

Frequently Asked Questions and Answers

Secondary Analyses of Existing Datasets of Tobacco Use and Health (R21 Clinical Trial Not Allowed)

Updated July 15, 2019

Eligibility for the R21

1. Are foreign investigators eligible to apply as Principal Investigators (PIs) for this Funding Opportunity Announcement (FOA)?
 - A. Foreign individuals are eligible to apply but must demonstrate that the proposed research can directly contribute to the U.S. Food and Drug Administration's (FDA) regulatory authority over the manufacture, marketing, and distribution of tobacco products. Individuals must also demonstrate that they will be employed by an eligible institution for the full award period of the grant.
2. Are foreign institutions eligible to apply?
 - A. Yes. However, research proposed in applications from foreign institutions must be specific to the U.S. population and provide information that will be useful to U.S. regulations.

Budget

3. Is there a budget cap on R21 applications?
 - A. Yes. The combined budget for direct cost for the entire project period may not exceed \$275,000. No more than \$200,000 in direct cost may be requested in any single year.
Two years maximum.

Application Requirements/Submission

4. Where can the applicant find additional information regarding application submission?
 - A. The National Institutes of Health (NIH) provides multiple resources for applicants with submission questions. Below is a list of resources, depending on the type of question being asked:
 - For questions regarding Grants.gov registration and submission, as well as downloading forms and application packages, please contact Grants.gov Customer Support at support@grants.gov.
 - For questions regarding application instructions, process, and finding additional NIH grant resources, please contact GrantsInfo at GrantsInfo@nih.gov.
 - For questions regarding Application Submission System & Interface for Submission Tracking (ASSIST), electronic Research Administration (eRA) Commons registration, submitting and tracking an application, documenting system problems that threaten submission by the due date, and postsubmission issues, please contact [Finding Help Online](#). Telephone: 301-402-7469 or 866-504-9552 (toll free).
 - For peer review questions, contact Dr. Delia Olufokounbi Sam from the NIH Center for Scientific Review at delia.olufokounbisa@nih.gov.

- For financial/budgetary questions, please contact the appropriate grants management contact listed in Section VII of the FOA.
 - For scientific and responsiveness questions, please contact the appropriate scientific contact listed in Section VII of the FOA.
5. When are applications due?
- A. Applications are due October 8, 2019, August 7, 2020, and March 8, 2021.
6. Am I required to submit a letter of intent (LOI)?
- A. An LOI is not required, and it does not enter into the review process. However, it allows NIH staff to estimate the potential review workload and plan the review. Investigators are encouraged to communicate with NIH scientific research contacts to discuss their research ideas and specific aims prior to submitting applications as all proposed research must be within the scientific interest areas covered in this FOA. We suggest submitting an LOI 60 days before the application due date. Applications that are non-responsive will not move forward to the review process.
- Suggested content of an LOI:
- Descriptive title of proposed activity
 - Name(s), address(es), and telephone number(s) of the Principal investigators/PI(s)
 - Names of other key personnel
 - Participating institution(s)
 - Number and title of this funding opportunity
 - Specific aims
7. Where do I send the LOI?
- A. The letter may be sent by email to: TRSP@mail.nih.gov
or by regular mail to:
Tobacco Regulatory Science Program
Office of Disease Prevention
6100 Executive Boulevard
Room 3B01, MSC 7530
Bethesda, MD 20892-7530 (Use Rockville, MD 20852 for Express Mail)
Telephone: 301-451-7464
Fax: 301-480-2230

Responsiveness

8. How do I know if my application is responsive to this FOA?
- A. This is a critical question, as **each of the specific aims** in the application must meet the following criteria to be considered responsive. The project must:
- Address one or more of the scientific interest areas listed in the FOA, **and**
 - Fall within the scope of the FDA Center for Tobacco Product's (CTP) regulatory authority.

As such, applicants are strongly encouraged to contact the scientific research contacts listed in Section VII of this FOA for feedback about responsiveness prior to submitting an application.

Note that upon receipt, applications will be **evaluated for responsiveness** by the FDA CTP and participating NIH Institutes. **Only applications that are within the scope of the scientific research areas listed in the FOA and the FDA CTP's regulatory authority will be peer reviewed.** Your application title, abstract, and specific aims are used to make this determination, so it is important that you are clear about your proposed scientific aims and how they may potentially inform the FDA CTP's regulatory authority. Staff reviewing your application will refer to other parts of the application if responsiveness is unclear based on title, abstract, and specific aims. If your application is deemed responsive, it will undergo scientific peer review by experts convened specifically for this FOA (by the NIH Center for Scientific Review). If your application is deemed non-responsive, it will be withdrawn prior to evaluation of its scientific merit (i.e., peer review).

9. The FDA CTP has regulatory authority over the manufacture, marketing, and distribution of tobacco products. What are some examples of these authorities?

A. [The Family Smoking Prevention and Tobacco Control Act](#) gave the FDA responsibility and authority to, among other things:

- Restrict cigarettes and smokeless tobacco retail sales to youth.
- Restrict the sale and distribution of tobacco products, including advertising and promotion, as appropriate to protect public health.
- Review modified risk tobacco products, such as those marketed for use to reduce harm, prior to their introduction to the market.
- Adjust warning labels for cigarettes and smokeless tobacco products in order to promote greater public understanding of the risks of tobacco use.
- Establish standards for tobacco products—for example, setting limits on harmful and potentially harmful constituents and nicotine levels—as appropriate to protect the public health.
- Review new tobacco products prior to their introduction to the market.

For more information, see the overview of the [Family Smoking Prevention and Tobacco Control Act](#).

10. What research areas are not within FDA CTP regulatory authorities?

A. In general, CTP's regulatory authorities do not extend to:

- Setting tax rates for tobacco products
- Regulating therapeutic products, such as those marketed to treat tobacco dependence (regulated by other parts of FDA)
- Setting clean indoor air policies
- Regulating tobacco growing
- Requiring the reduction of nicotine yields to zero
- Providing cessation services

- Banning all cigarettes, smokeless tobacco products, little cigars, other cigars, pipe tobacco, or roll-your-own tobacco products
- Changing the minimum age to purchase tobacco products

11. What type of innovative analysis with existing datasets might be relevant to this FOA?

Applications **should not propose** to carry out currently ongoing data analysis or the maintenance and distribution of data sets. Research using extant data that analyzes effects or outcomes that were not previously examined in the original scope of research **is a priority** for this announcement. Thus, the proposed research should be distinct from the aims and methods of the primary research under which the data were collected. For example, datasets collected for other purposes might be reanalyzed to identify:

- 1) patterns of tobacco use, including associated factors
- 2) tobacco product characteristics, such as flavors
- 3) perceptions of product harm
- 4) health effects from tobacco use, and
- 5) tobacco marketing and communication practices

12. What are the research interest areas for this FOA?

- A. Priority research questions that fall within the scope of this FOA include, but are not limited to the following:
- Identify and explain between-person differences and within-person changes in tobacco-use patterns, including the frequency and duration 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).
 - Examine the role of electronic nicotine delivery systems (ENDS) in the initiation of and use of other tobacco products, including the increase in tobacco product(s) use, cessation of tobacco product(s) use, or relapse to tobacco. Planned analyses should take into consideration product characteristics such as flavors and/or device types.
 - Identify tobacco use behavior patterns associated with cigarette smoking initiation, cessation, relapse, and switching among tobacco products. Planned analyses should take into consideration product characteristics including flavors.
 - Assess between-person differences and within-person changes over time in attitudes, behaviors, exposure to tobacco products, and related biomarkers among and within population subgroups identified by such characteristics as race/ethnicity, gender, age, sexual orientation, socio-economic status, urban/rural, and/or time in the United States or by risk factors, such as pregnancy, or co-occurring substance use, or mental health disorders, or by disease status.
 - Examine the effect of different quantities and counts of tobacco products—amount of loose smokeless tobacco per package, number of cigars per package, number of snus pouches/portioned moist snuff per package—on trial, experimentation, and initiation among never tobacco-using youth and young adults and increased use/frequency, product switching, and delayed cessation among current tobacco users.

- Examine the pattern of use of flavored tobacco products—what flavors are used at what point during tobacco use transitions—associated with: (1) transitions from never used to established use of tobacco products (including ENDS), and (2) transitions from established use of tobacco products (including ENDS) to complete cessation of all tobacco products.
- Examine how measures of comprehension and understanding of tobacco product risk—both absolute and comparative—relate to tobacco product use.
- Examine how tobacco product marketing, packaging, and/or labeling of newly deemed tobacco products—across various types of tobacco product categories—relate to patterns of product use—including dual use, transitions, and switching behavior—among youth, young adults, and adults.
- Examine health outcomes from various tobacco product types, not to include cigarettes.
- Examine the long- and short-term health effects of transitioning from combustible to non-combustible tobacco, and from non-combustible to combustible tobacco, using biomarker and/or health outcomes.
- Compare biomarker expression profiles with self-reported use of tobacco products, and analyze measures associated with biomarkers of exposure that may inform risk associated with tobacco exposure for mortality/morbidity by age, sex, and race/ethnicity.

13. Could researchers include datasets collected in other countries in their proposal?
- A. Foreign datasets may be included only if the dataset is relevant to the U.S. population and U.S. regulation of tobacco. Applications not using nationally representative datasets will need to provide justification of why the dataset is unique, and why the research questions cannot be answered from a (publicly available) national representative dataset.

14. What are some examples of existing datasets applicants can use in their proposed research?

- A. This FOA may be used to analyze cross-sectional or longitudinal data including knowledge, attitudes, perceptions, behaviors, dependence, toxicity, and health effects. This includes, but is not limited to data from:

- The Population Assessment of Tobacco and Health (PATH) Study
- The National Youth Tobacco Survey (NYTS)
- The Tobacco Use Supplement to the Current Population Survey (TUS-CPS)
- The National Adult Tobacco Survey (NATS)
- The National Health Interview Survey (NHIS)
- The Behavior Risk Factor Surveillance System (BRFSS)
- The Monitoring the Future (MTF) Surveys
- The National Survey on Drug Use and Health (NSDUH)
- The National Health and Nutrition Examination Survey (NHANES)
- The Health Information National Trends Survey (HINTS)
- The NIH sponsored National Longitudinal Mortality Study ([NLMS](#)) – Tobacco Use Follow-Up.

Additional [NIH Data Sharing Repositories](#) are available. Survey datasets may also be merged or linked to other existing datasets—geographic characteristics or policy information by region, state, or locality—and can be linked to existing national survey data, as appropriate to address a research question(s). Another type of example is linking directly or indirectly to the TUS-CPS public use datasets or to other CPS supplement data due to the panel nature of the CPS such as the Internet and Computer Use, Annual Social and Economic Supplement (ASEC), and American Time Use Survey (ATUS), etc.

15. What topics are non-responsive to this FOA?

- A. Although the following research topics may be within the FDA CTP's regulatory authorities to fund, they are not to be included in the FOA and will be deemed out of scope and not reviewed:
- Applications that do not use existing data
 - Applications focusing on non-tobacco products
 - Graphic health warnings for cigarette packages and advertisements
 - Communicating harmful and potentially harmful constituents to the public

- Impacts of marketing restrictions on adults
- Studies of demographics and/or risk perceptions that describe only exposure to advertising without linking exposure to tobacco use behaviors.

16. What are some ethical considerations when preparing applications?

A. Data used for these research projects should meet the below ethical conditions:

- Data used should be de-identified before release to the researcher.
- Study participants should have provided their consent, or it can be reasonably presumed that consent has been received.
- Outcomes of the analysis must not allow re-identifying participants.
- Use of the data should not result in any damage or distress to study participants.
- Tobacco Industry Funding of Applicants: the FDA CTP has adopted the following guidance regarding tobacco industry funding of applicants responding to this FOA.
 - The National Advisory Council on Drug Abuse (NACDA) has set forth points with regard to existing or prospective sponsored research agreements with tobacco companies or their related entities and the impact of acceptance of tobacco industry funding on National Institute on Drug Abuse's (NIDA) credibility and reputation within the scientific community. Please see [Points to Consider Regarding Tobacco Industry Funding of NIDA Applicants](#) for details. While this guidance was originally issued for NIDA applicants, it is relevant for all applications submitted under this FOA.

Review

17. Will more weight be assigned in the review for applications that address more than one of the scientific interest areas?

A. No. Reviewers will be looking to see if the research question is addressed adequately and appropriately. When approaching which research priorities to address, we recommend that investigators think about what scientific evidence the FDA would need to support a product review process or regulatory decision.

18. On what basis are applications selected for funding?

A. Applications will be selected for funding based on scientific merit, current availability of funds, and the FDA CTP's current research priorities.

19. What are some special review considerations for R21 applications?

A. The R21 exploratory/developmental grant supports investigation of novel scientific ideas or new model systems, tools, or technologies that have the potential for significant impact on biomedical or biobehavioral research. An R21 grant application need not have extensive background material or preliminary information. Accordingly, reviewers will emphasize the conceptual framework, level of innovation, and potential to significantly advance our knowledge or understanding. Appropriate justification for the proposed work can be provided through literature citations, data from other sources, or, when available, from investigator-generated data. Preliminary data are not required for R21 applications; however, they may be included if available.

20. What review criteria has been modified from the typical NIH review to fit this FOA?

A. Significance, Innovation, and Approach criteria have been modified for this FOA:

- **Significance:** Does the project address an important problem or critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, and technologies related to the manufacture, distribution, and marketing of tobacco products?
- **Innovation:** Does the application challenge and seek to shift current research in the field of tobacco science as it relates to the manufacture, distribution, and marketing of tobacco products? Is a refinement, improvement, or new application of theoretical concepts, approaches, or methodologies, or instrumentation proposed? Will the outcomes of the project provide new information to further develop the knowledge base that informs the manufacture, distribution, and marketing of tobacco products in order to protect public health?
- **Approach:** Are the variables selected to define participant groups appropriate for fulfilling the specific aims of the study? Are the types, numbers, and volumes of biospecimens justified? Have the proposed assays been validated for use with the specific types of biospecimens requested? Have sufficient preliminary data been presented to demonstrate accuracy and robustness of the proposed assays? Have the investigators provided assay validation data? If multiple assays are available for a proposed analyte, have the investigators justified their choice for using a particular assay? Have the investigators described the laboratory quality control plan, and if so, is it adequate? Have the investigators provided effect sizes and used power calculations to determine the sample sizes needed to detect significant effects for each aim? Did they state the power levels they wished to achieve with the proposed sample sizes? Does the statistical analysis plan adequately describe the data that will be analyzed and the statistical methods that will be used? Does the plan address statistical issues germane to the research such as measurement error, multiple comparison testing, bias, interactions, and data adjustments? Are individuals with sufficient expertise and experience proposed to conduct the data analyses?

Post-Award Management and Reporting

21. Which NIH Institute/Center (IC) will manage my award?

- A. It depends on the nature and scope of the research projects proposed. Applicants may request assignment to a particular Institute in their cover letter, but the NIH will make the final determination regarding Institute assignment.

22. Are the reporting requirements for these awards the same as other NIH grants?

- A. No. A mid-period progress report will be due every 6 months following the project start date, as well as the annual progress report and all reports required by the NIH at the time of grant closeout.

23. Are policies and procedures different for these awards?

- A. Yes. This includes exclusion from the [Streamlined Noncompeting Award Process \(SNAP\)](#) and all carryover requests requiring prior approval from both the NIH and the FDA CTP.

24. Some researchers are under limitations with respect to accepting funds from the tobacco industry. How will these FDA research awards be funded?

- A. As mandated in the Family Smoking Prevention and Tobacco Control Act, the FDA is authorized to collect fees from tobacco product manufacturers and importers for its activities related to the regulation of the manufacture, distribution, and marketing of tobacco products. Although the tobacco user fees are specified in statute, Congress must actually appropriate the funds before the FDA can obligate them. The tobacco industry has no control over FDA CTP funding decisions. The FDA uses some of these funds to award research grants.

NIH Guide FOA:

Secondary Analyses of Existing Datasets of Tobacco Use and Health (R21 Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/rfa-files/RFA-OD-19-022.html>

NIH-FDA Tobacco Regulatory Science Program website

<https://prevention.nih.gov/tobacco-regulatory-research>