

Frequently Asked Questions and Answers

Tobacco Regulatory Science (R01 Clinical Trial Optional) RFA-OD-19-019

Updated February 21, 2019

1. What does the “clinical trials” option mean for my study?
 - A. Note that the NIH [defines](#) a clinical trial as “a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.” As this definition can apply to studies that investigators may not have previously considered to be a “clinical trial,” we highly recommend investigators review the resources available at <https://grants.nih.gov/policy/clinical-trials/definition.htm>. Located at this site are [Case Studies](#), [FAQs](#), and a [Decision Tree](#) that will help determine if your investigation is considered a clinical trial or not. Additionally, investigators are encouraged to discuss proposals and research ideas with the appropriate scientific research contacts listed in Section VII of the funding opportunity announcement (FOA) to which you plan on applying.

2. Are foreign individuals eligible to apply as PIs for this RFA?
 - A. The intent of this RFA is to develop a cadre of new investigators in the early stages of establishing independent careers in tobacco regulatory research. 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.

Eligibility for the [R01](#)

3. 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

4. Is there a budget cap on R01 applications?
 - A. Yes. R01 budgets submitted to this funding announcement are limited to \$300,000 in direct costs per year. **Three years maximum.**

Application Requirements/Submission

5. Where can the applicant find additional information regarding application submission?

- A. The 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 ASSIST, eRA Commons registration, submitting and tracking an application, documenting system problems that threaten submission by the due date, and post-submission issues, please contact [Finding Help Online](#). Telephone: 301-402-7469 or 866-504-9552 (toll free).
 - For peer review questions, contact Dr. Weijia Ni from the Center for Scientific Review at niw@csr.nih.gov.
 - For financial/budgetary questions, please contact the appropriate grants management contact listed in Section VII of the RFA.
 - For scientific and responsiveness questions, please contact the appropriate scientific contact listed in Section VII of the RFA.

6. Am I required to submit a letter of intent?

- A. A letter of intent 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-specific aims must be within the regulatory authority of the FDA [Center for Tobacco Products \(CTP\)](#) in order to be deemed responsive to this FOA. Applications that are non-responsive will not be reviewed.

Suggested content of letter of intent:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PD(s)/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 letter of intent?

- 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)
Tel: 301-451-7464
Fax: 301-480-2230

Responsiveness

8. How do I know if my application is responsive to this funding opportunity announcement (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 seven interest areas listed in the RFAs, **and**
 - Fall within the scope of the FDA CTP's regulatory authority.

As such, applicants are strongly encouraged to contact the scientific research contacts listed in Section VII of the RFAs 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 seven areas listed in the RFAs 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 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 these RFAs (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 "[Overview of the Family Smoking Prevention and Tobacco Control Act.](#)"

10. What are the research interest areas for these RFAs?
- A. These RFAs are focused on the following **seven** FDA CTP interest areas. **Only** applications proposing research projects relevant to one or more of these **seven** areas will be considered for funding:

1. Toxicity
 2. Addiction
 3. Health effects
 4. Behavior
 5. Communications
 6. Marketing influences
 7. Impact analysis
11. Are the seven research priorities in the RFA listed in order of priority to the FDA, or are they of equal priority?
- A. The research priorities are not listed in priority order. They are of equal priority to the FDA CTP.
12. May researchers include foreign populations in their proposed research?
- A. Foreign populations may be included if the product under study is the same as the one(s) used in the United States. Results from foreign populations must be relevant to the U.S. population and U.S. regulation of tobacco.
13. In general, what areas of research are **not within the FDA CTP's regulatory authority**?
- A. The Family Smoking Prevention and Tobacco Control Act gives the FDA the authority to regulate the manufacture, marketing, and distribution of tobacco products to protect public health and to reduce tobacco use by youth. In general, the CTP's regulatory authorities do NOT extend to the following:
- Setting tax rates and prices for tobacco products.
 - Regulating therapeutic products, such as those marketed to treat tobacco dependence.
 - Setting clean indoor air polices.
14. Is a research proposal in which the primary outcome identifies differential effects of various tobacco products on disease risk, incidence, or progression of disease considered responsive?*
- A. Yes. A proposal identifying differential effects of various tobacco products on disease would be responsive. Examples* might include:
- Pulmonary function-testing outcomes following use of various combustible tobacco products
 - Oral manifestations following use of various tobacco products, especially new and emerging tobacco products.
- * The examples provided are illustrative and should not be viewed as definitive or comprehensive.**
15. Within the scientific domains of "toxicity" or "health effects," is a research proposal which investigates the mechanisms and/or etiology of tobacco-related disease responsive?
- A. It depends. Mechanistic and/or etiologic research is largely relevant to disease prevention or treatment, neither of which is within the CTP's regulatory authority, so would not be considered responsive. These types of research may in some cases be responsive, but only if the outcomes of the research inform the mandate of the FDA CTP. For example, research comparing the mechanistic processes or underlying disease etiology of different tobacco products or their constituents may be considered

responsive. As such, it is important to discuss your research concept with an NIH scientific research contact and to consider submitting a letter of intent.

16. Within the scientific domains of “addiction,” “toxicity,” or “health effects,” is a treatment intervention study designed to compare the effectiveness of various tobacco products on tobacco cessation considered responsive?

A. No. The CTP’s regulatory authority does not extend to regulating therapeutic uses of tobacco products as this authority rests with other Centers within the FDA. Examples of research projects that would be considered responsive include: (1) an observational study to examine the natural history of whether participants quit smoking cigarettes while using a different tobacco product, and (2) assessing if communications regarding the health consequences of using tobacco products have an impact on usage rates.* In many of its key regulatory areas, the CTP is charged with assessing the impact of tobacco products on the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products—as well as the increased or decreased likelihood that existing users of tobacco products will stop using such products, and the increased or decreased likelihood that those who do not use tobacco products will start using such products.

*** The examples provided are illustrative and should not be viewed as definitive or comprehensive.**

17. Within the scientific domains “toxicity” or “health effects,” is a research proposal in which the primary outcome informs treatment of disease considered responsive?

A. No. The CTP does not regulate products or support development of clinical interventions intended for the treatment of disease. For example pharmacotherapy for treatment of cancer or emphysema, screening, physical activity, or dietary interventions for heart disease would all be considered non-responsive.*

*** The examples provided are illustrative and should not be viewed as definitive or comprehensive.**

18. What types of biomarker research may be appropriate for FDA CTP funding?

A. Proposals identifying biomarkers of specific tobacco product exposure and/or disease and those with the potential to differentiate exposure of differing tobacco products could be considered responsive.

Examples* include:

- Biomarkers to measure exposure to new and emerging tobacco products
- Biomarkers of disease (e.g., cancer, cardiovascular disease, pulmonary disease, reproductive and developmental effects) that can be associated with specific measures of tobacco exposure
- Development of a non-clinical biomarker of disease coupled to traditional toxicology and/or pharmacology studies to provide a relevant framework for the regulatory application
- Studies linking biomarkers of disease in non-clinical models that translate to biomarkers that are measurable in the clinical setting
- Magnitude of changes in biomarkers that translates into clinically meaningful impacts on human health outcomes.

Biomarker research may fall within the scope of one or more of the seven interest areas, depending on the intended use of the biomarker. However, there is research that will remain outside of FDA CTP authorities such as biomarker research for which the primary focus is to inform treatment.

*** The examples provided above are illustrative and should not be viewed as definitive or comprehensive.**

19. What types of research on nicotine and/or nicotinic receptors are appropriate for consideration of funding by the CTP?
- A. If the research provides information on outcomes such as motor activity, memory, or neuronal responses to particular ligands, the research is likely not appropriate. Research to rapidly screen tobacco constituents for activity at the nicotinic receptor to determine their dependence potential would be considered responsive.*
- * The examples provided above are illustrative and should not be viewed as definitive or comprehensive.**
20. Are studies on the impact of state and local tobacco control policies responsive?
- A. It depends upon the specific policies being examined and whether they fall under the purview of the FDA CTP. Studies evaluating the impact of a tobacco tax increase are not responsive, as the CTP does not have regulatory authority regarding tax rates on tobacco products. Similarly, the CTP does not have authority over the sale of tobacco cessation medications, so, for example, a study evaluating the effectiveness for tobacco cessation of providing free nicotine replacement therapy would not be considered responsive. Studies evaluating the impact of a tobacco advertising restriction, a ban on the sale of flavored tobacco products, or restrictions on the sale of single serving products, however, may be considered responsive.*
- * The examples provided above are illustrative and should not be viewed as definitive or comprehensive.**
21. Are public opinion polls about tobacco regulations responsive to FDA CTP regulatory authorities?
- A. Unlike state or local policymaking, where public support can be an important factor in the adoption and implementation of policies, public opinions cannot be used to support federal regulations.
22. Is the CTP interested in graphic health warning research given that the U.S. government did not seek Supreme Court review of the court decision that blocked the implementation of graphic health warnings on cigarette packages and advertising?
- A. No, as indicated in the non-responsive research topics in the RFA, studies on graphic health warnings for cigarette packages and advertisements are not allowed. However, the FDA is committed to funding and conducting research on graphic health warnings on alternative tobacco products.
23. What topics are considered responsive within the scientific domain of “impact analysis”?
- A. The following types of analyses are examples* of topics that would be considered responsive under “impact analysis”:
- Computational/mathematical modeling and simulation and/or statistical modeling of the public health impact of potential FDA/CTP action

- Health and economic impact of tobacco use and/or tobacco regulatory policies on vulnerable populations
- Economic burden (e.g., healthcare cost, productivity loss) of tobacco-related diseases on users and non-users (e.g., secondhand and thirdhand exposure)
- Studies evaluating the impact of tobacco regulatory actions (e.g., mandated changes in product characteristics) on consumer behavior or behavioral intentions.

*** The examples provided above are illustrative and should not be viewed as definitive or comprehensive.**

24. Will applications that propose to study products not yet available in the United States be considered responsive?
- A. Yes, if the product(s) meets the statutory definition of a “tobacco product” under the Tobacco Control Act (i.e., any product made or derived from tobacco and intended for human consumption, including any component, part, or accessory of a tobacco product), then studies examining these products could be considered responsive to the RFA. However, the application must demonstrate that the proposed research can directly contribute to the FDA’s regulatory authority over the manufacture, marketing, and distribution of tobacco products within the United States. As the relevance may be dependent on not only the product, but also the types of research being conducted, we recommend that you discuss any particular proposed research with one or more of the scientific research contacts listed in Section VII of the RFAs.
25. Would an application that proposed to study a heat-not-burn product that is already included in a modified-risk tobacco product (MRTP) application be considered responsive?
- A. Potentially, yes. While heat-not-burn products would be considered a “tobacco product” under the Tobacco Control Act and would fall under the regulatory authority of the FDA CTP as a result of the [deeming rule](#), both the responsiveness of a research proposal investigating this product and its relevance to the FDA CTP priorities would depend upon the type of research being proposed. As such, we recommend that you discuss any particular proposed research with one or more of the scientific research contacts listed in Section VII of the RFAs.
26. The RFA states that “short-term studies of the acute effects of reduced nicotine content cigarettes” would be deemed non-responsive to the RFA. What does this RFA consider “short-term”?
- A. There is no a specific timeframe that defines “short-term” or acute outcomes. However, the appropriate length for any study is dependent upon the research question. Applicants are encouraged to familiarize themselves with the funded research and published literature in this area through the [NIH](#), the [Tobacco Regulatory Science Program \(TRSP\)](#), and other [CTP-supported tobacco regulatory research](#) and see how their proposed research could expand on the current understanding of reduced nicotine cigarette use.

Review

27. Will more weight be assigned in the review for applications that address more than one of the seven priority 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.

28. On what basis are applications selected for funding?

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

Post-Award Management and Reporting

29. 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.

30. 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 close-out.

31. Are policies and procedures different for these awards?

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

32. 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 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 CTP funding decisions. The FDA uses some of these funds to award research grants.

33. What will be the availability of confidential information obtained by the FDA, for example, product and constituent reporting?

- A. Several laws govern the confidentiality of tobacco product information submitted to the FDA, including sections 301(j) and 906(c) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the Trade Secrets Act, and the Freedom of Information Act, as well as the FDA's implementing regulations. The FDA's general regulations concerning the public availability of FDA records are contained in 21 CFR Part 20. Regarding the reporting of constituents, the FD&C Act requires tobacco product manufacturers and importers to report quantities of harmful and potentially harmful constituents (HPHCs) in tobacco products or tobacco smoke by brand and sub-brand. The FD&C Act also directs the Agency to publish a list of HPHCs by brand and by quantity in each brand and sub-brand, in a format that is understandable and not misleading to a layperson.

34. If a scientific study proposes to make ANY change to a commercialized tobacco product (e.g., manipulating the size of the product; putting the tobacco product in different colored packaging), then an investigational tobacco products (ITP) request is recommended by the FDA (Reference: [Draft Guidance Use of Investigational Tobacco Products](#)). What information is required in the ITP request?

- A. The information needed in an ITP request may vary depending on the proposed ITP and the type of study. The FDA needs to determine whether the product is a tobacco product, whether the tobacco product is within our current jurisdiction, whether the

tobacco product is an ITP, and whether the study products will be provided to human subjects. For example, if one makes a change in labeling of a commercially marketed tobacco product and it will not be used by human subjects, no ITP request is needed. If one makes a change in labeling of a commercially marketed tobacco product and there will be actual use by human subjects, then the FDA recommends that an ITP request come to the CTP for review; but it is likely that chemistry, engineering, and manufacturing will not be needed. If you have questions about ITP, please contact Debbie Cordaro (debbie.cordaro@fda.hhs.gov).

Research Resources

35. What is the PhenX Toolkit, and why does the RFA encourage its use?
- A. The [PhenX Toolkit](#) is a web-based catalog of freely-available standard measures that can be easily incorporated into research studies. The measures span many scientific domains, and include Specialty Collections in Tobacco Regulatory Research (TRR). As noted in [NOT-OD-17-034](#), the TRR Collections provide a common set of recommended measures that, when incorporated across studies, will facilitate data sharing, comparing, and integration, as well as replication and validation of findings. The measures that are included in the PhenX Toolkit were identified by working groups of experts within each of the scientific domains, followed by outreach to the relevant scientific communities to establish a consensus for the prioritized, recommended measures. PhenX measures are typically well-established, broadly validated measures that are low-burden to the participant and investigator. The TRR Collections include standard measures like the Fagerstrom Test for Nicotine Dependence and questions found in large and/or nationally representative surveys like the Population Assessment of Tobacco and Health (PATH) and the National Youth Tobacco Survey (NYTS). For more information about the TRR Collections in the PhenX Toolkit, see the [TRSP website](#).
36. Will the National Institute on Drug Abuse research cigarettes be available for research funded through this RFA on a similar basis as currently?
- A. Yes. NRC* Spectrum Cigarettes will be available for these awards and research investigators need to prepare a request package. Please visit the [Nicotine Research Cigarettes Drug Supply Website](#) for more information and to learn about the request process. For further questions, email NIDANRCSupply@mail.nih.gov and specify NRC in the subject line.

Address correspondence to:
Rik Kline, Ph.D.
National Institute on Drug Abuse
Chemistry and Pharmaceuticals Branch
Division of Therapeutics and Medical Consequences
6001 Executive Boulevard, Room #4119, MSC 9555
Bethesda, MD 20892-9555
Phone: (301) 827-5243
Fax: (301) 443-2599

*NRC: Nicotine Research Cigarettes

37. Might it be possible to obtain other research tobacco products (e.g., cigars, roll-your-own tobacco or e-cigarettes) with known nicotine concentrations for use in research funded through this RFA?

- A. At this time, we are aware of one additional research tobacco product, the standardized research e-cigarette (SREC) developed by the National Institute on Drug Abuse (NIDA), NIH. Unlike the SPECTRUM combustible cigarette provided by NIDA to researchers at no cost, the SREC was developed under a small business contract issued by NIDA to NJOY, LLC. Consequently, researchers will purchase the SREC directly from NJOY. Researchers with NIH funding to use the SREC are guaranteed to be able to purchase the devices; however, there is no expectation that NJOY will be limiting access to the SREC. For more information and how to request SREC click [here](#).

NIH Guide FOA:

Tobacco Regulatory Science (R01 Clinical Trial Optional)

<https://grants.nih.gov/grants/guide/rfa-files/RFA-OD-19-019.html>

NIH-FDA Tobacco Regulatory Science Program website:

<http://prevention.nih.gov/tobacco/>