interviewing review	Interviewers followed protocol and questions performed as expected.	Interviewers had difficulty with some portions of the protocol and some questions were hard to read as intended.	The protocol has been simplified to make it easier for interviewers to follow. Questions have been revised and restructured to make them easier to read as intended. Training procedures have been improved.

Note. The sampling design assumptions are national, whereas the field test results are for a purposive selection of 15 PSUs.

A.2d Uses of Information by NIDA

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

As a research study, the PATH Study will collect and analyze population-based data over time to enhance the evidence-based framework FDA uses in meeting its regulatory mandates under the TCA. The PATH Study's baseline data will provide a comprehensive baseline to support this framework, first through the analyses of between-person differences in tobacco use behaviors and health and, over time, by analyzing within-person changes, both in parallel with FDA's tobacco-related decisions and actions. Analyses include but are not limited to identifying key transitions in the course of nicotine dependence (from the earliest experiences of initiation, to daily use, poly-tobacco use, cessation attempts, and relapse) and assessing how these transitions are associated with tobacco use-related health conditions, the implementation of specific tobacco-related policies and programs, or changes in the tobacco product marketplace.

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

A.2e Use of Information by Other Agencies and Organizations

As NIDA's principal partner in conducting the PATH Study, FDA has specific plans for use of its data to meet its mandate by the TCA for meaningful and effective tobacco product regulations. As mentioned in Section A.1, the TCA authorizes FDA to regulate tobacco-product advertising, labeling, marketing, constituents, ingredients and additives; it also mandates FDA to report back

to Congress within specific periods of time its progress and effectiveness in implementing key TCA provisions. The TCA mandates the regulation of tobacco products using a population health standard including users and non-users of tobacco products The PATH Study is critical to facilitating this process. Its nationally representative longitudinal cohort design will provide epidemiological, population-based data on tobacco use behaviors, attitudes, exposures, and health to help inform FDA's regulatory decisions and actions under the TCA.

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

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

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

data disclosure, sharing, and confidentiality for qualified researchers with interests in analyzing the PATH Study data.

Data sharing plans promulgated by the NIH dictate dissemination of appropriately de-identified data. After data collected by the PATH Study are stripped of personally identifiable information (PII) and subjected to disclosure limitation procedures, they may be deposited in a repository such as the National Addiction and HIV Data Archive Program (NAHDAP) at the University of Michigan's Inter-University Consortium for Political and Social Research (ICPSR); data from other NIDA-funded research projects, including research studies and surveys, are routinely deposited in NAHDAP for public or restricted use.

A.3 Use of Information Technology and Burden Reduction

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

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

1. Use of an automated computer-assisted personal interviewing (CAPI) household screener to determine household eligibility and to select sample persons for the PATH Study;

2. Use of automated audio computer-assisted self-interviewing (ACASI) extended instruments (separate instruments for youth and adults) and an automated CAPI parent instrument to collect PATH Study data;

3. Use of lead-in questions and logic-based question routing to skip entire sections or questions that are not relevant to a sample person;

4. Use of flashcards or on-screen displays of lists and images to aid sample persons with multiple response categories;

5. Arrangement of sections and questions in the PATH Study extended interviews that will make sense to the sample person and will facilitate the flow of administration from one topic area to another;

6. Use of data collectors who are bilingual in English and Spanish; and

7. Use of versions of all instruments, consent forms and other study documents in Spanish where English is not spoken or it is the respondent's preferred language for the interview.

The majority of the PATH Study data will be gathered via computer-assisted questionnaires (i.e., CAPI or ACASI). The adult and youth questionnaires are designed with separate modules, and all but a few sections have lead-in questions that respondents can check for relevance in order to quickly skip out of non-relevant modules. This design was successfully used in the National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC) study (OMB #0925-0628, expiration date 4/30/2014). Brief tests of the PATH Study instruments with fewer than 9 individuals indicated that the average adult or youth respondent answered questions in about one-third of the total number of sections in the adult or youth instrument, respectively. Further, within each instrument, about one-third of the associated questions were applicable to any particular respondent, leaving two-thirds inapplicable and, therefore, requiring no answer from either the adult or youth respondent taking the respective interview.

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

Tobacco-related data collections supported by the Federal government and subject to OMB review require strategic coordination to assure they maximize the utility of data collected, minimize burden on participants, and comply with HHS standards. To achieve these objectives, NIH and FDA are working with the Assistant Secretary for Planning and Evaluation (ASPE) at HHS to facilitate the coordination and integration of tobacco-related data-collection efforts, to the extent feasible, practicable, and desirable, across HHS agencies. From a feasibility perspective, the current funding mechanism (the TCA) requires that the research data collected by the PATH Study be

relevant to FDA’s regulatory priorities, needs, and authorities related to the manufacture, marketing, and distribution of tobacco products. Consequently, within the limits and authorities of the TCA, the PATH Study has flexibility to integrate the data-collection needs of other HHS agencies, such as by including questionnaire items and priority measures of shared interest.

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

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

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

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

Longitudinal Design. The PATH Study's longitudinal design gives it the capacity to generate data on between-person differences and within-person changes in tobacco-use behaviors, attitudes and risk perceptions, biomarkers of harm associated with tobacco use, and related health outcomes over the lifespan. This is important for understanding factors associated with the uptake of new products, in product switching, in poly tobacco use, and in cessation and relapse. By contrast, cross-sectional surveillance surveys such as NYTS, NATS, and TUS-CPS are designed to generate representative "snapshots" of the U.S. population at a given point in time, but not between-person differences or within-person changes over time.

The PATH Study's probability-based sample (n=58,916) 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), including attitudes and risk perceptions, biomarkers of harm associated with tobacco use, tobacco dependence, and tobacco use-related health outcomes over the lifespan. 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 ensure adequate representation of this subpopulation for reliable statistical analyses.

As a longitudinal cohort study, the PATH Study has the capability to follow youth as they age into young adulthood. This places the PATH Study in position to assess between-person differences and within-person changes over the life course, from youth to adolescence, young adulthood, and adulthood, to understand contemporary trends in tobacco-use patterns, including onset and progression, cessation efforts and relapse, and successful cessation, all in the context of changes in the tobacco product marketplace, in marketing techniques and messages on different types and brands of tobacco products, and in FDA's regulatory decisions and activities.

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

Scope of Data Collection. The PATH Study is distinguished by the breadth and depth of its coverage of tobacco use, tobacco products (e.g., cigarettes, cigars, pipes, smokeless and new and emerging products such as snus, hookah, and e-cigarettes), and tobacco product brands and sub-brands. Data-collection methods, which include an image database of tobacco products, brands, and sub-brands, will enhance the specificity of the tobacco-use data, for example, by allowing the differentiation of traditional cigars, little filtered cigars, and cigarillos. It also provides for the assessment of respondents' recognition, exposure, and receptivity to tobacco marketing. In addition to respondent interview data, the PATH Study is collecting three biospecimens from consenting adults (i.e., urine, buccal cells, and blood) in the baseline year, to serve as the basis for examining and comparing biomarkers of exposure, including exposure to tobacco products, tobacco brands and sub-brands . This multi-component data-collection protocol distinguishes the PATH Study's capacity to enhance the evidence base FDA needs for its tobacco-related regulatory activities with timely, specific, population-based data.

A.5 Impact on Small Businesses or Other Small Entities

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

A.6 Consequences of Collecting the Information Less Frequently

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

Not conducting the PATH Study as scheduled (or delaying its annual follow-up interviews of each cohort respondent) would significantly reduce FDA's ability to capitalize on the strengths of the cohort study design to examine associations between enacted policies and tobacco use uptake, cessation, and relapse in the population. The dynamic environment of ever-changing policies and tobacco industry efforts requires annual data and biospecimen collection. Data collected less frequently would be considerably less precise, and would significantly decrease the capacity of the study to meet the scientific needs of NIDA and FDA to establish a science framework that informs FDA's efforts to protect the Nation's public health.

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

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

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

A.8a Federal Register Notice

The 60-day Federal Register Notice, required by 5 CFR 1320.8 (d) to solicit comments on the information collection prior to submission to the OMB, was published on May 18, 2012 in the Federal Register (Vol. 77, No. 97 pgs. 29667 - 29668). Two comments were received. One was a letter in support of the collection of data for the PATH Study. The other offered four suggestions to "improve the quality, utility, and clarity of information NIDA intends to collect in the PATH Study." The comments and NIDA's responses to these comments are included in Attachment 10.

A.8b Efforts to Consult Outside Agency

Individuals from within NIH, FDA, and other units within DHHS and numerous outside agencies, institutions, and universities were consulted from October 2011 to the present, and these consultations are ongoing. The individuals consulted include the PATH Study questionnaire workgroup and sampling workgroup, which include individuals from Roswell Park Cancer Institute, Legacy/The Schroeder Institute for Tobacco, Pinney Associates, University of California San Diego Moores Cancer Center, University of Waterloo, Dartmouth College, University of Illinois at Chicago, Westat, CDC, and FDA. These workgroup members represent experts in the fields of tobacco research and survey methodology, and provided significant input on questionnaire content, sampling design, and methodology. Numerous other individuals also contributed their expertise regarding sample design and methodology, questionnaire content, and related issues. The names, affiliations, and phone numbers of all individuals consulted are presented in

Attachment 11. During the aforementioned consultations, all issues raised were satisfactorily resolved.

A.9 Explanation of Any Payment or Gift to Respondents

The design of the PATH study involves significant burden to respondents, both in terms of interview time, multiple visits, and the provision of biospecimens. To assist in meeting the response rate goals of the PATH Study, multiple incentives are proposed (see Table A-4). A $2 incentive is proposed to be included in the advance mailing letters sent to households sampled for the PATH Study to ensure that potential respondents read the letters. Research has found that including an incentive in mailings increases the likelihood that respondents will read the letter (Singer, 2002).

Table A-4. PATH planned incentives

	Incentive
Advance Mailing	$2
Adult Visit #1 (conducted by interviewer)	
Adult Extended Interview	$35
Biospecimen collection	$25
Adult Visit #2 (conducted by health professional) -- additional biospecimen collection	$25
Youth Interview	$25
Parent Interview*	$10
Contact Information Update**	$10

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

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

An incentive of $35 is proposed for adult respondents who complete the adult extended interview at the first 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. In addition, at the first home visit, an incentive of $25 is proposed for adult respondents who consent to and provide biospecimens and related information to the interviewer. An incentive of $25 is planned for adult respondents who consent to and provide additional biospecimens and related information to a health professional at a second home visit. 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. Several research studies have shown the importance of providing a significant incentive at the baseline interview to increase response rates (Rodgers, 2011; Goldenberg, et al., 2009). Use of separate incentives for completion of different components of a study has been used by other studies approved by OMB (e.g., National Children's Study OMB #'s 0925-0661 expiration date 6/30/2015, and 0925-0647 expiration date 1/31/2015).

To encourage retention of PATH Study respondents over time, an incentive is proposed for adult respondents who provide updates to their contact information in between data collection waves. Adults will receive $5 each time they update their contact information up to a total of $10 per year.

Youth respondents will receive $5 each time their parent updates their contact information up to a total of $10 per year. Research also supports the use of incentives between data collection waves as they boost response rates and increase the amount of updated locator information received from respondents (McGonagle, et al., 2011; Castiglioni, et al., 2008).

The incentives will be mentioned in several study materials: in the advance letter sent to each selected household prior to contact by the data collector; in the study brochure enclosed with the letter; and in the consent document provided to each respondent prior to the start of the PATH Study extended interview (see Attachments 12 and 13). These materials will clearly state that the household screener will identify whether any household member is eligible to be selected for the PATH Study, and if selected for the study, that incentives will be provided as a thank you for completing each visit and associated tasks (the first adult visit for completing the adult extended interview and, separately, for consenting to and providing biospecimens; a second adult visit for consenting to and providing additional biospecimens; the parent interview; the extended youth interview; and for providing contact information for future follow-up by the PATH Study). Biospecimens will only be collected from adults who complete the PATH Study extended interview.

Thus, as part of the PATH Study baseline data collection and prior to the first follow-up data collection wave, an adult respondent may receive up to $97 as a thank you for participating in the PATH Study: $2 in the advance mailing, $35 for the extended interview at a first home visit (OMB approved a $90 incentive for the NESARC study [OMB # 0925-0628 expiration date 4/30/2014], which did not include a separate visit to collect blood from study respondents), $25 for biospecimens and related information at the first home visit, $25 for additional biospecimens and related information at a second home visit, and a maximum of $10 for updating 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)[1]. A youth respondent may receive up to $35 for participating in

[1] In households with multiple births, parents may complete a total of 4 interviews for 4 youth to receive a maximum of $40.

the PATH Study: $25 for completing the youth extended interview, and a maximum of $10 for having their parent provide updated contact information.

The PATH Study proposes to pay some of the incentives by means of cash or check, and others by means of debit cards. For small, stand-alone incentives (advance mailing and contact information updates), the study will use cash or checks. For larger incentives that may be combined for a given respondent (i.e., as thank-you incentives for completing the first and second home visits), the study will use debit cards. In these cases, trained field interviewers will distribute a blank debit card to each respondent who completes the first visit, and the PATH Study will transfer the correct funds to the debit card within approximately 3 business days. If the respondent consents to a second home visit for additional biospecimen collection, the incentive for that follow-up visit will also be transferred to the card.

A.10 Assurances of Confidentiality Provided to Respondents

A.10a Overview

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

psychological, and social consequences. The COC issued to the PATH Study on August 31, 2012 and amended on June 6, 2013 is included in Attachment 14.

Law governing Federal employees conducting this research study, 18 U.S.C. 1905, (which prohibits disclosure of individuals' identifying information or confidential statistical data by Federal employees) is also relevant to the maintenance of confidentiality of data. In addition, all study activities under this contract will be conducted in compliance with 45 CFR Part 46, Protection of Human Subjects, HHSAR 352.270-8(a) (January 2006), the Privacy Act of 1974, and the Systems of Records Notice 09-25-0200 (regulations pertaining to confidentiality of data).

The PATH Study will implement a range of procedures to protect respondents' Personally Identifiable Information (PII) and the confidentiality of all data. All data collection staff will be proficient in data security, confidentiality, and privacy issues and procedures. PATH Study field interviewers will be required to sign a pledge of confidentiality (see Attachment 15) and to complete training on standards and ethics in research that includes detailed content on topics such as confidentiality and informed consent.

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

Data will be identified by unique identification numbers assigned to each respondent. These will then be used to link responses to the PATH Study extended interview and the biospecimen collection. Crosswalks that match

these numbers to PII will be stored in secure, encrypted files accessible only to authorized staff whose roles on the study necessitate access. NIDA will not have access to identifying information, and personal identifiers will not be included in the data received by NIDA. The prime contractor will transfer all data for the PATH Study and associated products and documents to NIDA at the time of compiling final data files, and will not retain any records of the data. Procedures for the storage and disposition of data collected as part of the PATH Study are described in Section A.10b.

All PATH Study respondents will be informed of the sponsor, the nature, purpose and uses of the study data, legal authorities, the voluntary nature of the PATH Study, and the protection of the information in an advance letter (Attachment 12) mailed to all dwelling units 1 to 2 weeks prior to the data collector's visit. Prior to administration of the household screener, the data collectors will ask if the household received the introductory letter. Those respondents who do not recall receiving or reading the letter will be provided with a copy of it, and sufficient time will be allowed for them to read it and ask any questions related to the letter.

All respondents will be informed in writing that the information they provide will be kept private to the extent permitted by law under the Privacy Act. Participation is voluntary; respondents may decline answer particular questions without any consequence. An informed consent form, which includes descriptions of risks, benefits, and privacy protections, will be reviewed with each potential PATH Study respondent and will be signed by all those choosing to participate in the study. Separate consent forms (see Attachment 13) and procedures have been developed for adults and youth. For youth, parental permission will be obtained in writing prior to seeking youth assent to participate in the PATH Study. There is also a separate consent form for adult biospecimen collection. Information in the consent documents is presented in language that is easily understood and covers many topics, including the (1) voluntary nature of the data collection; (2) purposes and uses of the data; (3) storage and use of the biospecimen samples; (4) privacy of the information; (5) whether study results or information are available to the respondent; (6) benefits/risks; and (7) contact information regarding questions about the PATH Study.

As noted previously in A.3, two PIAs for the PATH Study were promoted on July 6, 2012 (see Attachment 7). The PATH Study also received approval from the prime contractor's Institutional Review Board (IRB) (Attachment 16).

A.10b Storage and Disposition of the Information

Information collected in the PATH Study is covered by NIH Privacy Act SORN 09-25-0200, "Clinical, Basic, and Population-based Research Studies of the National Institutes of Health (NIH), HHS/NIH/OD" published in the Federal Register on September 26, 2002 (67 FR 60776) (Attachment 17). The NIH Privacy Act Officer has also reviewed the information contained herein and determined that the Privacy Act applies to the PATH Study data collection.

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

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

The prime contractor for the PATH Study is responsible for storing identifiers in a secure, database environment in accordance with the security guidelines defined by the Federal Information Security Management Act (FISMA) and NIST Special Publication 800-53 for Moderate information system security. All systems and databases handling or storing PII and/or PHI (protected health information) will be reviewed for FISMA compliance by the NIDA Chief Information Officer (CIO) and Information Systems Security Officer (ISSO), and will not be operated in production mode until granted an Authority To Operate (ATO) by NIDA. All computerized data will be maintained in a manner that is consistent with the FISMA Moderate requirements. No reports or analysis files will contain PII. A complete list of the procedures the contractor will take to keep the study data private are found in Attachment 18.

Access to the PII is limited to a small number of immediate staff working on the study, and all staff members will sign a pledge of confidentiality prior to beginning work (Attachment 15). In addition, all contract staff members are required to undergo background screening commensurate with their role on the project and their access to study data, and are required to complete NIH Computer Security Awareness Training as well as Privacy Awareness Training.

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

A detailed inventory of all files, including hard copy consent forms, which include respondent names, and all other PII, will be secured separately from research data and accessible only to authorized staff. All records, including hard copies of informed consent and other documentation, will be retained

and disposed of under authority of the NIH Records Control Schedule contained in NIH Manual Chapter 1743, Appendix 1B "Keeping and Destroying Records" (HHS Records Management Manual, Appendix B-361) (see Attachment 17).

A.10c Plans for Data Sharing

NIDA and FDA will create a public use dataset from each wave's data, making it available to the public on-line, consistent with OMB's Memorandum 13-13 (March 2013). The time period from completion of a wave to availability of a public use dataset is anticipated to be within 18 months. Data underlying all government-funded scientific publication will be made available to the public at the time of publication, to the greatest extent feasible and consistent with applicable laws. Such transparency is particularly important in the regulatory context (see the Office of Science and Technology's Scientific Integrity Guidance, December 2010).

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

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

Upon receiving DAC approval, researchers will be required to submit a Data Use Agreement to the data repository, such as NAHDAP/ICPSR (see Attachment 19) to gain access to the restricted data files. These data files will include PATH Study questionnaire data and may include data from biospecimens, however, qualified researchers interested in accessing PATH Study biospecimens to conduct analyses will be required to apply to the PATH Study Biospecimen Access Committee (BAC). This committee will manage the: sharing of biospecimens; instruct the PATH Study biospecimen repository subcontractor to ship specimens to approved labs/researchers; track the progress of researchers; and if necessary recall biospecimens.

A.11 Justification for Sensitive Questions

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

A.11a Tobacco

The mission of CTP at FDA is to protect Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products; and by educating the public, especially young people, about tobacco products and the dangers their use poses to themselves and others. The PATH Study is central to this mission and will

provide population-based scientific evidence to inform FDA's regulatory activities. Tobacco use questions are the critical core of the PATH Study – without these questions, FDA's ability to achieve its mandated mission under the TCA would be significantly impaired.

The PATH Study's focus is on tobacco use. Most of the items in its instruments are similar to or slight variations of items common to widely-used surveys on tobacco that have been approved by OMB. The PATH Study adult instrument contains questions that assess tobacco use in great detail and breadth. Answers to these questions will provide a resource to NIDA and FDA to understand risk factors associated with tobacco use initiation, as well as motivations for product-switching, use of multiple tobacco products, and quitting. Such questions are not generally considered sensitive when administered to adults.

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

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

A.11b Psychological Problems and Conditions

Tobacco use is highly associated with an array of psychological problems and conditions, including depression and anxiety. Adults (John, et al., 2004) and youth (Udaphyaya, et al., 2002) with mental health concerns use tobacco at higher rates and find it more difficult to quit using tobacco (Snyder, 2006). Epidemiologic and clinical studies have shown that psychiatric disorders are important moderators of nicotine dependency severity (as measured by Fagerstrom Test of Nicotine Dependency or FTND scores, for example), withdrawal, craving, quitting, and responses to changes in cigarette pricing. As reported by Legacy (2011): “People with mental illnesses smoke at rates almost twice as high as the general population (41 percent versus 22.5 percent, respectively). Nearly half the cigarettes smoked in the United States (44-46 percent) are consumed by people with co-occurring psychiatric or addictive disorders.” Moreover, remission from nicotine was moderated by comorbid psychiatric disorders and substance use disorders, findings that have been replicated in cross-sectional and longitudinal analyses. In summary, including these constructs in PATH Study instruments will facilitate understanding of how various program and policy changes may affect tobacco use behaviors in the population.

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

The PATH Study has developed a handout (Attachment 20) 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 Global Appraisal of Individual Needs Short Screener (GAIN SS). These are a series of questions designed to identify respondents who have one or more behavior health disorders, including internalizing or externalizing psychiatric disorders and substance use disorders.

A.11c Substance Abuse

Substance abuse and tobacco use are frequently comorbid conditions. In numerous household surveys conducted since 1960 in the U.S., the results indicate that such questions have not been considered sensitive by respondents. Item nonresponse for such questions was low (generally less than 5.0 percent), and interview break-offs and refusals related to these questions were negligible (less than 1.0 percent). Examples of these surveys, all of which obtained OMB approval, include: SAMHSA's NSDUH conducted since the early 1980s (OMB #0930-0110, expiration date 8/31/2014); the Bureau of Labor Statistics' National Longitudinal Survey of Youth (NLSY) conducted periodically since 1973 (OMB# 1220-0109, expiration date 12/31/2013); and CDC's National Health and Nutrition Examination Survey (NHANES) (OMB # 0920-0237, expiration date 11/30/12).

A.11d Income

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

administered item (rather than an interviewer-administered item); it includes household income categories that a respondent selects.

A.11e Sexual Identity, Orientation, and Attraction

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

The PATH Study adult interview includes three items from the National Health Interview Survey 2013 (Miller, et al, 2011) that ask about sexual identity/orientation. The PATH Study youth interview includes the same three items 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 (Centers for Disease Control and Prevention, 2011). The NHIS does not ask about sexual attraction.

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

A.12 Estimates of Annualized Burden Hours and Costs

The average annual hour burden for the baseline wave is presented in Table A-5. Annualized cost to respondents associated with the PATH Study baseline wave is presented in Table A-6. Burden estimates were based on the results from the field test conducted with 1,170 household screener respondents, 480 adult interview respondents, 122 youth interview respondents, and 128 parent respondents. These estimates include the time needed to respond to the entire interview, read the introductory letter, and to potentially respond to the data quality verification interview.

Table A-5. PATH Study baseline hour burden estimates

Type of Respondent and Instrument	Estimated Number of Respondents	Estimated Number of Responses per Respondent	Average Burden Hours per Response	Estimated Total Annual Burden Hours Requested
Adults – Household Screener	104,725	1	14/60	24,436
Adults – Individual Screener	59,500	1	6/60	5,950
Adults – Extended Interview	42,730	1	54/60	38,457
Adults – Biospecimen Collection: Urine	42,730	1	10/60	7,122
Adults – Biospecimen Collection: Buccal Cell	42,730	1	18/60	12,819
Adults – Biospecimen Collection: Blood	42,730	1	18/60	12,819
Adults – Tobacco Use Form	42,730	1	4/60	2,849
Adults – Follow-up/Tracking Participant Information Form	42,730	2	8/60	11,395
Youth – Extended Interview	16,186	1	32/60	8,633
Adult – Parent Interview	16,186	1	14/60	3,777
Adults – Follow-up/Tracking Participant Information Form for Youth (completed by parents)	16,186	2	$^{8}/_{60}$	4,316
Adults – Follow-up/Tracking Participant Information Form for Shadow Sample Youth (completed by parents)	16,186	2	8/60	4,316
Total				136,889

Table A-6. PATH Study baseline annualized cost to respondents

Type of Respondent and Instrument	Number of Respon-dents	Frequency of Response	Average Time Per Respon-dent	Annual Hour Burden	Hourly Wage Rate	Respondent Cost
Adults – Household Screener	104,725	1	14/60	24,436	$16.27	$397,571
Adults – Individual Screener	59,500	1	6/60	5,950	$16.27	$96,807
Adults – Extended Interview	42,730	1	54/60	38,457	$16.27	$625,695
Adults – Biospecimen Collection: Urine	42,730	1	10/60	7,122	$16.27	$115,870
Adults – Biospecimen Collection: Buccal Cell	42,730	1	18/60	12,819	$16.27	$208,565
Adults – Biospecimen Collection: Blood	42,730	1	18/60	12,819	$16.27	$208,565
Adults – Tobacco Use Form	42,730	1	4/60	2,849	$16.27	$46,348
Adults – Follow-up/Tracking Participant Information Form	42,730	2	8/60	11,395	$16.27	$185,391
Youth – Extended Interview	16,186	1	32/60	8,633	$7.25	$62,586
Adult – Parent Interview	16,186	1	14/60	3,777	$16.27	$61,448
Adults – Follow-up/Tracking Participant Information Form for Youth (completed by parents)	16,186	2	8/60	4,316	$16.27	$70,226
Adults – Follow-up/Tracking Participant Information Form for Shadow Sample Youth (completed by parents)	16,186	2	8/60	4,316	$16.27	$70,226
Total				136,889		$2,149,298

The estimates for hourly wage of adult respondents is based on the national median hourly estimate for all occupations reported in the Bureau of Labor Statistics' Occupational Employment Statistics, May 2010 National Occupational Employment and Wage Estimates United States. See http://www.bls.gov/oes/current/oes_nat.htm. Estimates for youth hourly wages are based on the federal minimum wage. See http://www.dol.gov/dol/topic/wages/minimumwage.htm.

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 total estimated annual cost of the 5-year PATH Study to the Federal government is $1.3 million. This estimate is based on the mean weighted salaries (average of $116,000 each) of the 11 FTEs of federal staff at NIH and FDA responsible for this work. It includes quantification of hours (full time) plus estimates for operational expenses (including equipment, overhead, printing, and support staff) that would not be incurred without this collection of information. The PATH Study contract is funded by FDA through an Interagency Agreement to NIH/NIDA using tobacco user fees assessed under the authority of the TCA (PL 111-31, June 22, 2009). Contractor expenses for conducting information collection activities, including the design and development of the sample, field testing, interviewer training, mailing list compilation and maintenance, printing forms and materials, mailing and enumeration, data and biospecimen collection, editing, coding, tabulation, data analysis, and the reporting and dissemination of results are estimated to be a total of $207 million for all 5 years.

A.15 Explanation for Program Changes or Adjustments

This is a non-substantive change request to begin the baseline wave of data collection for the PATH Study. This data collection is based on the completion of a field test approved by OMB on 11/30/12. The estimated burden for the baseline wave is 136,889 hours. This is lower than the estimated burden of 138,514 hours reported for the baseline in the original package approved for the field test. The lower number results from a combination of fewer youth and parent interviews estimated for the baseline

and refinements made to several instruments based on the field test to reduce burden on participants.

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

A.16a Plans for Tabulation and Publication

Analyses will be conducted by Westat pursuant to plans agreed upon in concert with NIDA and FDA. Plans for tabulation, statistical analysis, and publication of the PATH Study data are driven by its research design and major objectives presented in Section A.2. As a longitudinal cohort study, the PATH Study involves repeated observations on the same individuals to examine between-person differences and within-person changes over the same period of time. Benefits of the longitudinal research design include observing changes more accurately over time because the same persons are observed at multiple points over the same temporal order of events. For the baseline data, the PATH Study plans to focus on establishing a comprehensive assessment for the cohort that will serve as the "anchor" against which individuals will be compared to examine within-person changes over the follow-up waves. The baseline data will provide the PATH Study with the capability to screen respondents for participation in small-scale research studies, such as in cognitive testing or methodological studies under the PATH Study's existing generic clearances, or in other types of research studies that focus on new and emerging tobacco-related issues of interest to FDA. The PATH Study's baseline data may also be useful in corroborating the prevalence and incidence estimates produced by major cross-sectional surveillance surveys on health conditions in the U.S. population, such as NHANES and NHIS.

In addition, baseline data will be used to inform the PATH Study's major objectives, primarily by examining between-person differences in: (1) tobacco-use patterns, including specific product type and brand, product/brand switching over time, uptake of new products, and dual- and

poly-use of tobacco products (i.e., use of multiple products within the same time period, and switching between multiple products) (Objective 1); (2) risk perceptions regarding HPHC, new and emerging tobacco products, filters and other design features of tobacco products, packaging, and labeling, and other factors that may affect use (such as social influences and individual preferences) (Objective 2); (3) tobacco use dependence, cessation, and relapse, including readiness and self-efficacy to quit, motivations for quitting, the number and length of quit attempts, and the length of abstinence related various tobacco products (Objective 3); and (4) potential early markers of tobacco use exposures and related disease processes (Objective 4). Key analyses for papers planned after completion of the baseline wave include, but are not limited to: (1) description of rates of use and levels of dependence by tobacco product type for youth and adults; (2) demographic correlates of the use of each tobacco product type for youth and adults; (3) description of reasons for use of non-cigarette tobacco products; (4) description of risk perceptions, attitudes, and knowledge by tobacco product type; (5) description of youth and adult exposure to tobacco industry marketing; and (6) description of levels of biomarkers of exposure and harm by tobacco product type and health measure. (See Attachment 21 for detailed examples of some, but not all, of the analyses planned after completion of the baseline wave.)

Pending sufficient sample sizes and non-response bias analyses, PATH Study data will be used to assess and compare samples of former and never users of tobacco products for between-person differences and within-person changes in relapse and uptake, risk perceptions, and indicators of tobacco exposure and tobacco use-related disease processes. All such analyses will attempt to account for other potential factors that may influence these measures (e.g., demographics, local tobacco-control policies, and economic, social network, peer group, and family factors(Objectives 5 through 7). Major outcome variables represent dependent variables, while tobacco policy variables and major demographic and socioeconomic variables will serve as independent, confounding, mediating or moderator variables. Many of these analyses will include the use of logistic regression models, however, specific multivariate procedures to be performed 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 the PATH Study biospecimens. These analyses will focus on comparing intermediate endpoints (i.e., markers of exposure and tobacco-related disease processes) and health outcomes. Examples of specific analytes for which some of the biospecimens will be tested are presented in Attachment 6.

A.16b Project Time Schedule

The following table outlines the key activities and time schedules for the PATH Study baseline wave of data collection.

Table A-7. Baseline timeline

Activity	Time Schedule
OMB approval for field test	November, 2012
Begin baseline data collection	10 Months after OMB approval
Process and clean questionnaire data	12 – 36 Months after OMB approval
Data Analyses	13 – 36 Months after OMB approval
Publish preliminary study results/release public use data files for questionnaire data	Within 18 Months after completion of data wave
Publish preliminary study results/release public use data files for biospecimen data	Within 18 months after completion of data wave

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

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

A.18 Exceptions to Certification for Paperwork Reduction Act Submissions

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

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