REQUEST FOR PROPOSAL: BIOMARKERS OF NICOTINE PRODUCT USE

BACKGROUND

Smoking is the single greatest preventable cause of death and disability in the world today: more than a billion people smoke, and there will be a billion premature deaths from smoking in this century.

More and better research is needed to help accelerate the end of smoking. Much of this research will depend on well-designed longitudinal studies to gauge the use patterns and effects of traditional and emerging nicotine products. However, these studies often rely on survey data and can be susceptible to recall bias. There is a need for sensitive and accurate biomarkers of exposure that can determine a subject's product-use status (e.g., cigarette smoker, vaper, smokeless user, nicotine-replacement therapy [NRT] user, nonuser).[1] Although a large body of evidence concerning biomarkers for combusted products exists, efforts focused on the development and validation of biomarkers of emerging nicotine products are less advanced. A recent Foundation-commissioned landscape review of biomarkers of exposure associated with tobacco and nicotine-delivery products concluded that additional research is needed to develop biomarkers that can discern between nicotine product–use groups, identify dual- and multi-product use, and distinguish product use from environmental sources.

Additionally, the development of digital biomarkers (i.e., physiological and behavioral data collected by biosensors, wearables, or other devices) could provide new information, which, if used in concert with traditional biospecimen-based biomarkers, could further improve the ability to determine patterns of product use and exposure.

DESIRED END PRODUCT

At the end of the funding period, the Foundation expects delivery of a prototype diagnostic (biomarker or panel of biomarkers) that can reliably discriminate between the nicotine-delivery product groups. This will include proof-of-concept bench testing, in-field/clinic validation of the diagnostic, and a plan for scale-up in developed and low- and middle-income economies.

Successful diagnostics should meet the following minimal criteria:

- Display clear dose–response relationship with exposure. The signal should increase with an increase in product use and decrease on cessation or switching
- Include qualitative and quantitative identification of a wide range of concentrations or behavior signatures so that high and low levels of use would produce measurable signals
- Have sufficient resolution between product-use groups
- Have relatively low levels of background exposure or signals
- Be detected in readily collectable biospecimens (e.g., saliva, blood, urine) and/or data transmitted by biosensor or wearable device
- Have acceptable time course of detection after product use
- Provide a rapid, low-cost analysis

This RFP welcomes research that can reliably discriminate between, and ideally within, the use-groups in Table 1.

Table 1. Preliminary Product-Use Groups

Combusted Tobacco	Heated Tobacco	E-cigarettes	Oral Tobacco	Oral/Dermal Nicotine
• Cigarettes • Cigars • Cigarillos • Little cigars • Water pipes • Bidis	• Heat-not-burn	• + Nicotine • – Nicotine	• Chew • Moist snuff • Snus • Gutka	• NRT gum/lozenge • NRT patch • Oral nicotine (e.g., Zyn, Zonnic)

In addition to the groups in Table 1, it will be necessary to ensure that nonusers are correctly identified, including those who might have been exposed to secondhand tobacco smoke or to other background environmental exposures. Because nicotine users occasionally switch between products depending on personal preferences or in different social situations, the ability to distinguish between dual- and multi-use conditions would fall under this RFP. For instance, a cigarette smoker may smoke daily, except when at work where they use an e-cigarette or snus. The ability to distinguish between many permutations of behavior will be essential for researchers to evaluate subject exposures. Given the complexity of the exposures from each product, it is likely that the result could include some combination of biomarkers or data collection methods.

Traditional biomarkers are dependent on the time-course of metabolism and clearance of the chemical of interest, whereas digital biomarkers are capable of continuous and real-time data collection. We anticipate that proposals will include an analysis of the detection period of biomarkers in the context of clinical and epidemiological research projects. For example, the diagnostic must be able to detect recent use (e.g., hours); but, to provide a more holistic look at the subject's behavior, it must also be capable of detecting product use over longer periods of time (e.g., days to weeks).

Given that 80% of smokers live in low- and middle-income countries, the end-product diagnostic from this effort must be one that can, with further development, be scaled up for, and affordable for use in, these countries.

APPLICATION PROCESS

The Foundation will be using a two-phased approach to the funding of this RFP. From the initial scoping proposals, the Foundation will select several groups to fund for two months of in-depth project scoping/planning work. The Foundation will then evaluate the submitted plans and choose up to three organizations for two years of direct research funding.

- Deadline for receipt of scoping proposals: Sep 28, 2018
- Communication of application status to all applicants: Oct 12, 2018
- Submission of final scoping work: Nov 30, 2018
- Announcement of final grants: Dec 21, 2018

Phase One: Scoping Proposal

- Deadline for receipt of scoping proposals: Sep 28, 2018
- Number of scoping grants to be awarded: ~5
- Budget for project scoping/planning award: $100K
- Deadline for submission of scoping work: Nov 30, 2018

Phase Two: Biomarker Research

- Funding duration: 24 months
- Max number of funded projects: 3
- Budget for biomarker work: up to $3M per project

The Foundation expects that at the end of the 24-month project, deliverables will include proof-of-concept bench testing, in-field/clinic validation of the diagnostic, and a plan for scale-up in developed and low- and middle-income countries. This funding is intended to be the first phase—successful tests/techniques may be further supported for pilot testing and additional development.

Expected Qualifications

- The Foundation encourages participation by groups whose mission aligns with the Foundation's mission to eliminate smoking within a generation. These groups may include institutions of higher education, nonprofits, commercial enterprises, governmental agencies, or other research-based organizations.
- Applicants should have a proven track record in biomarker development and validation, particularly in diagnostics suitable for use in longitudinal cohort studies. Previous research of tobacco and/or nicotine is appreciated but is not a requirement for funding.
- Successful applicants will likely have an interdisciplinary group of key personnel who can approach this project from their individual fields of expertise (e.g., analytical chemists, pharmacologists, epidemiologists, biomedical engineers, clinicians).

Scoping Proposal Structure

All interested parties should submit a detailed proposal for scoping work to the Foundation. Although there is no page requirement for submissions, we expect submissions to be around 10 to 20 pages. The Foundation has recently commissioned a comprehensive third-party landscape analysis of nicotine-product biomarkers of exposure that may be of use to applicants.

Please be sure to cover the following in your submission:

1. Summary of Organizational Capabilities and Experience
Please describe your organization's experience with biomarkers in biosamples that could be used to determine product use, and with digital biomarkers (e.g., wearables, biosensors). Please give a description of your organization's capabilities and experience with similar projects, as well as the organization's experience in low- and middle-income countries.

2. Project Team Information
Please list your organization's key personnel and collaborators who will be involved in this project. Include CVs for key personnel and highlight experience relevant to this project.

3. Detailed Approach to Phase One (scoping proposal)
Please describe the concept and the overall approach you will take to develop your scoping project. You should include the format for the final deliverable of the scoping product, experts you plan to consult, a summary of all potential scoping activities, and a detailed timeline for the duration of the project.

4. High-Level Approach to Phase Two (biomarker research)
While the final approach to the full research project will be developed during the scoping process, please provide a high-level description of the potential approach you will be taking to develop a diagnostic for nicotine-product use, the technologies you foresee being used/developed, and your view of potential challenges to the success of this project and how these difficulties might be mitigated.

5. Costs
Please include a detailed budget for all scoping/planning activities, personnel, and resources.

Evaluation Criteria

The following criteria will be used to evaluate submissions:

- Alignment with the Foundation's mission to eliminate smoking globally within a generation
- Technology expertise and prior experience
- Demonstrated ability to perform on similar projects
- Cost and timeline
- Probability of meeting the objectives of the RFP
- Potential for further scale-up (either internally or in collaboration with partners)
- Key organizational documents provided to the Foundation as part of our due diligence process, as outlined in our Grant Policies and Procedures

Submission Instructions

Applications should be submitted through our online portal that can be accessed here.
You may save a started application at any time by using the Save & Finish Later button at the end of each page. If you do so please use this link to return to the log-in screen to access the saved form.

A list of FAQs can be found here.
For all other inquiries, please contact us at support@smokefreeworld.org.

KEY INFORMATION

The Foundation may disclose proposals, documents, communications, and associated materials submitted in response to this RFP to its employees, consultants, legal counsel, contractors, and potential co-funders. Applicants should carefully consider the content of submitted materials if they have any doubt about the impact of disclosure of confidential or proprietary information. Although submissions will not be disclosed publicly during the evaluation process, all funded projects (scoping and final awards) will be made public. The Foundation will work with awardees to ensure that any materials made public will not disclose any protected information.

To be considered for an award, the applicant agrees that the Foundation may:

- Amend or cancel the RFP, in whole or in part, at any time
- Extend the deadline for submitting responses
- Determine whether a response does or does not substantially comply with the requirements of the RFP
- Issue multiple awards

The applicant must ensure that it has responded to the RFP with complete honesty and accuracy. If information in the applicant's response changes, the applicant will supplement its response in writing with any deletions, additions, or changes within five days of the changes. Any material misrepresentation, including omissions, may disqualify an applicant from consideration for an award.

1 Goniewicz ML, Smith DM. Are some e-cigarette users "blowing smoke"?: Assessing the accuracy of self-reported smoking abstinence in exclusive e-cigarette users. Nicotine Tob Res. 2018. Epub ahead of print. 02 May 2018. https://doi.org/10.1093/ntr/nty085.