Frequently Asked Questions
Center for Rapid Surveillance of Tobacco (CRST) to Assess Changes in Use Behaviors, Product Marketing, and the Marketplace (U01 Clinical Trial Not Allowed)

RFA-OD-22-002 (https://grants.nih.gov/grants/guide/rfa-files/RFA-OD-22-002.html)

Updated April 25, 2022

The frequently asked questions (FAQs) detailed below are an ongoing compilation of questions related to RFA-OD-22-002 and will be updated as new questions are compiled, so please check back. Potential applicants are strongly encouraged to consult with National Institutes of Health (NIH) scientific contacts listed in the Request for Applications (RFA) to confirm that their research ideas are responsive to the research priorities outlined in the RFA and to the Food and Drug Administration (FDA) Center for Tobacco Products' (CTP's) regulatory authority. Only applications within the scope of the RFA and within the regulatory authority of the FDA CTP will be sent forward for review. For additional information about TRSP and the work with FDA CTP, visit the **NIH-FDA Tobacco Regulatory Science Program website.**

This document's questions and examples are for illustrative purposes only and should not be viewed as definitive or comprehensive.

General Information

What are the upcoming dates to keep in mind?

Letters of Intent (LOI) must be RECEIVED by March 20, 2022.
CRST applications must be RECEIVED by May 18, 2022.

Am I required to submit an LOI?

An LOI is not required, and it is not part of the peer review process. However, it allows NIH staff to estimate the potential review workload and plan the review. We *strongly recommend* sending the LOI 60 days before the application due date **with a current draft of your specific aims** so that NIH scientific research contacts can review your rapid surveillance ideas and specific aims before submitting applications. All proposed specific aims must be within the regulatory authority of the FDA CTP to be deemed responsive. Applications that are non-responsive will **not** be reviewed.

Suggested content of the LOI:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the Program Director(s) (PD(s))/Principal Investigator(s) (PI(s))
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity
- Specific aims

Where do I send the LOI?

The letter may be sent by email to: TRSP@nih.gov
Tobacco Regulatory Science Program
Office of Disease Prevention
Tel: 301-451-7464
Fax: 301-480-5588

If an applicant sends specific aims with an LOI and obtains feedback that even part of the Aims is off target or non-responsive, can they resubmit a revised LOI?

Yes, it is recommended that applicants communicate with the appropriate scientific contact listed in Section VII. Agency Contacts as early as possible. Also, it is important to note that an LOI is not required, not binding, and not part of the review of an application.

How will NIH ensure that the members of the review panel who will be reviewing CRST applications have the appropriate expertise?

The CRST applications will be reviewed by an NIH Center for Scientific Review (CSR) Special Emphasis Panel and reviewers will be recruited per the type of expertise needed. If you feel that specific expertise is needed, you may include the type of expertise you recommend in a cover letter when submitting your application. You should not include names of any individuals as the CSR would deem those individuals in conflict.

Responsiveness

How do I know if my application is responsive to RFA-OD-22-002?

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*:

1) Fall within the scope of the FDA CTP's regulatory authorities, **and**
2) Address the Research Objectives that are listed in the RFA.

As such, applicants are *strongly encouraged* to contact the scientific research contact listed in the RFA for feedback about responsiveness before submitting an application. Sharing your rapid surveillance ideas and specific aims when submitting an LOI before applying will allow NIH staff to provide responsiveness feedback.

If your application is deemed responsive, it will undergo scientific peer review by experts convened specifically for that purpose (by the NIH CSR). If your application is deemed non-responsive, it will be withdrawn before evaluation of its scientific merit (i.e., peer review). Program officials will let you know if the application must be withdrawn before peer review.

For a CRST application to be considered responsive, it must fall within the scope of FDA CTP's regulatory authorities. What are these regulatory authorities?

The Family Smoking Prevention and Tobacco Control Act amended the Food, Drug, and Cosmetic Act to provide FDA authority over the manufacture, marketing, and distribution of tobacco products to protect public health and to reduce tobacco use by youth. This gives FDA CTP the responsibility and regulatory authority for:

- Premarket review of new and modified risk tobacco products
- Post-market surveillance
- Product standards
- Reporting of ingredients
- Reporting of harmful and potentially harmful constituents
- Adverse event reporting
- Health warnings
- Advertising and promotion restrictions
- User fees.

For more information about these authorities, see Family Smoking Prevention and Tobacco Control Act - An Overview.

What are some examples of activities that are *not* within the FDA CTP's regulatory authority?

In general, FDA 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
- Public opinion polls about current, potential, or proposed tobacco regulations

Note these are FDA CTP's broad authorities, and the CRST RFA seeks rapid surveillance for some, but not all areas within FDA CTP's regulatory authorities. Please examine the RFA closely for the relevant areas to be addressed in your application. However, for more examples of the general types of research considered responsive versus non-responsive under FDA CTP's regulatory authorities, see the FAQs document addressing general responsiveness questions.

For a CRST application to be considered responsive, it must address the Topic Areas, including bulleted content, listed in the RFA. What are these requirements?

Applicants **must** address the following Topic Areas listed in the RFA:

Rapid surveillance of changes in tobacco product use behaviors:

- Changes in tobacco use behaviors (e.g., type of tobacco product, quantity, frequency) among youth, young adults, and other populations with tobacco-related disparities such as racial/ethnic minorities, those with lower socioeconomic status, people with mental health comorbidities, and sexual or gender minorities, underserved rural populations, those pregnant or trying to become pregnant, and those in the military or veterans , and factors that contribute to their use behaviors, e.g., access, labeled product characteristics (e.g., brand, packaging, nicotine concentration, flavors, components, design features), price promotions, advertising, social media marketing, social media discussions.
- Changes in how youth, young adults, and populations with tobacco-related disparities access or obtain tobacco products.
- Emerging use behaviors such as:
    - Users adjusting the components, ingredients, or features of their products (including devices and/or contents) and the result of those modifications.
    - Users producing their own flavored tobacco products (including mixing their own flavors into ENDS liquids or refilling e-liquid cartridges with their own mixtures).

Rapid surveillance of tobacco product marketing:

- Describe recent changes in the mechanisms or platforms of current tobacco product marketing in traditional and non-traditional communication channels, including owned or earned media, social media influencers, brand ambassadors, outreach events, or other digital marketing of tobacco products.
- Describe recent changes in industry tobacco product marketing strategies, including retailer (online or brick and mortar), promotional practices, such as point-of-sale marketing, price promotions, coupons, and/or affiliate marketing. Is there evidence that these marketing strategies have disparate effects on populations with tobacco-related disparities?

Rapid surveillance of tobacco product marketplace:

- Describe recent changes in the tobacco retail environment for existing and/or emerging tobacco products including traditional stores such as grocery, convenient, and “big-box” stores, and gas stations; as well as tobacco specialty shops such as vape shops, “head” shops, cigar bars and hookah bars.
- Describe recent changes and/or trends in tobacco product sales in tobacco specialty shops (e.g., vape shops, cigar bars, hookah bars), as well as online retailers, for deemed tobacco products (e.g., ENDS, cigars, hookah/waterpipe) and products that have recently obtained a marketing authorization.

The following types of studies are considered non-responsive to this RFA:

- Human laboratory studies, e.g., topography, fMRI
- Laboratory analysis of tobacco products, e.g., smoking machine, device analysis
- Biospecimen collection or analysis
- Environmental scan of policies

Are there activities that are outside the scope of this RFA?

Yes, the RFA specifies that the following types of studies are considered non-responsive to the CRST RFA:

- Human laboratory studies, e.g., topography, functional magnetic resonance imaging (fMRI)
- Laboratory analysis of tobacco products, e.g., smoking machine, device analysis
- Biospecimen collection or analysis
- Environmental scan of policies

Are studies addressing specific populations that experience tobacco-related disparities responsive?

Yes, studies of populations with tobacco-related disparities are responsive to FDA CTP regulatory authorities. However, the population needs to be appropriate to the research question. Note that this RFA specifies that the CRST must address rapid surveillance of changes in tobacco product use behaviors among populations with tobacco-related disparities, such as youth, young adults, racial/ethnic minorities, those with lower socioeconomic status, people with mental health comorbidities, and sexual or gender minorities, underserved rural populations, those pregnant or trying to become pregnant, and those in the military or veterans.

Can the CRST assess questions of interest not directly referenced in the RFA? For example, would monitoring appeal of tobacco ads be considered in scope/responsive?

If added questions are within the scope of FDA CTP's regulatory authority and are closely related to and enhance the work of the CRST, then it is likely it would be an appropriate activity. In the above scenario, the application must explain how the CRST will conduct rapid surveillance of tobacco product marketing, including recent changes in industry tobacco product marketing strategies, to be responsive to the RFA, and could then justify the inclusion of measures of appeal related to these strategies.

Application Requirements

Given the requirement to address three rapid surveillance Topic Areas, how should the application be organized within the U01 application format guidelines?

We recommend that applications specify the activities to address these areas in separate specific aims and include a graphic representation of the organizational structure and associated activities within the application. Note that the page limit requirements for writing a U01 are similar to those of an R01. For more information see NIH Application Guides.

What does the specification "clinical trial not allowed" mean for my application?

The RFA limits the rapid surveillance conducted within the CRST to activities that do not fall within the NIH definition of a clinical trial. The activities of the CRST should focus on observations of behavior, marketing, and the marketplace in real time. 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.

I am engaging in research that I think would be useful as a sentinel site, how can I get involved?

You may partner with an investigator who plans to submit an application for CRST to be a sentinel site or you may contact the CRST PI to offer your data as a sentinel site once the CRST award is made.

Are foreign institutions eligible to apply?

No, foreign institutions *are not eligible* to apply, including Non-domestic (non-U.S.) Entities (Foreign Institutions) and Non-domestic (non-U.S.) Components of U.S Organizations. However, Foreign Components, as defined by the NIH Grants Policy Statement (see Chapter 16) are allowed. Note that justification for foreign collaboration and applicability of the research to U.S. regulations would need to be included.

May applicants include NIH intramural researchers as part of the transdisciplinary/multidisciplinary team?

Yes. In general, NIH intramural researchers may collaborate or consult with extramural researchers who apply for a U01 award. However, NIH intramural investigators may not receive salary support through the grant award. See Chapter 17 of the NIH Grants Policy Statement for more information.

Suppose the applicant proposes to collaborate with one or more organizations in carrying out the proposed research. Is there a limit to the percentage of work that can be subcontracted from the applicant organization?

No, applicants are not subject to a maximum allowable percentage of work that can be subcontracted from the applicant organization. NIH policy requires that the grantee is the one responsible and accountable for the performance of the grant. The grantee must perform a substantive role in the planned research and cannot simply be a conduit of funds to another party. This includes providing appropriate oversight of all scientific, programmatic, financial, and administrative matters related to the grant. However, depending on the nature of the science, it is possible that it would be appropriate for the consortia budget (i.e., subcontracts) to account for a larger portion of the requested budget. In short, there is no cap on subcontracts.

Can a single scientist serve as an investigator on the CRST application *and* a Tobacco Center of Regulatory Science (TCORS) and/or Center for Coordination of Analytics, Science, Enhancement, and Logistics (CASEL) application?

While an investigator may participate in more than one center application, note the following restrictions for participating on these grants once they are funded: A CRST PD/PI cannot serve as PD/PI of a TCORS grant, although a CRST PD/PI or other key personnel can serve as key personnel on a TCORS grant. Also, the CRST grant can include key personnel from a TCORS. However, no CRST personnel (PD/PI or other key personnel) can serve as a member of a CASEL awardee team. In addition, applicants are encouraged to carefully consider the effort they will carry in these large grants as level of effort will be considered.

The RFA outlines a sentinel network to include FDA CTP as well as other sites such as FDA CTP-funded research projects, on-going surveys, and/or other surveillance programs proposed by the applicant. Does that mean data from these sources or sites are available to CRST to analyze, for instance the PATH Study data or data from grantees?

This would depend on the specific data source and the agreements CRST will establish with sites participating in the sentinel network. Note that data sources could include grants or contracts funded through the FDA CTP, NIH, and/or other funding agencies, and as such may have different requirements or approval processes for data sharing. For example, some sentinel sites will collect data for the CRST, whereas other sites may allow the CRST access only to restricted or public-use data files, and still others may perform CRST-requested analyses without access to the data. As such, the applicant should address these issues for each site and data source.

Given that FDA CTP has access to several data sources and will serve as a sentinel site, how do I address data sources in my application?

As covered in the CRST pre-application webinar on January 13, 2022, FDA CTP has access to the following surveillance data sources: sales data, advertising data, poison control data, adverse event data, social media monitoring, consumer use behaviors and perceptions, and news and regulation tracking. Applicants should not rely solely on the FDA CTP data sources and should include data sources and associated costs it expects to be part of its surveillance program. Once the award is made, the NIH and FDA CTP staff will meet with the awardee to discuss coordination of data sources.

Will TCORS sites automatically be included as sentinel sites?

No, the TCORS will not automatically become sentinel sites as they are expected to have a broader range of research topics and methodologies, which may or may not include surveillance topics appropriate for collaboration with the CRST. As the next round of TCORS will be funded after the submission date for the CRST applications, the CRST applicant(s) will not be able to pre-identify TCORS partners. Therefore, the CRST applicant should address the sentinel network through a combination of pre-identified partners and how they will build collaborations with future TCORS and/or other relevant research projects with input from federal partners post-award.

Budget

What is the budget cap? Will applications that exceed the budget cap be considered?

The budget cap is $2.8 million total costs for the first year of the grant, and $3.8 million total costs per year for subsequent years (up to five years). Year 1 funding is capped at $2.8 million total cost to account for lead time needed for project start-up. Budget needs, reflecting actual needs of the proposed project and future year funds after Year 1, will depend on the availability of funds. Proposed budgets *cannot* exceed the budget cap, and applications exceeding the budget cap risk being returned as non-responsive.

Should salary increases due to escalation or inflation be included in the application's budget?

No, escalation or inflation costs should not be included in the application. Only costs required by the work needed for the study should be included. Changes in cost due to level of effort changes and fluctuations associated with the science performed will be honored. Applicants should request what is needed to complete the work proposed. Grants management will make any necessary modifications according to current funding guidelines if the application is selected for award. Specific questions regarding an application's budget should be directed to the appropriate grants management contact listed in Section VII of the RFA.

Should the application budget for invited and potential future sentinel site partners, for instance for investigators time in meetings or to conduct requested analyses?

Yes, the CRST should budget for all aspects of sentinel site collaboration with CRST., For example, sentinel site investigators' time for participation in meetings, analysis of data, or access to resources that would not be already included in the partners' organizational resources.

Post-Award Management and Reporting

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

The CRST grant will be assigned to the National Cancer Institute (NCI).

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

No. A Mid-Period Progress Report (MPPR) will be due every 6 months following the project start date, in addition to the annual progress report and all grant close-out reports required by the NIH.

Are policies and procedures different for these awards?

Yes. This includes exclusion from the Streamlined Noncompeting Award Process (SNAP), which means that all carryover rDequests require prior approval from both the NIH and the FDA CTP. These special requirements will be listed as special terms of the award on the grantee's Notice of Award letter.

Would the CRST have final scientific say on the work, with input from NIH/FDA, or would NIH/FDA have final say (e.g., publications)?

The CRST is awarded as an NIH grant, and as such the Institution/PI is ultimately responsible for the work. That said, the grant funding mechanism is a cooperative agreement, and as such there will be substantial involvement from federal partners. Within the RFA it is further clarified that "Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities."

Research Resources

What is the PhenX Toolkit, and why does the RFA encourage its use?

The PhenX Toolkit is a web-based catalog of freely-available standard measures 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 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, and 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) Study and the National Youth Tobacco Survey (NYTS). For more information about the TRR Collections in the PhenX Toolkit, see the PhenX website.

Additional Resources

NIH Guide FOA: Center for Rapid Surveillance of Tobacco (CRST) to Assess Changes in Use Behaviors, Product Marketing, and the Marketplace (U01 Clinical Trial Not Allowed)
https://grants.nih.gov/grants/guide/rfa-files/RFA-OD-22-002.html

NIH-FDA Tobacco Regulatory Science Program website: http://prevention.nih.gov/tobacco/
Includes FAQs regarding responsiveness to FDA's CTP Regulatory Authority

FDA CTP Regulated Products Guidance and Regulations: The CTP website includes information about a variety of topics, including information on the products, guidance, and regulations.

Where can the applicant find additional inforSmation regarding application submission?

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 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 post-submission issues, please contact Finding Help Online. Telephone: 301-402-7469 or 866-504-9552 (toll free).
- For peer review questions, email the CSR at FOAReviewContact@CSR.NIH.gov.
- For financial/grants management questions, please contact Crystal Wolfrey, NCI, Crystal.Wolfrey@nih.gov.
- For scientific and responsiveness questions, please contact Dr. Maria Roditis, Maria.Roditis@nih.gov.