MARCH 17, 2021 | BIOHEALTH INNOVATION

WRITING YOUR SPECIFIC AIMS PAGE

DEEPA NARAYANAN
SBIR DEVELOPMENT CENTER
NATIONAL CANCER INSTITUTE

SBIR
DEVELOPMENT CENTER

FROM IDEA TO AWARD…

01 HAVE AN IDEA??

02 ARE YOU ELIGIBLE FOR SBIR?

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05 WRITING A SPECIFIC AIMS PAGE

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09 HOW ARE FUNDING DECISIONS MADE?

10 TACKLING RESUBMISSIONS

SBIR DEVELOPMENT CENTER

WHO ARE SBIR/STTR APPLICANTS?

Aruna Gambhir, MS, MBA

CEO and Co-Founder, CellSight Technologies

"Investors want to see that a technology works. SBIR funding has been critical to our company to show that our technology works."

CellSight Technologies

Modulation Therapeutics, Inc

"My laboratory was working in drug development and it takes a long time to license a technology. It was hard to push forward with only R01 funding and we had neat technology, worth pursuing."

Lori Hazlehurst, Ph.D.

Professor, Pharmaceutical Sciences
West Virginia University

President and Co-founder, Modulation Therapeutics

WHAT IS THE NIH LOOKING FOR?

Innovative solution to significant **unmet clinical need**

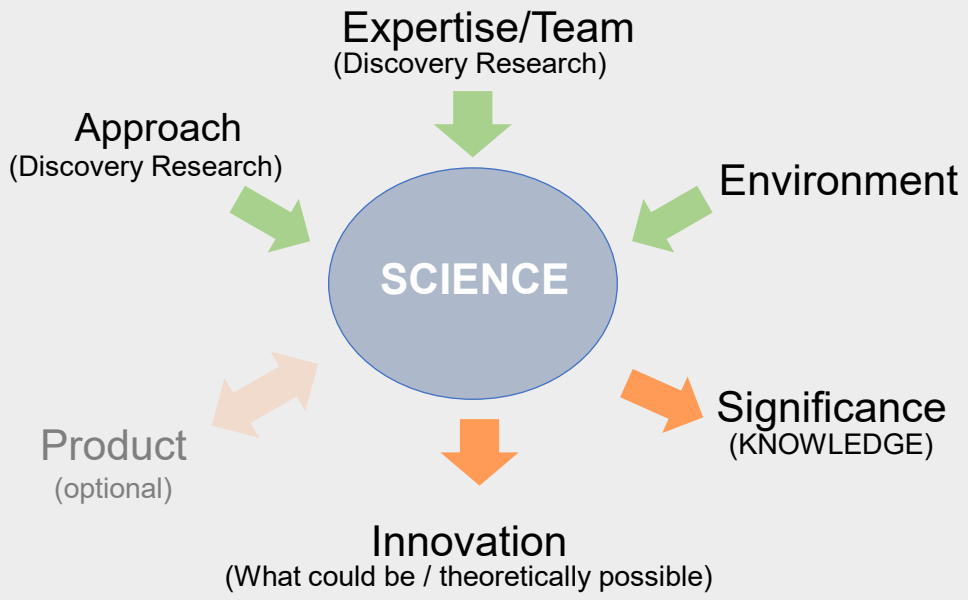
Leverage the expertise of the company/ founder

Solution that has **significant commercial potential**

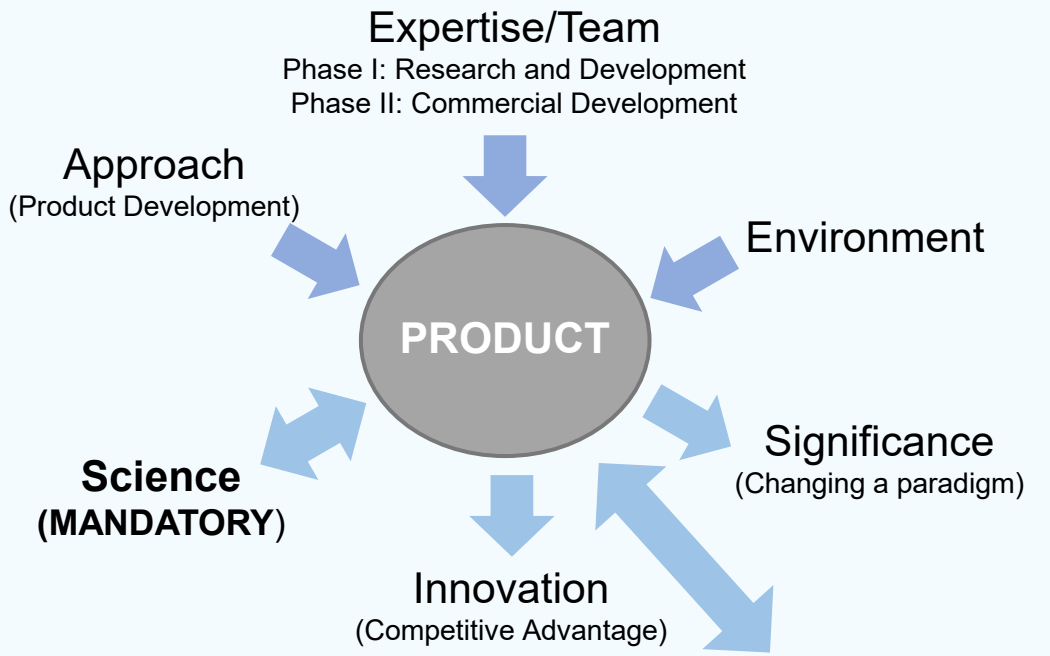
Product focused Science

PRODUCT FOCUSSED SCIENCE

ACADEMIC GRANT



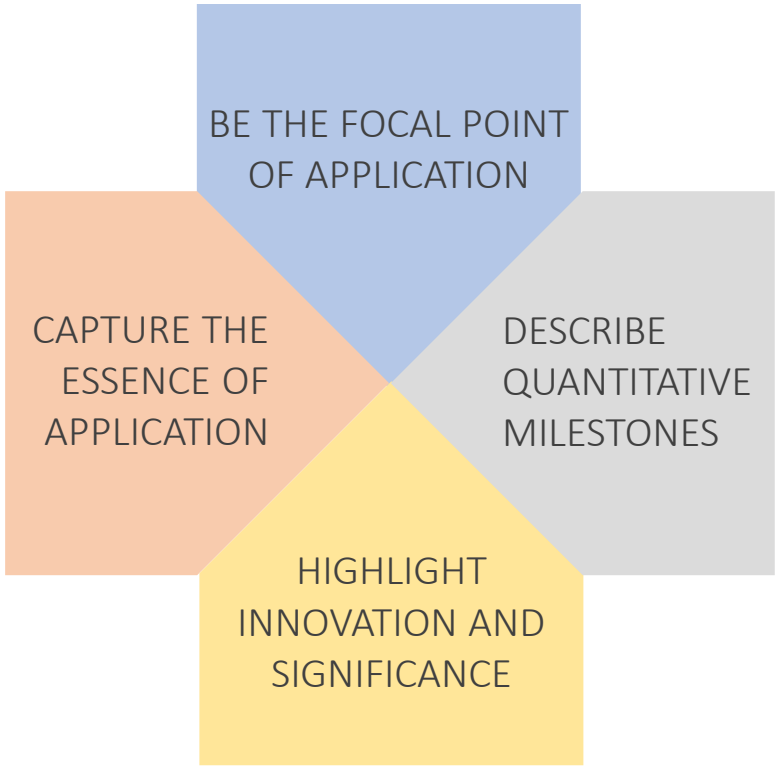
SBIR/STTR GRANT

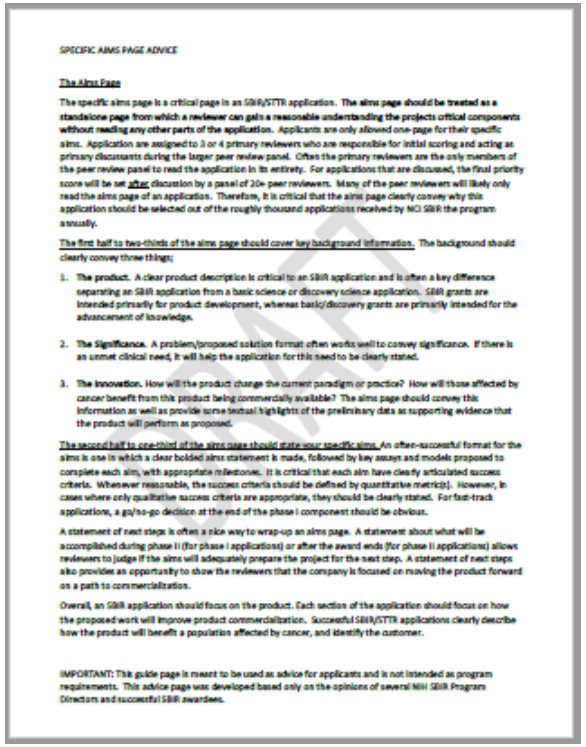


WHY IS SPECIFIC AIMS PAGE IMPORTANT?

- **Focal point of the application : First impression matters**
- **Single Page to Persuade Reviewers and Program about the importance of your technology**
- **Serves as a guide to the rest of the application**
- **Look at some sample applications.**
  https://www.niaid.nih.gov/grants-contracts/sample-applications#r43r44

THE SPECIFIC AIMS PAGE





SPECIFIC AIMS PAGE ADVICE

The Aims Page

The specific aims page is a critical page in an SBIR/STTR application. **The aims page should be treated as a standalone page from which a reviewer can gain a reasonable understanding the projects critical components without reading any other parts of the application.** Applicants are only allowed one-page for their specific aims. Application are assigned to 3 or 4 primary reviewers who are responsible for initial scoring and acting as primary discussants during the larger peer review panel. Often the primary reviewers are the only members of the peer review panel to read the application in its entirety. For applications that are discussed, the final priority score will be set after discussion by a panel of 20+ peer reviewers. Many of the peer reviewers will likely only read the aims page of an application. Therefore, it is critical that the aims page clearly convey why this application should be selected out of the roughly thousand applications received by NCI SBIR the program annually.

The first half to two-thirds of the aims page should cover key background information. The background should clearly convey three things;

1. **The product.** A clear product description is critical to an SBIR application and is often a key difference separating an SBIR application from a basic science or discovery science application. SBIR grants are intended primarily for product development, whereas basic/discovery grants are primarily intended for the advancement of knowledge.

2. **The Significance.** A problem/proposed solution format often works well to convey significance. If there is an unmet clinical need, it will help the application for this need to be clearly stated.

3. **The Innovation.** How will the product change the current paradigm or practice? How will those affected by cancer benefit from this product being commercially available? The aims page should convey this information as well as provide some textual highlights of the preliminary data as supporting evidence that the product will perform as proposed.

The second half to one-third of the aims page should state your specific aims. An often-successful format for the aims is one in which a clear bolded aims statement is made, followed by key assays and models proposed to complete each aim, with appropriate milestones. It is critical that each aim have clearly articulated success criteria. Whenever reasonable, the success criteria should be defined by quantitative metric(s). However, in cases where only qualitative success criteria are appropriate, they should be clearly stated. For fast-track applications, a go/no-go decision at the end of the phase I component should be obvious.

A statement of next steps is often a nice way to wrap-up an aims page. A statement about what will be accomplished during phase II (for phase I applications) or after the award ends (for phase II applications) allows reviewers to judge if the aims will adequately prepare the project for the next step. A statement of next steps also provides an opportunity to show the reviewers that the company is focused on moving the product forward on a path to commercialization.

Overall, an SBIR application should focus on the product. Each section of the application should focus on how the proposed work will improve product commercialization. Successful SBIR/STTR applications clearly describe how the product will benefit a population affected by cancer, and identify the customer.

IMPORTANT: This guide page is meant to be used as advice for applicants and is not intended as program requirements. This advice page was developed based only on the opinions of several NIH SBIR Program Directors and successful SBIR awardees.

BACKGROUND:
Product
Innovation
Significance

AIMS:
Goals-based statements
Key assays and models
Quantitative milestones

CONTEXT:
These studies will get us to…
Next we will…
This data will be used for…

EXAMPLE PAGE

SIGNIFICANCE & UNMET NEED →

PRODUCT & INNOVATION →

AIMS →

SPECIFIC AIMS

HIV infection remains a major public health crisis both in the United States and worldwide. There is increasing awareness that acutely infected individuals disproportionately contribute to disease spread (1). Yet these individuals remain the most difficult to identify, as infectivity is highest prior to the appearance of the HIV antibodies that serve as the basis for serological diagnostics (2). There are currently no FDA-approved point-of-care (POC) tests that are sensitive to acutely infected individuals. An HIV-1/2 antigen/antibody (Ag/Ab) combination assay – the so-called "4th generation" immunoassay – in an inexpensive, simple to use, POC format would fundamentally improve HIV-1/2 screening efforts in the United States and worldwide (3, 4).

MBio Diagnostics, Inc. is developing a point-of-care infectious disease testing platform for multiplexed HIV and coinfection serodiagnostic screening. Prototype devices have been placed in field sites in San Diego, Mozambique, Kenya, and Brazil. Due to cost and labor constraints, current acute infection diagnosis is typically based on pooled sample nucleic acid amplification testing algorithms, with 7 to 14 day turnaround times. 4th gen Ag/Ab assays in the clinical laboratory have been approved recently (Abbott ARCHITECT HIV Ag/Ab combo, Bio-Rad GS HIV 1/2 Ag/Ab Combo), but the 4th gen clinical analyzers do not offer the improved linkage to care associated with rapid, POC HIV testing. Here we propose an inexpensive device that delivers the performance of lab-based 4th gen Ag/Ab combo assays in a simple, POC package. We build on successes of our Phase I SBIR program and propose continuation of our translational research on a novel system with high commercial potential, offering:

- Parallel HIV-1/2 antibody and p24 antigen detection on a single point-of-care platform.
- Workflow and ease-of-use comparable to conventional HIV rapid tests.
- Robust, low cost, minimally instrumented system for use in emergency departments, public health labs, STD clinics, and targeted outreach programs.

Aim 1: Assay Development. Combine the Phase I p24 antigen detection assay with the MBio multiplexed serology assay cartridge, addressing issues of final monoclonal antibody (mAb) pair selection, HIV-1 Ag and HIV-2 Ag selection, reagent conjugations, cross-reactivity, and minimization of assay steps and complexity. The Aim 1 milestone is an HIV-1/2 antigen/antibody detection assay with performance equivalent to FDA-approved laboratory 4th gen Ag/Ab combo assays for the MBio early/acute sample collection [a set of 5 commercially available HIV-1 seroconversion/performance panels, two anti-HIV-1/2 combo performance panels, an anti-HIV-2 performance panel, and a unique collection of acute samples from San Diego.]

Aim 2: Cartridge Integration. Modify the MBio Cartridge, Rack, Reader, and Software to deliver an automated HIV-1/2 Ag/Ab combo result, and incorporate heat stable assay reagents into the MQ cartridge. The Aim 2 milestone is a portable, integrated system delivered to clinical collaborators that meets FDA CLIA waiver guidance requirements.

Aim 3: Assay Validation. Validate system using well characterized early HIV infection specimens including a panel of 200 HIV positive specimens comprised of 20 acute infection samples (RNA+ / Ab -), early seroconversion (Western Blot indeterminate) and seropositive (HIV-1 and HIV-2) samples. 200 HIV-negative samples will be used for specificity testing. The Aim 3 milestone is a dataset demonstrating performance equivalent to FDA-approved laboratory 4th gen HIV-1/2 Ag/Ab assays.

Aim 4: Pre-Market Field Evaluation. Place systems in intended use setting and capture operational and usability feedback in advance of design lock; and generate a preliminary dataset on capillary whole blood samples from 100 study participants in San Diego. The Aim 3 and 4 milestone is a system design and dataset for an FDA investigational device exemption (IDE) meeting in advance of clinical trials.

The assembled group of investigators is uniquely capable of executing this project in a timely and cost

EXAMPLE PAGE WITH QUANTITATIVE MILESTONES

Aim 1. Complete development of an optimized HIV incidence rapid test based on the rIDR-M antigen or synthetic peptides derived from it.

a. Optimization of antibody capture format, colorimetric detection system, dissociation conditions, interpretation criteria, test strip format and housing to yield <2% false recency compared to LAg ELISA;

b. Preparation and validation of plasma controls (incident, prevalent, negative) using dried tube specimens [2] or lyophilization. Validation will involve comparison with standard controls' ability to detect introduced error. Correlation of ≥95% will signal success.

c. Simultaneous preparation of instructions for use, interpretation spreadsheet and training package, including photographs or video of test method process and interpretation;

d. Design of cassette, transfer to manufacturing and manufacture of pilot lots of the rapid test for laboratory and field evaluations.

e. Field testing of device and peripherals for accuracy, ease of use, reproducibility, and clarity of interpretation; data review and analysis; modifications as required. Four resource-limited sites from among CDC sites in Malawi, Botswana and Kenya and MHRP sites in Nigeria, Tanzania, and Thailand will test 200 sequential unlinked samples each in parallel with LAg ELISA or their current population surveillance method. The goal will be ≥98% correlation. Discrepants will be investigated to the extent possible, and appropriate modifications made to the assay.

Aim 2. Validate the final-format HIV incidence rapid test performance using plasma panels with closely estimated HIV infection dates and other relevant sample sets from DOD, CDC, CEPHIA, Blood Systems Research Institute and SeraCare.

a. Analysis of sensitivity and specificity of antibody detection and discrimination of recent vs. long-term infections across multiple subtypes with seroconversion series and other repository samples from known long-term infections, elite controllers, and ART-treated and non-treated individuals with a goal of ≤ 2% false recency;

b. Evaluation of a rapid plasma separation device [17] to allow population surveillance with whole blood samples when necessary: comparison of fresh plasma samples (incident and prevalent) from spun whole blood and membrane-separated whole blood will be performed at Blood Systems Research Institute with a goal of ≥98% correlation between specimen types.

Dos & DON'T's

DO

- Write product driven /technology driven objectives than traditional hypothesis driven research
- Keep the aims scientific
- Provide Alternative strategies
- Remember there is only one page
- **Contact Program**

DON'T

- Propose aims that cannot be achieved in the time & budget specified
- Don't rush through your specific aims page
- Do not make claims that are not backed by data
- Do not use jargon or acronyms

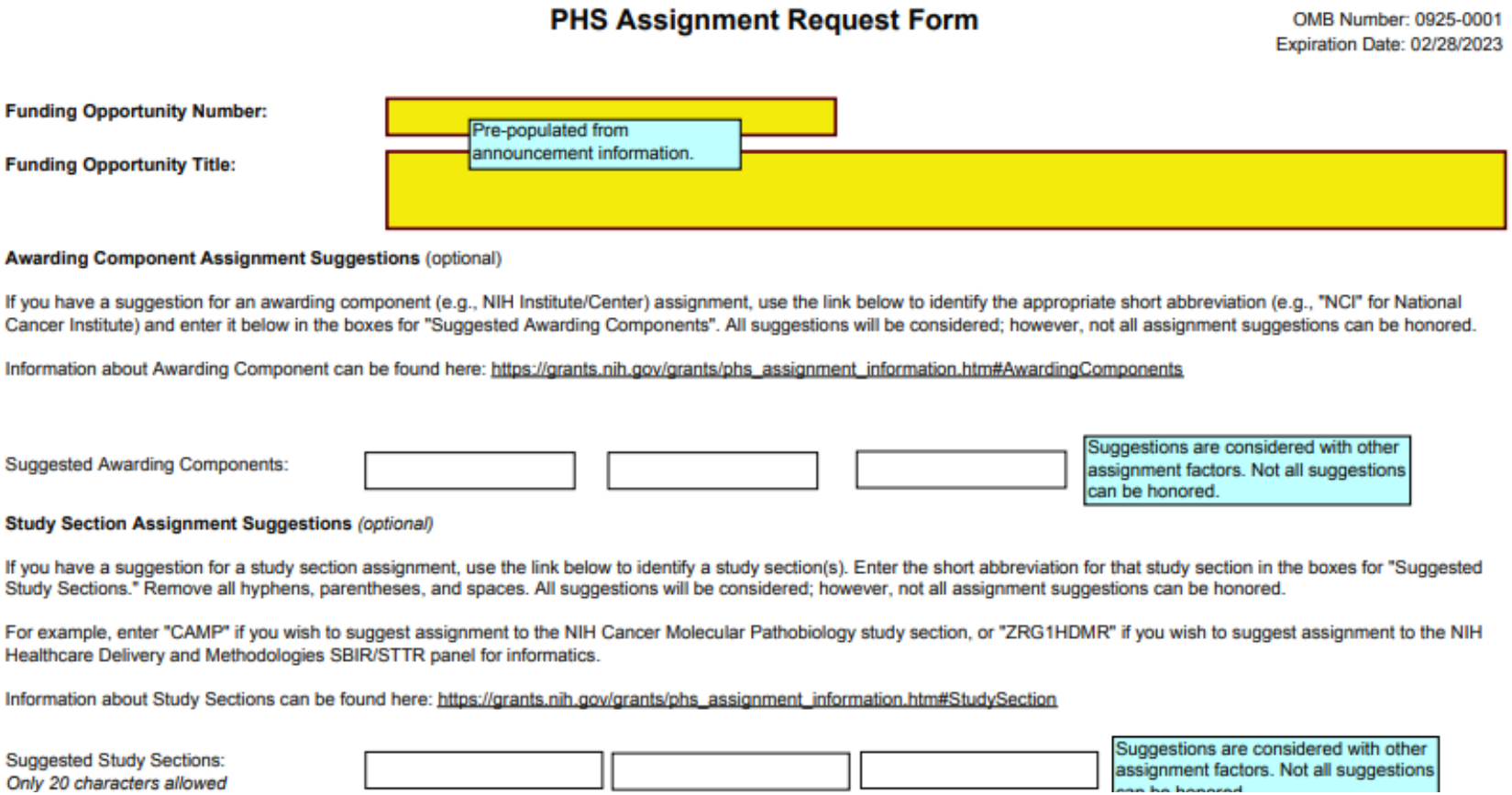
IMPORTANCE OF ABSTRACT & TITLE

PI: **Garrett, Patricia**	Title: Rapid Test for Recent HIV Infection	
Received: 09/09/2013	FOA: PA10-123	Council: 01/2014
Competition ID: ADOBE-FORMS-B1	FOA Title: NIAID ADVANCED TECHNOLOGY SBIR (NIAID-AT-SBIR [R43/R44]	
2 R44 AI098567-03	Dual:	Accession Number: 3620271
IPF: 2755701	Organization: IMMUNETICS, INC.	

To accurately monitor the HIV epidemic with respect to the rate of new infections, and to determine optimal interventions to prevent further transmission, a test that can identify recent infections is essential. Currently, such HIV incidence tests are few, mostly suboptimal in performance, and require a sophisticated laboratory to perform. We propose to develop the first rapid HIV incidence test than can be used in field conditions, without a laboratory, and will deliver results as or more accurate than the best laboratory tests now available. This test will put a powerful tool for identification of new HIV infections at the disposal of individuals and organizations responsible for monitoring and managing HIV prevention in the field.

Monitoring the HIV epidemic to understand rates and patterns of growth, as well as targeting intervention efforts to populations exhibiting high rates of HIV transmission, are wholly dependent on determining the frequency of new infections using an assay that discriminates recent from long-term HIV infection. However, very few HIV assays have been developed specifically to distinguish incidence from prevalence. An added barrier has been the lack of an incidence assay for field work and resource-poor settings. Most HIV serologic assays are aimed at diagnostic use, while RNA assays have been used largely to determine viral load for clinical management purposes. Furthermore, HIV incidence testing currently requires access to well-equipped centralized laboratories capable of running the few sophisticated assays available for this purpose; these have been ELISAs requiring microplate handling and reading instrumentation, including the BED ELISA and the Vironostika detuned ELISA. Dependence on a central laboratory also implies the requirement for a system to transport serum specimens from where they have been collected to the laboratory, a separate and acute logistical challenge.

SELECTING IC/ REVIEW SECTION



PHS Assignment Request Form

OMB Number: 0925-0001
Expiration Date: 02/28/2023

Funding Opportunity Number:

Funding Opportunity Title:

Pre-populated from announcement information.

Awarding Component Assignment Suggestions (optional)

If you have a suggestion for an awarding component (e.g., NIH Institute/Center) assignment, use the link below to identify the appropriate short abbreviation (e.g., "NCI" for National Cancer Institute) and enter it below in the boxes for "Suggested Awarding Components". All suggestions will be considered; however, not all assignment suggestions can be honored.

Information about Awarding Component can be found here: https://grants.nih.gov/grants/phs_assignment_information.htm#AwardingComponents

Suggested Awarding Components:

Suggestions are considered with other assignment factors. Not all suggestions can be honored.

Study Section Assignment Suggestions *(optional)*

If you have a suggestion for a study section assignment, use the link below to identify a study section(s). Enter the short abbreviation for that study section in the boxes for "Suggested Study Sections." Remove all hyphens, parentheses, and spaces. All suggestions will be considered; however, not all assignment suggestions can be honored.

For example, enter "CAMP" if you wish to suggest assignment to the NIH Cancer Molecular Pathobiology study section, or "ZRG1HDMR" if you wish to suggest assignment to the NIH Healthcare Delivery and Methodologies SBIR/STTR panel for informatics.

Information about Study Sections can be found here: https://grants.nih.gov/grants/phs_assignment_information.htm#StudySection

Suggested Study Sections:
Only 20 characters allowed

Suggestions are considered with other assignment factors. Not all suggestions

SF424 Forms F (Lastest Version):
https://grants.nih.gov/grants/ElectronicReceipt/files/Annotated_Forms_SmallBus_FORMS-F.pdf

SELECTING IC/ REVIEW SECTION

PHS Assignment Request Form

List individuals who should not review your application and why *(optional)*

Entry is limited to 1000 characters.

Provide sufficient information (e.g., name organization affiliation) to correctly identify each individual. Provide specific reason why an individual should not review your application. Information will be considered, but listing an individual does not guarantee they will not be on review panel.

Identify scientific areas of expertise needed to review your application *(optional)*

Note: Do not provide names of individuals

	1	2	3	4	5
Expertise: *Each entry is limited to 40 characters*					

Limit your answers to expertise. DO NOT enter the names of individuals you'd like to review your application.

UNDERSTAND PEER REVIEW PROCESS

- Application is submitted to NIH (not the institute)
- Study section assigned is in Commons at least 30 days before review.
  - Finding the appropriate Study Section: https://public.csr.nih.gov/StudySections/SmallBusinessAndTechnologyTransfer
  - Use G.600-PHS Assignment Request Form, to request Study section, suggested review expertise, conflicted reviewers with rationale.
- Get Review Experience

UNDERSTAND PEER REVIEW PROCESS

INVESTIGATOR

Are the investigators, collaborators and consultants appropriately trained and **capable** of completing all project tasks?

SIGNIFICANCE

Does the product address an important **problem**, and have commercial potential? Is there a market pull for the product?

ENVIRONMENT

Does the **scientific environment** contribute to the probability of success? **Facilities**? Independence?

APPROACH

Are **design and methods** well-developed and appropriate? Are problem areas addressed? Are potential pitfalls and alternative approaches provided?

COMMERCIALIZATION

Is the company's **business strategy** one that has a high potential for success?

INNOVATION

How novel is the **technology/product** and **approaches** proposed to test feasibility?

KNOW THE APPLICATION COMPONENTS

RESEARCH STRATEGY

- Provide background information
- Preliminary data not required (Phase I), but needed to be competitive
- Provide detailed technical plan to achieve the Specific Aims
  - Expand on quantitative milestones & success criteria
  - Describe potential pitfalls and alternative angles of attack
- Propose a project scope within the budget and time constraints
  - Timeline/GANTT chart is a good idea

OTHER APPLICATION COMPONENTS

BIOSKETCHES	Bio-sketches for all senior/key personnel (<4 pages each)
FACILITIES	Provide description of facilities and equipment relevant to this grant.
BUDGET	Provide budgets for each project period & sub-contractors.
TITLE/ABSTRACT	CSR uses this to assign IC and Study section.
HUMAN/ANIMAL STUDIES	Complete VAS or Human Subjects section Check if you have an NIH defined clinical trial.
COMMERCIALIZATION PLAN	Important Element of Phase II; Program views it seriously.
LETTERS OF SUPPORT	Necessary from consultants and collaborators Helpful endorsements from clinicians, end-users, investors.

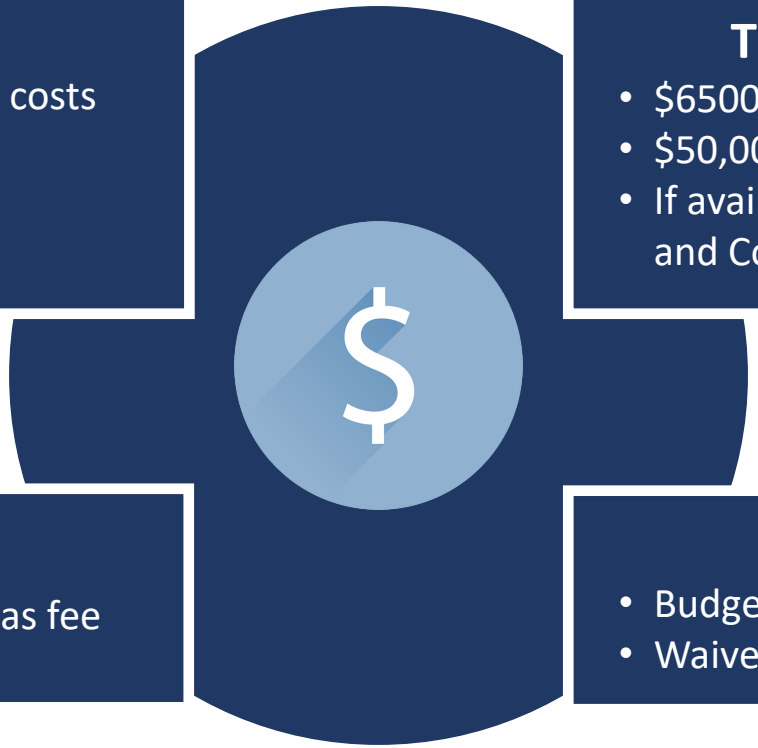
BUDGET SPECIFICS

TOTAL COSTS

- SBIR Budgets are defined by total costs
- Subcontracting is limited
- Know what you can or cannot subcontract

TECHNICAL ASSISTANCE

- $6500 for Phase I
- $50,000 for Phase II
- If availed, cannot participate in Needs and Consultant TABA



FEES

- Companies can request up to 7% as fee

CHECK IC LIMITS

- Budgets vary by IC
- Waiver for technology specific areas

RESUBMISSION: HOW TO RESUBMIT

INTRODUCTION

Here we provide an overview of revisions included in this grant resubmission. According the Summary Statement for the original submission, "there was significant enthusiasm for this Phase II application." Cited strengths included the success of Phase I studies, promising preliminary data, and the significance of point-of-care (POC) technology. Cited weaknesses were minor. Here we attempt to address all weaknesses in order of appearance in the Summary Statement. Reviewer comments are in bold, followed by the MBio response. Italic items highlight where edits have been made to the Research Strategy.

Not as sensitive as PCR. PCR is definitely more sensitive than antigen-based approaches, including the approach outlined here. We believe, however, that the cost and ease-of-use advantages of immunoassays will continue to result in high impact diagnostic tests, particularly at the point-of-care in limited resource settings. Very low cost POC PCR is still years away (in our opinion). *Cost and ease-of-use are addressed more clearly in the Significance section.*

Uses serum or whole blood not saliva which may be more difficult. Finger stick whole blood is widely accepted worldwide and will be necessary for the antigen detection part of the proposed assay. Oral fluid is very convenient, but antigen detection in saliva is not likely to meet analytical sensitivity requirements.

Clinical assays are available to detect HIV-1 antibody/antigens. Clinical lab assays indeed exist (e.g., Abbott and Bio-Rad). But high quality POC antigen/antibody combination assays have still not been well established. Published data for the antigen detection component of the Alere Determine® HIV-1 Ag/Ab Combo assay (e.g., recent posters from CROI 2013, Atlanta) show significant opportunity for improvement, particularly in the context of acute infection detection.

POC kits based on nucleic acid based testing for early HIV infection may be a more appropriate technology. Nucleic acid tests perhaps pose the greatest commercial threat to the proposed antigen-based system. As discussed above however, we believe the cost advantages and ease-of-use of immunoassay approaches will keep antigen detection very competitive in cost-driven applications such HIV screening in global markets. *Cost and ease-of-use are addressed more clearly in the Significance section.*

No details are given for VDSA (trade secret). A detailed description of the viral disruption formulation is not critical for the scientific review of this proposal. As the reviewer correctly notes, viral disruption and immune complex disruption have "standard" elements, and the details of the formulation are not at the core

RESUBMISSION: HOW TO RESUBMIT

[Edits to the original submission are included in bold brackets in this resubmission]

SIGNIFICANCE

HIV/AIDS remains a critical public health crisis in the United States and worldwide:

- CDC estimates there are 1.2 million Americans with HIV, and 1 in 5 do not know their disease status (1).
- Because the early/acute phase of infection is marked by very high titers of active viral particles (>3E05 particles/mL), infectivity is significantly higher for individuals during the early/acute phase of infection compared to those with chronic HIV infection and a mature antibody response.
- New guidelines from CDC for laboratory testing of HIV infection recommend initial screening with a sensitive, "4th generation" antigen/antibody combination assay (2).
- The global impact of HIV/AIDS remains enormous, with approximately 2.7 million new infections per year, 2 million AIDS-related deaths, and ~33 million people living with HIV (3).

Effective ELISA tests for the HIV-1 p24 antigen have been available for some time, but are not approved for human diagnostics. Importantly, the ELISA protocol includes pre-treatment to break antigen-antibody (Ag-Ab) complex, long incubations, various wash protocols, and added cost that make this test format incompatible with sensitive POC testing. The system proposed here avoids the Ag-Ab complex issue by reporting parallel Ag and Ab results. Other sensitive p24 assays have appeared in the literature recently (11), including POC devices with clinically relevant sensitivities and workflow (12, 13). The POC systems are promising, but they require multiple steps and, because they are built on lateral flow technology, those systems will not have the multiplexing capabilities of the system described in this proposal.

[While PCR and lab-based methods provide outstanding sensitivity, they will be limited in impact in high disease burden, resource-limited settings where cost and ease-of-use are major drivers. The system proposed here addresses a major unmet public health screening need.]

KEYS TO A STRONG SBIR APPLICATION

CONTACT SBIR PROGRAM BEFORE APPLYING

✓	Innovative Product Focused Science
✓	Demonstrated Clinical/Market Need & Commercial Potential
✓	Understanding the Review Criteria
✓	Projects Should Involve Appropriate Collaborators
✓	Well Written Specific Aims Page with Quantitative Milestones
✓	Review Sample Applications & other Funded Projects
✓	Submit Early

GET IN TOUCH WITH US!

- Keep in touch with your PD
  - Reach out to PDs at Conferences
  - Outreach Activities in your area
  - If you are in DC – stop by!
- Share success stories with us
  - Key Milestones
  - Fundraising Activities
- Web: https://sbir.cancer.gov
  Email: ncisbir@mail.nih.gov
  Twitter: @NCISBIR
  LinkedIn: http://bit.ly/ncisbirlinkedin

SBIR
DEVELOPMENT CENTER

THANK YOU

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