

AMENDMENT ONE (1)

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PURPOSE OF SOLICITATION AMENDMENT

The purpose of this amendment is to:

- Provide slides, recording, and transcript of the pre-proposal conference;
- Regarding Solicitation Section 2.5 *I-Corps™ at NIH*: To clarify that CDC/NIOSH (National Institute of Occupational Safety and Health) does participate in the iCorps program, but not as a part of this solicitation;
- Amend Solicitation Section 12, NCI Topic 433 *Developing Unbiased Medical Technologies to Reduce Disparities in Cancer Outcomes*, to remove paragraph one under *Project Goals*, which was included in error; and,
- Respond to Questions received regarding the solicitation.

The hour and date specified for receipt of Offers remains unchanged.

Except as provided herein, all terms and conditions of the solicitation remain unchanged and in full effect.

A recording of the pre-proposal conference and associated materials have been posted on the NIH SBIR/STTR News Flash Page <https://sbir.nih.gov/engage/news> and are also made available below:

- [Webinar Slides](#)
- [Recording](#)
- [Transcript](#)

SECTION 12 Component Instructions and Technical Topic Descriptions, National Cancer Institute (NCI), Topic 433: *Developing Unbiased Medical Technologies to Reduce Disparities in Cancer Outcomes*, is amended to remove paragraph one under *Project Goals* as follows:

NIH/National Cancer Institute (NCI):

Topic 433: Developing Unbiased Medical Technologies to Reduce Disparities in Cancer Outcomes

Fast-Track proposals **will be** accepted.

Direct-to-Phase II proposals **will be** accepted.

Number of anticipated awards: 3-5

Budget (total costs, per award):

Phase I: up to \$400,000 for up to 12 months

Phase II: up to \$2,000,000 for up to 2 years

PROPOSALS THAT EXCEED THE BUDGET OR PROJECT DURATION LISTED ABOVE MAY NOT BE FUNDED.

Summary

There is an urgent need to spur innovation in developing unbiased medical technologies to reduce disparities in cancer outcomes. Structural inequalities in health and medicine, including in cancer control, have garnered the attention of leading clinicians, researchers, and journals. One insidious symptom of, and contributor to, structural inequalities in cancer outcomes is biased medical technology.

For example, existing pulse oximeters overestimate oxygen saturation when used by people with darker skin, and particularly women of color. This is consequential for cancer, given that pulse oximeters are an important prognostic tool for lung cancer. Similarly, Black, Indigenous, or other People of Color (BIPOC) individuals are at risk of getting inaccurate readings from smartwatches and fitness trackers that monitor heartbeat, due to increasing inaccuracy in darker skin. This is consequential for cancer because activity guidelines for cancer prevention recommend the use of heart rate monitors. Algorithms and machine learning-informed artificial intelligence (AI) used to guide clinical cancer decisions are often adjusted for race/ethnicity (with no explanation or explanations based on outdated/biased data); such algorithms guide decisions in ways that direct greater resources to white patients, compared to BIPOC patients. Similarly, computer-aided cancer diagnostic tools (e.g., for medical imaging) may be biased because the datasets they are developed on are imbalanced with respect to race/gender. If underlying data informing algorithms, AI, and imaging reflect structural inequalities, these will perpetuate bias and widen existing cancer disparities. As such, there is a critical need to develop unbiased medical technologies to improve cancer disparities.

Project Goals

Proposals should identify existing, racially/ethnically biased medical technologies integral to cancer prevention and control; identify the mechanisms contributing to such bias (e.g., targeted development and testing, inability to work effectively with a variety of skin tones, biased data inputs or outcome measurements); and develop new, unbiased replacement technologies. Potentially biased technologies could be identified in the existing literature or by the applicant.

Activities that fall within the scope of this solicitation include development of unbiased medical technologies to replace existing bias in technologies that contribute to disparities in cancer control outcomes. Proposals should target existing technologies integral to cancer control and with demonstrated bias, including (but not limited to): pulse oximeters or other measures of blood oxygen to be used at home or in clinical settings; heart rate monitors to be used at home to guide appropriate intensity exercise for weight loss and maintenance; and algorithms and artificial intelligence (AI) designed to inform clinician decision making individualized to the patient, such as those used for diagnosis, prognostic prediction, distribution of medical resources, and assessment of patient-reported outcomes (including pain). Projects could also involve integration of large biomedical data sets containing genomic, proteomic, histological, and clinical information to develop new technologies or algorithms, as prioritized in the Cancer Moonshot Blue Ribbon Panel. Activities can involve the development of any medical technology that could complement or replace existing, racially/ethnically biased technologies that are widely

employed in the medical care system or recommended for at home use.

Phase I Activities and Deliverables:

- Establish a project team including personnel with training and research experience in the specific type of medical technology targeted, knowledge of the relevant area of cancer prevention and control, and expertise in structural inequalities/health disparities;
- Provide a report including a detailed description and/ or documentation of:
 - o Existing racial/ethnic bias in the targeted medical technology;
 - o The role of such biased technology in perpetuating or exacerbating disparities in cancer prevention and control;
 - o Potential mechanisms underlying biases in the target medical technology;
 - o Description of the technical strategy that would be used to correct the bias in the existing technology or develop a new technology that could replace the cancer prevention and control function of the target biased technology;
 - o Analysis of the cost-effectiveness and ability to disseminate/ implement/ integrate technology into standard cancer prevention and control practices or healthcare settings;
 - o A detailed plan of methods that will be used to validate and evaluate the acceptability of the new technology in performing requisite cancer prevention and control strategies among the racial/ ethnic group for whom the initially targeted technology produced biased results;
 - o A detailed plan of methods that will be used to validate and evaluate the efficacy of the new technology in performing requisite cancer prevention and control strategies among the racial/ ethnic group for whom the initially targeted technology produced biased results;
 - o A detailed plan of methods that will be used to examine the reliability of the new technology in performing requisite cancer prevention and control strategies among the racial/ ethnic group for whom the initially targeted technology produced biased results across time;
 - o A plan for marketing and distribution of the novel medical technology after it has passed cost-effectiveness and efficacy/ acceptability tests described above;
 - o Any original data collected to demonstrate the bias in the target technology; and
 - o A list of all references and research informing the description and documentation outlined above.
- Develop a functional prototype of the newly developed technology;
- Provide preliminary evidence for potential efficacy for newly developed technology in reducing or eliminating bias;

Phase II Activities and Deliverables:

- Evaluate and document cost of and time to development of technology, compared to the existing biased technology;
- Scale the production of the technology, if necessary, to accommodate efficacy/acceptability research as described in the plan requested above;
- Conduct studies of acceptability, efficacy, and reliability, based on the detailed methodological plan outlined as described above;
- Prepare a report describing the cost-effectiveness and acceptability/efficacy/reliability findings;
- Execute marketing and dissemination/ implementation plan;
- In the first year of the contract, provide the program and contract officers with a letter(s) of commercial interest; and
- In the second year of the contract, provide the program and contract officers with a letter(s) of commercial commitment.

End of Topic 433

General Solicitation Questions

Question 1: Is a company allowed to submit more than one proposal to the same topic, assuming the proposals represent clearly different approaches, under the PHS 2022-1 SBIR Contracts solicitation?

Answer 1: Yes, a company is allowed to submit more than one proposal under the same topic, if the proposals represent separate and distinct projects.

Note that for proposal submission in eCPS, the company would need to create entirely separate submission packages. The company would go through the eCPS submission process for the 1st submission and then repeat the process for the next submission. If a company is planning to submit more than one proposal under the same topic, it is recommended that the Company differentiates between their different Phase I proposals by using a unique identifier in the file names/naming conventions. For example: if each submission has a different PI, include the PI name in the submission file names, etc., to ensure reviewers will be aware that the submissions are different proposals from the same vendor not a duplicate submission of the same proposal.

Question 2: Can you clarify when letters of support are requested?

Answer 2: When a subcontractor or consultant collaborator is proposed, a letter must be included from each individual confirming his/her role in the project and extent of involvement; when facilities other than those of the applicant are proposed, a letter must be included stating that leasing/rental arrangements have been negotiated and will be available for the use of the SBIR applicant; and, for Phase II proposals under a Fast Track submission, letters should be included in the Finance Plan section of your Commercialization Plan.

In addition, some of the specific Topic Descriptions in Section 12 refer to additional and/or more specialized letter requirements, so check your individual Topic of interest carefully.

*All of these letters should be included in your **Technical Proposal** to ensure that they are reviewed by all reviewers.*

*In addition, costs associated with collaborators should be addressed in Appendix C of the **Business Proposal**, and letters that discuss or confirm financial information for collaborators can also be included in the Business Proposal to support the evaluation of the proposed project budget. For NIH Topics, please note that information submitted in the **Business Proposal**, however, will not be seen by all evaluators, some of whom will **only** review the Technical Proposal.*

Question 3: How should I determine and document indirect rates?

Answer 3: The solicitation allows for small business to charge indirect costs at a rate of up to 40% of total direct costs without requiring that the small business negotiate an indirect rate agreement with the NIH Division of Financial Advisory Services (DFAS).

However, this does not mean that an indirect rate of 40% will be acceptable for every business.

Your business should complete a table such as the one found at the website below to be able to justify your rate (of up to 40%), and include this information in your Business Proposal:

- <https://oamp.od.nih.gov/dfas/indirect-cost-branch/indirect-cost-submission/indirect-cost-definition-and-example>

After reviewing the DFAS website above, if you have further questions, you are encouraged to contact the DFAS staff at dfas-idc@nih.gov for assistance in understanding how to determine an appropriate indirect rate.

Questions: Section 12 Component Instructions and Technical Topic Descriptions

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES (NCATS)

National Center for Advancing Translational Sciences (NCATS), Topic 022: Technological Development and Validation of Remote Measures for Use in Clinical Trials in Individuals with Rare Diseases

Question 1: Are you seeking a mobile / tech platform for data gathering? Measuring devices or IoT connected monitoring devices?

Answer 1: The objective of this contract is to develop and validate digital health technologies for data capture that can be used to assess individuals with rare diseases in remote settings in a manner that is suitably sensitive and specific for use in clinical trials. Technologies should be reliable, secure, and easy to use to monitor study participants remotely.

Technology developers, clinicians, researchers, and patients/patient groups will work collaboratively to develop validated digital health technologies specifically for outcomes data capture for clinical trials for rare diseases, and not for the purposes of recruitment, retention, or as the intervention itself. Digital health technologies may include clinical outcome assessments including new or modified: Patient-reported outcomes (PROs), Observer-reported outcomes (ObsROs), Performance outcomes (PerfOs), ClinicianReported outcomes (ClinROs) and devices for gathering physiological data. The technology must be reliable, secure, and easy to use to monitor study participants remotely, either in the home or while participating in activities of daily living. The technology should also be appropriate for use in three or more different rare diseases, (e.g., tool to assess movement in neurodegenerative diseases, PRO for reporting level of pain).

Question 2: Wearables are mentioned: A smartphone could theoretically be used as a wearable data collection device, from which an App such as Outpatient could then collect from it. For clinical trials, especially with distributed and remote people involved, the ability to track patient activity and confirm actions (and log those actions), could be very valuable. Track , collect, and coordinate vs Diagnostic measuring platform.

Answer 2: The objective of this contract is to develop and validate digital health technologies for data capture that can be used to assess individuals with rare diseases in remote settings in a manner that is suitably sensitive and specific for use in clinical trials. Technologies should be reliable, secure, and easy to use to monitor study participants remotely.

Technology developers, clinicians, researchers, and patients/patient groups will work collaboratively to develop validated digital health technologies specifically for outcomes data capture for clinical trials for rare diseases, and not for the purposes of recruitment, retention, or as the intervention itself. Digital health technologies may include clinical outcome assessments including new or modified: Patient-reported outcomes (PROs), Observer-reported outcomes (ObsROs), Performance outcomes (PerfOs), ClinicianReported outcomes (ClinROs) and devices for gathering physiological data. The technology must be reliable, secure, and easy to use to monitor study participants remotely, either in the home or while participating in activities of daily living. The technology should also be appropriate for use in three or more different rare diseases, (e.g., tool to assess movement in neurodegenerative diseases, PRO for reporting level of pain).

Question 3: In the Phase I Activities and Expected Deliverables, question #1 it asks about intended populations/age groups. Our app can assist with remote health management of rare diseases and more general (Covid) clinical trials, across all age groups. Do we have to list specific diseases?

Answer 3: Please describe intended populations a. Describe intended population(s) i. Rare diseases ii. Age group.

Question 4: Intended population - describe intended population: Are you expecting the offeror to determine the rare disease for this project? We usually work with a healthcare company that provides us with the disease and the patient conditions that need to be monitored/measured?

Answer 4: The offeror is expected to describe intended populations a. Describe intended population(s) i. Rare diseases ii. Age group.

Question 5: Measurement Property: Are you expecting the offeror to provide the measurement metrics? Typically, the healthcare company that we are working with provides us with the measurement metrics.

Answer 5: The offeror is expected to provide all information requested in the Phase I Activities and Expected Deliverable section.

Question 6: Technical Performance: Are you expecting the offeror to test with patients? Typically, the healthcare company that we are working with does the testing with their patients.

Answer 6: The offeror is expected to provide all information requested in the Phase I Activities and expected deliverables including safety specifications and human factor specifications.

NATIONAL CANCER INSTITUTE (NCI)

General Questions Applicable to All NCI Topics:

Question 1: May Technical and Business Assistance costs be added on top of the Topic's budget?

Answer 1: Yes, for proposals submitted in response to National Cancer Institute (NCI) Topics, these costs may be included in addition to the budget set forth for the Topic, by the amount allowed in the solicitation provision discussing Technical and Business Assistance.

Question 2: Is there a recorded version of the webinar that NCI SBIR and FDA held on August 24th?

Answer 2: Please email ncioasbir@mail.nih.gov and a copy will be sent to you once available.

National Cancer Institute (NCI), Topic 430: Development of Senotherapeutic Agents for Cancer Treatment

Question 1: Would it be within the scope of this Topic to propose the use of our novel ADC in combination with an inhibitor of BCL-2 for solid tumors to “fire-up” tumor microenvironment and promote drug response to immune checkpoint inhibitors?

Answer 1: If a proprietary ADC exerts its biological effects through senomorphic or senolytic activities, it may be a good fit for contract Topic 430. If the only senolytic/senomorphing agent is the already approved BCL-2 inhibitor, then it is not a good fit for this Topic, since that is not the product being developed.

Question 2: We would be interested in proposing medicinal chemistry and scale-up chemistry of next generation compounds, coupled to in vivo testing in a model for an age related lung cancer. Please let me know if this fits the intent of the solicitation?

Answer 2: Yes, the proposed work would likely be appropriate for the topic. Please be sure to justify the rationale in selection of the specific in vivo animal model (e.g., model with accumulated senescent cells through aging and/or observed therapeutic effect caused by clearing of senescent cell).

National Cancer Institute (NCI), Topic 431: Cancer Treatment Technologies for Low-Resource Settings

Question 1: There seems to be some overlap with NCI topic 431 and PA-21-259. Are these the same opportunity with different funding mechanisms? Does applying to one preclude applying to the other?

Answer 1: NOT-CA-21-062 (<https://grants.nih.gov/grants/guide/notice-files/NOT-CA-21-062.html>) is related to the

general Omnibus solicitation PA-21-259. If the applicant applies for NOT-CA-21-062, for funding consideration, the applicant must include “NOT-CA-21-062” (without quotation marks) in the Agency Routing Identifier field (box 4b) of the SF424 R&R form. Applications without this information in box 4b will not be considered for this initiative.

The Omnibus Grant Solicitation PA-21-259 is the investigator- initiated grant solicitation and is generally open to any technology that fits the mission of **NIH**. Depending on the grant application, it is assigned to a study section at CSR and to the appropriate institute.

Topic 431 is a National Cancer Institute specific topic and is a contract solicitation. You should only apply to the contract if you are working in this exact space and can meet the expectations and deliverables.

You cannot apply to both the contact and grant opportunities at the same time since you cannot have two essentially similar applications under review at the same time. If your project fits squarely within the parameters of contract Topic 431, we would recommend that you consider submitting a contract proposal under Solicitation PHS2022-1, since this is a one-time proposal submission opportunity that NCI has designated as a priority area. (NCI may or may not decide to include the same or similar Topic in future annual SBIR contract solicitations.)

Question 2: Is a clinical trial phase I (conducted in low-resource settings) testing the drug candidate in participants with advanced solid tumors, within scope of this solicitation/topic?

Answer 2: If the drug candidate is proposed to target low-resource setting areas or underserved populations in the US, it would likely fit within the scope of Topic 431. However, if the drug candidate targets general patient population with advanced solid tumors, the applicant should consider the general SBIR/STTR Omnibus solicitation. Link: <https://sbir.cancer.gov/funding/opportunities/SBIR-STTR-omnibus-solicitation>.

Question 3: Would a repurposed IND vaccine be a fit for Topic NCI 431 for oncolytic virus therapy for low-resource settings?

Answer 3: If the repurposed IND vaccine is proposed to target low-resource setting areas or underserved populations in the US, it would likely fit within the scope of SBIR Topic 431. However, if the vaccine targets general patient population with triple negative breast cancer, the applicant should consider the general SBIR/STTR Omnibus solicitation. Link: <https://sbir.cancer.gov/funding/opportunities/SBIR-STTR-omnibus-solicitation>

Question 4: Would the development of an injectable cytotoxic cancer drug that targets the generic market be suitable for topic 431?

Answer 4: This would not be likely to fit within SBIR Topic 431. It fits well with the general SBIR/STTR Omnibus solicitation. Link: <https://sbir.cancer.gov/funding/opportunities/SBIR-STTR-omnibus-solicitation>.

National Cancer Institute (NCI), Topic 432: Synthetic Biology Gene Circuits for Cancer Therapy

Question 1: Are the following concepts within the scope of Topic 432? 1) Applying genetically encoded biocontainment technology to mammalian cancer cell lines to provide control over timing and dose of therapeutic cell lines, and controlling location within the body with CARs, to ultimately be applied to cancer cell lines that can be engineered to behave as antigen presenting cells. 2) Combining genetic control and containment elements to therapeutically modified organisms that intrinsically colonize solid tumors and switching into a cytotoxic state when the microbial density reaches a certain point.

Answer 1: Both comments are likely to fall within the scope of this Topic; however, remember that the proposal should reach the development stage defined in the solicitation by the end of Phase I.

National Cancer Institute (NCI), Topic 433: Developing Unbiased Medical Technologies to Reduce Disparities in Cancer Outcomes

Question 1: It seems like the 3rd paragraph on page 72 of the solicitation is a mistake as it doesn't fit in with the rest of the topic, can you please confirm?

Answer 1: Yes, you are correct – this paragraph was inadvertently included. Please disregard the paragraph that states: “The goal is to create scalable health IT-based informatics tools... The researchers will gain access to tools that measure the variability in cancer care coordination and patient engagement in diverse settings, which will help identify the characteristics of clinical teams, processes and health systems associated with delivery of high-quality care and to test interventions based on these characteristics”

Question 2: For the Direct to Phase II option, does the concept of digital pain management technology with the engagement of clinical research (comparing patient guessing their pain score with a future state of objective unbiased quantified pain measurement, then comparing the two data results with the intent of improving cancer outcomes by validating patient stated pain level, reducing the cost of care, and reducing disparities in care and outcomes due to clinical bias) fall in the scope of topic 433?

Answer 2: Yes, this is likely to be within the scope of Topic 433.

National Cancer Institute (NCI), Topic 437: 3D Spatial Omics for Molecular and Cellular Tumor Atlas Construction

Question 1: Is the contract topic also interested in projects that aim to build a metabolomics tumor atlas that is not based on spatial or imaging information?

Answer 1: In order to be considered for award under Topic 437, the solicitation states that “Cellular or sub-cellular resolution imaging is a requirement”. Unless the offeror proposes to combine their metabolomics information with spatial/imaging data, it would not fall within the scope of this Topic.

National Cancer Institute (NCI), Topic 438: Understanding Cancer Tumor Genomic Results: Technology Applications for Community Providers

Question 1: Would innovative technology that can specify which cancer drug will work on which genetic variant leading to targeted therapy and tailored to the cancer patient’s genetic profile be within the scope of this topic area?

Answer 1: Yes, this would likely be within the scope of this Topic.

National Cancer Institute (NCI), Topic 439: Advanced Sample Processing Platforms for Downstream Single-Cell Multi-Omic Analysis

Question 1: In reference to the scope of the integration, what is the final step that needs to be integrated? Is it isolation and enrichment of cancer cells or extraction of their nucleotides? Or is there any freedom of choice?

*Answer 1: According to the solicitation, the final product is an integrated platform, “The offerors are encouraged to integrate the preanalytical workflow from tumor cell dissociation/isolation, enrichment, tracking, cell lysis, to biomolecular isolation **on a single platform** to enable **single cell multimodal-omic analysis.**”*

Question 2: Please confirm if following methods mentioned are acceptable as long as they can provide high efficiency separation: droplet microfluidics, microwell technologies, valves and chambered microchannels, tube-based kits.

Answer 2: These methods are acceptable as long as the project fits the requirement stated above and in the solicitation.

National Cancer Institute (NCI), Topic 440: Cancer Prevention and Diagnosis Technologies for Low-Resource Settings

Question 1: Would the development of a low cost compact CT for diagnostic imaging fit into this topic description?

Answer 1: If the low cost compact CT for diagnostic imaging is developed for targeting low- and middle-income countries (LMICs) or low-resource settings in the US, it fits into the topic 440. NCI uses the [World Bank Country and Lending Groups](#) to categorize low- and middle-income countries (LMICs) for potential research sites and partnerships. Low-resource settings in the US are the areas that have populations with social economic disadvantage and cancer health disparities. If an applicant plans to include research in foreign countries, please pay attention to the policy statement regarding the foreign country involvement in the solicitation.

Question 2: Would research into prevention nutrition fit under topic 440?

Answer 2: If the applicant targets cancer prevention in a low-resource setting area or underserved populations, it could fit into the scope of the topic 440. However, if the applicant targets cancer prevention for general populations, the applicant should consider the general SBIR/STTR Omnibus solicitations. Link: <https://sbir.cancer.gov/funding/opportunities/SBIR-STTR-omnibus-solicitation>.

National Cancer Institute (NCI), Topic 441: At-Home Screening for Hepatitis C Virus

Question 1: If there is technology that has been successfully utilized to develop IVD test for other viruses, and a similar technology will be used to develop a new test for hepatitis C, would this be appropriate for this Topic, even though the core technology is not brand new and the basic principles are the same?

Answer 1: This is likely to be considered within the scope of this Topic.

Question 2: In Phase I, is it mandatory that we establish and provide proof of collaboration with a US-based medical facility / research group for human specimens for validation of the prototype POC assay?

Answer 2: The solicitation states that Offerors may need to establish a collaboration; however, if the Offeror already has the appropriate specimens, then no collaboration is necessary. Please ensure there is a description of the source of the specimens in the proposal.

Question 3: Regarding the prototype POC assay, should this assay have the capability to inform on both active infection (HCV antigens), as well as exposure (anti-HCV antibodies) or will one or the other component suffice?

Answer 3: The solicitation states the following: "The development of a rapid and accurate at-home test for HCV antibodies for HCV exposure or HCV antigens or RNA for active HCV infection will provide a readily acceptable and accessible modality that can eventually reduce the burden of liver disease and HCC cancer morbidity and mortality." Since the solicitation indicates "HCV antibodies for HCV exposure or HCV antigens or RNA for active HCV infection" it is up to the Offeror to decide if they can develop both capabilities in Phase I.

Question 4: Would the optimization of an AI based wearable monitoring system for accurate tracking of pulse oximetry, heart rate, and other indicators in people of different skin color, as described in the topic description align with topic 441?

Answer 4: The description provided would likely fall within the scope of Topic 441.

National Cancer Institute (NCI), Topic 442: Quantitative Biomarkers as Medical Device Development Tools for Cancer

Question 1: With regards to Topic 442, what is an appropriate proposal for biomarker 'device'? For example, if an ELISA assay detects a cancer biomarker PSA; would the ELISA assay be considered as the proposed device?

Answer 1: For more information on MDDTs, please see FDA guidance: <https://www.fda.gov/media/87134/download>. You may contact ncioasbir@mail.nih.gov for an MDDT inquiry template which may help you understand the requirements for a Biomarker based MDDT tool.

Question 2: Would methods and reference tools centering on a distinct and proven chemical labeling technology with the ultimate goal of converting our finding into a commercial diagnostic test fit the criteria for MDDT? The market size of the standards and methods are much smaller than a diagnostic test so our concern is that the application would have weak commercial significance.

Answer 2: It could potentially fall under the scope of this topic. There is an FDA process for reviewing whether a project would fit within MDDT; however, the Offeror would not receive a response in time to make a decision about submitting a contract proposal to NCI for this topic.

Regarding the market size, NCI does not strictly judge on market size alone for commercial strength. For example, we support the development of therapeutics for rare cancers where patients have no treatment options. From one perspective, this could be thought of as a small market size, but from NCI's perspective, a therapeutic like this could fill a significant unmet need.

National Cancer Institute (NCI), Topic 443: Development of Computer-Aided Diagnosis Tools for Upper and Lower Gastrointestinal Tract Cancer Prevention

Question 1: Do computer-aided detection (CADe) and diagnosis (CADx) systems of colonic polyps in “virtual” colonoscopy” (aka CT/MR colonography) fall in the scope of Topic 443?

Answer 1: Yes, it is likely that new computer/software tools for computer-assisted virtual colonoscopy would be within the scope of this contract topic.

Question 2: Is the development of Artificial Intelligence / Machine Learning algorithms capable of identifying normal, precancerous and cancerous cells in the anus, along with dysplasia, and metaplasia, something that NCI is looking for in response to Topic 443? Algorithms would also be able to evaluate endoscopic images for prediction of progression to more advanced disease and / or response to anal cancer interception intervention.

Answer 2: Yes, development of an algorithm to assist with diagnosis of anal cancer would likely be within the scope of Topic 443.

Question 3: Is this contract topic against computer aided diagnostic tools that use molecular probes? Or would it be open to molecular probes in general?

Answer 3: A novel fluorescence endoscope integrating molecular and structural information, based on the use of molecular probes would only be within the scope of this Topic if it also includes computer algorithm/software to assist in the identification of pre-cancer/cancer lesions. The focus of this topic is computer assistance for diagnosis of gastrointestinal tract cancers.

National Cancer Institute (NCI), Topic 444: Evaluation Datasets as Medical Device Development Tools for Testing Cancer Technologies

Question 1: It appears that the MDDT proposal requirements are included as part of the SBIR Phase I

deliverables. We understand that we need to submit our qualification plan to the FDA by the end of the Phase I contract. However, what we would like clarification on is when we submit our “proposal plan” to the FDA. Do we need to submit the “proposal phase” to the MDDT program and receive approval BEFORE we are allowed to submit the SBIR proposal? If so, how long does it take to receive approval and will we receive it in time to submit the full SBIR proposal?

Answer 1: The MDDT proposal phase can be submitted after a company is awarded the NCI Phase I contract. According to FDA guidance (<https://www.fda.gov/media/87134/download>), CDRH intends to notify companies of its decision regarding proposal acceptance ~60 days from receipt of the proposal. This should allow a company time to submit an MDDT proposal and qualification plan during the Phase I contract time period.

Question 2: Will the FDA require the dataset to be made available publicly, and if so, to what degree? Will we be expected to allow users of the data set through the MDDT process to inspect the data records at an individual data record level? It makes a difference to the organizations we intend to solicit data from for this project whether their data will be in a “black box” and protected from individual record examination versus having an “open” dataset where users are allowed to see individual records.

Answer 2: FDA only makes the SEBQ information about the tool publicly available. See <https://www.fda.gov/medical-devices/science-and-research-medical-devices/medical-device-development-tools-mddt>. The other information submitted is needed as part of the review for qualification decision, and is not made public. If the preference is a “black box” for datasets in the SEBQ, this would possibly be fine; FDA will not publish individual data record details, but may need some standard established criteria to define the “black box” in the SEBQ for the users so that it can be correctly utilized by external stakeholders and correctly reviewed by internal stakeholders.

Question 3: Is NCI interested in a radiation oncology tool that predicts failure points in the treatment delivery process? Would this idea meet any of the three categories described in FDA’s MMT program?

Answer 3: This would likely fall under the scope of this topic and potentially be a tool for consideration in the FDA MDDT program.

National Cancer Institute (NCI), Topic 445: Advanced Manufacturing to Speed Availability of Emerging Autologous Cell-Based Therapies

Question 1: Would the development of a cell expansion platform or the development of a cell-based therapeutic fall within the scope of this topic area?

Answer 1: The purpose of Topic 445 is to stimulate the development of advanced manufacturing technologies that substantially improve the speed and cost of producing autologous cell-based therapies. This Topic is focused on solving key bottlenecks in cell manufacturing to reduce time and cost. It is expected that offerors will have an end-to-end process in place. Offerors can use a candidate cell therapy to demonstrate their process or system is meeting the needs of the topic; however, if the goal of the proposal is primarily to advance a specific cell therapy then it would likely be a better fit under the omnibus SBIR grant solicitation, instead. If the goal of the proposal is to advance an NK cell manufacturing process or system, then it would likely fall within the scope of this topic.

Question 2: Would a proposal submission focused on a standardized medical device and protocols in order for physicians to prepare bioregenerative treatments with safe, robust, and consistent outcomes align with the goals of this topic?

Answer 2: This was not the type of therapeutic that NCI was contemplating for this Topic. NCI is instead primarily interested in immune cell-based therapies, thus the reason for the requirement that the team has an immunologist, an engineer, and a clinician. Therefore, the project described would be a better fit under the omnibus SBIR grant solicitation.

Question 3: Please clarify what was said in the solicitation for Topic 445: “*Activities not responsive to announcement: Projects proposing to use allogeneic cell-based therapies for technology validation will not be considered responsive under this solicitation. Projects improving a key part of the cell manufacturing process, but not being tested in an end to end process will be considered incomplete proposals and therefore not responsive to the topic.*”

Answer 3: All proposals must have a system or process that is reflective of the whole vein to vein process. If the system described is being incorporated into a cell therapy manufacturing process that would manufacture a clinical grade or research grade cell therapeutic, then it would likely be considered within the scope of this Topic. However, if the potential offeror is using the term “end to end” to describe the completion of a part of the overall cell therapy manufacturing process, that would not be considered within the scope of this Topic.

NATIONAL INSTITUTE ON AGING (NIA)

National Institute on Aging (NIA), Topic 004: Improving CNS Gene Delivery Systems for AD/ABDR Therapy Development

Question 1: I approach you with a question regarding the SBIR contract topic: “NIH/NIA 004 - Improving CNS Gene Delivery Systems for AD/ABDR Therapy Development”. Is this topic intended only for technologies that improve gene therapy delivery to the brain, or would it accept also projects aiming to improve drug delivery to the brain in general?

Answer 1: This solicitation is specifically for CNS gene delivery only.

Question 2: My reading of the contract topic is that it is aimed more for manipulations of drug structures and compositions that would allow them to pass through the BBB. Would you please advise as to whether a proposed project (to use focal electric field to open the BBB) would be responsive to the contract? We would use a “standard” gene therapy vector to test the opening of the BBB (e.g. AAV), rather than focus on modifying the vector?

Answer 2: NIA will allow novel delivery modalities such as ultrasound, as long as they meet the expected deliverables.

Question 3: I would like to ask you whether I can use other types of gene therapy, not limited AAV-mediated gene therapy that is stated in the announcement.

Answer 3: Offerors can use other types of gene therapy for delivery vehicle/modality, but it has to be delivery for gene therapy (not drugs). As stated in the solicitation: Novel delivery vehicles can include (but are not limited to) nanoparticles, liposomes, micelles, and Trojan horse approaches; examples of novel delivery modalities can include ultrasound, electroporation, and implantable pumps.

National Institute on Aging (NIA), Topic 005: Geroscience-based Chronic Wound Treatment Product Development

Question 1: Is NIA 005 interested in prevention of wounds or solely focused on wound healing?

Answer 1: This solicitation is focused on the treatment of wound and healing, but not prevention of wounds.

Question 2: If we have animal data, can we skip the animal study and go straight into the human usability study (since we have IRB approval already)?

Answer 2: A Phase I proposal could include human usability study if well-justified by existing preliminary studies, and appropriately designed.

Question 3: Would the NIA want us to propose multiple different contracts for specific indications, for example, would the NIA want us to submit one for diabetic foot ulcers, one for leg ulcers, one for pressure ulcers/bedsores?

Answer 3: The proposal should propose studies based on the product's intended indication, whether that is broader or more specific, and justify the choice of that indication.

Question 4: If we already have animal data, can we skip to a human usability study in these specific indications?

Answer 4: A Phase I proposal could include human usability study if well-justified by existing preliminary studies, and appropriately designed.

Question 5: Would studies to advance drug delivery to address degenerative joint ailments such as arthritis qualify under Topic 005 - Geroscience-based Chronic Wound Treatment Product Development?

Answer 5: No, the focus of this topic is on healing of skin wounds, particularly venous leg ulcers, diabetic foot ulcers and pressure ulcers, which occur more commonly in older adults. Proposals about arthritis treatment would not be responsive.

National Institute on Aging (NIA), Topic 006: The Development of Mechanism-based Adult Stem Cell Treatments to Combat Aging Pathologies

Question 1: What do we do if our product does not fall under a drug pathway but is approved by the FDA as a device? Can we skip the activities that are related to drug development? For example, if our product was a device or biologics.

Answer 1: The development of a device is also appropriate so long the goal will encompass the mechanisms of its benefit.

Question 2: If we have validated biomarkers and phenotypic analysis data, can we propose to move forward with animal studies? Furthermore, are we to believe that the 100 in vivo mice animal studies is related to mice and/or rodents and if so, can we propose to do a smaller number of animals if those animals are large animals such as pigs, dogs, etc? As these types of animal studies are a better representation of what will happen in humans.

Answer 2: Yes other animals maybe used and numbers are justified. Mice were used as only an example.

Question 3: We noticed that it states a need for a large-scale animal study. If we get better data off of the smaller study we asked in the prior question, can we move on to human studies, especially if we already have regulatory approval in that field of use?

Answer 3: As long as there is FDA regulatory approval which has already vetted the number of animals used to base the approval on that would be fine.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

National Institute of Allergy and Infectious Diseases (NIAID), Topic 103: Development of Diagnostics to Differentiate HIV Infection from Vaccine Induced Seropositivity

Question 1: Is a laboratory-based test sufficient to address the requirement of the solicitation? Is it necessary to include the point-of-care-based test, as well?

Answer 1: A laboratory-based test will be responsive to the solicitation.

Question 2: For the assay that is intended for use in research laboratory setting, is there a specified cost range of the instrument associated with the assay?

Answer 2: There is no request for the development of tests for "research laboratory settings," rather, for diagnostics. The cost of the instrument is not specified, but it will be considered in light of maintenance costs, price/test, high throughput capability, cost to operate, level of training necessary, power source dependability, reporting system, time to result, kind and volume of sample(s), foot print etc..

National Institute of Allergy and Infectious Diseases (NIAID), Topic 104: Adjuvant Discovery for Vaccines and for Autoimmune and Allergic Diseases

Question 1: In vitro correlates of adjuvanticity could easily encompass cytokine release, innate cell surface receptor expression, and even T cell proliferation/activity. For the Phase I Activities, what would constitute an acceptable in vitro correlate of tolerogenic clinical adjuvanticity for an a high-throughput screen?

Answer 1: In vitro correlates of adjuvanticity continue to be poorly defined, not only for infectious disease applications, but even more so for the new category of tolerogenic adjuvants. Furthermore, such in vitro correlates will likely not be the same for different indications, and will also likely be multi-parametric. It is, therefore, impossible to guide any offeror in regards to the choice of most appropriate in vitro readouts. Offerors are encouraged to provide preliminary data, ideally in the disease model they propose to use (either for Phase I or subsequent Phase II studies) to establish the relevance and appropriateness of the proposed readouts, ideally based on a prototype immunomodulator that induces the desired in vivo effect. Alternatively, the offeror may refer to studies in which the proposed in vitro readouts had shown predictive value.

National Institute of Allergy and Infectious Diseases (NIAID), Topic 106: Production of Adjuvants Mimics

Question 1: What is meant by mimic? Does this mean an exact replicate of an adjuvant formulation already in use, or does this mean a formulation will biosimilar chemical constituents? If the latter, can a proposal for an adjuvant mimic include a pre-clinical assessment differentiating between Th1 versus Th2 responses?

Answer 1: An adjuvant mimic is an adjuvant formulation with biosimilar chemical constituents and that is expected to promote an immune response to a co-delivered antigen similar to that induced by the adjuvant it seeks to mimic. Thus, the characterization of the responses induced by the adjuvant is an appropriate activity that may be used to confirm that the activity of the mimic is comparable.

Question 2: In Phase II, does the “lead product” refer to the chosen mimic adjuvant formulation that is desired to be carried forward?

Answer 2: Yes, the lead product is the mimic formulation that shows the greatest promise moving forward towards product development-related activities.

Question 3: Would Phase II support testing the immunological profile of a chosen adjuvant with more than one disease model?

Answer 3: Since not all adjuvants will be suitable for all pathogens or vaccine types, it is potentially useful to test an adjuvant mimic using more than one disease model (compared to a benchmark). However, offerors should keep in mind that the primary objective of Topic 106 is the “development, validation and production of adjuvant [mimics] for use by the broader research community, either as commercial products or through licensing agreements”. If the testing of the adjuvant mimic in different disease models goes beyond what is needed to simply validate the product and is aimed at determining the usefulness of the adjuvant for specific vaccines (and for further product development of certain adjuvant/antigen combinations), offerors should consider responding to Topic NIH/NIAID 105 (Adjuvant Development for Vaccines and Autoimmune and Allergic Diseases).

Question 4: Could you elaborate on what sort of pharmacological and toxicological studies would be appropriate for Phase II?

Answer 4: For this solicitation, NIAID does not specify the types of studies that need to be conducted to accomplish the objectives of the statement of work that the offeror develops. What types of PK/tox-studies an offeror proposes will also depend on the intended purpose of the adjuvant mimic produced under this program (e.g., use for preclinical studies only or does the offeror intend to produce a GMP lot under the SBIR program?)

Question 5: One of the Phase II deliverables is a “marketing plan”, is it allowed to budget Business Development individuals’ as part of the proposal?

Answer 5: The SBIR solicitation does not prohibit the proposing of business development personnel. If selected for further consideration, all proposals are subject to negotiations in which the Government may focus on specific cost elements for either removal or inclusion.

Question 6: What level of production scale would be appropriate to obtain by the end of Phase II?

Answer 6: The objective of the solicitation is to “[Develop adjuvant mimics] for use by the broader research community, either as commercial products or through licensing agreements”. The production scale will be capped by the costs associated with the production and testing of the adjuvant and factors such as the cost of goods, the complexity of the manufacturing process, and the purity/quality of the product (lab-grade, GLP-grade, GMP-grade).

National Institute of Allergy and Infectious Diseases (NIAID), Topic 108: Development of Rapid POC Diagnostics for Treponema pallidum

Question 1: A lot of the confusion is caught in the semantics of "direct detection" because that could mean two different things, particularly when it comes to syphilis testing. From the solicitation, under the project goals for Topic 108, it reads: "The goal of this project is to develop a rapid (\leq one hour), point-of-care diagnostic capable of detecting T. pallidum directly from patient specimens". In a clinical sense, a direct treponemal test usually involves antibody detection which in itself is not "directly" detecting T.pallidum, hence the confusion.

Answer 1: Direct detection” in the context of this topic means an assay or activity that shows that Treponema pallidum organisms, or constituents of T. pallidum such as DNA, RNA or proteins, are present in the patient specimen under examination.

National Institute of Allergy and Infectious Diseases (NIAID), Topic 110: Point of Care (POC) Diagnostics for Antimicrobial Resistant (AMR) Enteric Bacterial and Parasitic Pathogens

Question 1: By antibiotic resistance profiles, do you mean genotypic DNA markers?

Answer 1: For antibiotic resistance profiles, it is suitable to use genotypic DNA markers and/or phenotypic markers, which includes transcriptional markers.

Question 2: Can we use known antimicrobial resistance DNA markers or do we need to find new ones?

Answer 2: The use of established AMR DNA markers is acceptable, as is the use of new DNA markers.

National Institute of Allergy and Infectious Diseases (NIAID), Topic 112: Digital Tools Against Misinformation about Infectious Disease Treatments and Vaccines

Question 1: How critical will it be to propose solutions that will have as broad a reach as possible?

Answer 1: It is up to the offerors to determine the scope of the solution they propose.

Question 2: We understand that this SBIR does not support clinical trials. Given the broad definition of clinical trial used by the NIH, could we obtain clarity on the types of HSR that may fall within scope of this topic? For example, do studies exploring the efficacy of developed tools at guarding against misinformation qualify as clinical trials?

Answer 2: The proposed solutions should be digital tools that address disinformation bots or other digital mechanisms that spread disinformation. Therefore, it is not expected that human subjects or clinical trials would be involved within the scope of these projects.

CDC/NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION (NCCDPHP)

National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP), Topic 044: Algorithmic Database Food Product Tool to Align Food Service with Guidelines

Question 1: On the <https://www.sbir.gov/faqs/all> website, it was mentioned that we do not have to certify eligibility (establishing the business) until the time of award. Does this grant require us to found a company prior to submitting our proposal?

Answer 1: A copy of the completed SBA Company Registration for your organization must be submitted as part of your Business Proposal.

Funding Agreement Certification & Life Cycle Certifications – Required Prior to Award and During Contract Life Cycle. The SBA SBIR/STTR Policy Directive requires the collection of certain information from firms at time of award and during the award life cycle through use of the SBIR Funding Agreement Certification and the SBIR Life Cycle Certification, which can be viewed here: https://grants.nih.gov/grants/forms/manage_a_small_business_award.htm.

The Funding Agreement Certification is required at the time of award and may also be required at any other time that has been identified and incorporated into the contract delivery schedule. The Life Cycle Certification is required prior to final payment on the Phase I award, prior to receiving 50% of the total award amount on the Phase II award, and prior to final payment on the Phase II award, and may also be required at any other time that has been identified and incorporated into the contract delivery schedule. These certifications do not need to be included in your original proposal. The grants.gov submission/registration process requires that an applicant be a formal entity in order to submit an application to the federal government. However, applicants need not meet the SBIR and STTR eligibility requirements until the time of award.

Question 2: As the product/software requires constant updates to reflect new changes in dietary guidelines over the next few years, nutritional information to deal with new ingredients (i.e., cell-based meats), and new product databases, does the award agency (CDC) then have access to our software in perpetuity, with the updates done to the software for free?

Answer 2: Please see the solicitation's Sections 4.19 – "Identification and Marking of SBIR Technical Data in Contract Reports and Deliverables" and 5.12 "Technical Data Rights".

Question 3: Are you able to introduce us to connections in the food service operations, for us to talk to and learn more about the problems they are facing to better tailor our proposal?

Answer 3: No – this is the responsibility of the offeror. There are many types of potential subject matter experts in this area, selecting which one and figuring out how to get some of their time or partner with them is critical to success in this proposal.

CDC/NATIONAL CENTER FOR HIV/AIDS, VIRAL HEPATITIS, STD, AND TB PREVENTION (NCHHSTP)

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), Topic 052: Electronic Health Record Algorithm to Identify Persons with HIV Not in Care

Question 1: I would like to know the details about this program and application process?

Answer 1: All information related to Topic 052 is located in Section 12 - Component Instructions and Technical Topic Descriptions, pages 128 and 129. Information regarding the application process is located in Section 7 - Proposal Submission, beginning on page 35 and Section 8 - Proposal Preparation and Instructions, beginning on page 38. Please read the entire solicitation for additional information on the SBIR program and to assist with the application process.

CDC/NATIONAL CENTER FOR IMMUNIZATION AND RESPIRATORY DISEASES (NCIRD)

National Center for Immunization and Respiratory Diseases (NCIRD), Topic 035: Nanoparticle-based Multi-Antigen Influenza Vaccine that Induces both Antibody and Cell-Mediated Immune Responses

Question 1: In this solicitation, the required Phase I activities include animal studies. The also indicates that it will be 6-month Phase I and the funds will be \$243,500 for this program. We are just not sure if it is possible to extend the program to 9-12 months due to the animal studies when we submit the proposal? And the amount of funds could be also increased accordingly, or it is the maximum amount that we could budget for this program?

Answer 1: The funding amount for Topic 035 cannot exceed \$243,500. The period of performance may be extended but cannot exceed 12 months.

End of Amendment 1