Office of Biomedical Advanced Research and Development Authority (BARDA) Division of Research, Innovation & Ventures (DRIVe)

Special Instructions 018 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-20-100-SOL-0002

The purpose of these Special Instructions is the following:

1) Revise the descriptions of the following Areas of Interest (AOIs):

   AOI #8: Bringing Laboratory Testing to the Home
   AOI #9: Digital Health Tools for Pandemic Preparedness
   AOI #11a: Home-based, Over-the-Counter Diagnostics for the Detection of SARS-CoV-2
   AOI #11b: Enabling Technologies to Support Home-Based Diagnostics for SARS-CoV-2 Acute Infection

2) Add **AOI #13:** Endotyping for Host-Directed Therapeutics to the EZ-BAA.

3) Update the closing dates for abstract submissions for multiple AOIs.

I. INTRODUCTION AND OVERVIEW INFORMATION

A. Development Opportunity Objective:

Under these Special Instructions, DRIVe is doing the following:

1) Revising the descriptions of the following AOIs:

   AOI #8: Bringing Laboratory Testing to the Home
   AOI #9: Digital Health Tools for Pandemic Preparedness
   AOI #11a: Home-based, Over-the-Counter Diagnostics for the Detection of SARS-CoV-2
   AOI #11b: Enabling Technologies to Support Home-Based Diagnostics for SARS-CoV-2 Acute Infection

2) Adding **AOI #13:** Endotyping for Host-Directed Therapeutics to the EZ-BAA.
3) Updating the closing dates for multiple AOIs

Under these revised and new AOIs, we are seeking abstract submissions for the following:

AOI #8: Bringing Laboratory Testing to the Home

DRIVe is seeking platform technologies for on-demand, at-home detection of biochemical health markers, with a preference for multiplexed biochemical assays. The goal is to rapidly obtain quantitative information about patients' health status in a CLIA-waived environment without going through traditional central laboratory testing, which can be cumbersome, time-consuming, and lead to delays in receiving care. Such platforms could enhance the capabilities of telemedicine by enabling data-driven diagnosis by physicians without requiring sample shipping or travel to a sample collection site. By enabling such testing, chronic disease management, clinical trial management, etc. could potentially be greatly enhanced, leading to a healthier population with reduced healthcare costs.

While DRIVe does not specify a particular platform form factor or sensing modality, and will consider both desktop (portable) and wearable platforms, a successful platform will provide single time point quantitative measurements comparable to a central laboratory. The goal of projects funded through this AOI is detection and quantification of at least four different biochemical markers in a multiplexed manner. Respondents should address the following in their Abstract submissions:

- The scientific premise for interrogating a specific set of biomarkers using the proposed sample and method, and the clinical relevancy of those biomarkers.
- A comparison between the proposed solution and the laboratory standard in function and clinical value, including how the novel technology is intended to replicate the central laboratory function and/or outcome.
- A plan for assay validation, including how data collected during the project will be compared to a laboratory standard.
- The desired limit of detection and accuracy of the proposed sensing modality.
- A plan to detect at least four biochemical markers from a clinical sample in a multiplex assay.
- Relevant preliminary data.

Examples of desired use cases include detection of host biochemical markers relevant to infectious diseases, rapid results of critical cardiac functions, complete blood counts, and wellness testing. Biochemical markers of interest include, but are not limited to, host lipids, proteins, nucleic acids, and small molecules (examples include bilirubin, creatinine, CRP, uric acid, triglycerides, glucose, hemoglobin, iron, calcium, potassium, IP-10, TRAIL, cortisol, etc.).

If specific interest lies with informing on infection severity, Respondents may want to review AOI #2 Infection Severity and Solving Sepsis which addresses late-stage development, clinical validation, and de-risking regulatory path activities.

Responsiveness Criteria:

- Novel platform technologies must provide quantitative biomarker data/detection of biomarkers when used by untrained personnel in the home or other CLIA-waived environment. Both desktop/portable and wearable form factors will be considered. Among wearable form factors, microneedle patches, smart tattoos, and other innovations are particularly desired.
- The proposed platform technology should produce quantitative test results and be readily adaptable to a broad menu of test panels to cover a wide range of disease states as well as standard health assessments.
- Technologies do not need to interpret or analyze the quantitative output of biomarkers for diagnostic purposes and to inform on care.
- Sample specimens should preferably be collected non-invasively at home by an untrained individual 18 years of age or older. Acceptable samples include saliva, urine, sweat, breath, nasal swabs, or minimally invasive samples such as finger stick blood or interstitial fluid. However, analytes measured from novel sample types should demonstrate comparability to values from venous blood samples.
- The entire testing process including sample collection, sample application to test, and test readout should preferably take no more than 2 hours. The test must be designed to be performed in the home by untrained personnel 18 years of age or older.
- Any visual readouts confirming proper use of the system should be easy to interpret by lay individuals.
- The analytical performance of the test should be commensurate with up-to-date regulatory and public health guidance.

Other Characteristics:

- The system may include a smartphone, mobile device, portable desktop device, or instrument for collection and transfer of data to a medical care provider, however, projects focusing chiefly on data transfer mechanisms will not be prioritized.
- The collection and transfer of data by the device or a mobile device should follow accepted data standards to allow connectivity with medical professionals, as well as comply with current privacy laws and guidelines.
- Plans for product commercialization, including a regulatory pathway, are desired but not required.
- Priority will be given to platforms being developed in the United States.

Out of Scope Topics:

- Platform technologies that directly detect pathogens.
- Technologies requiring venous blood draws or other invasive samples.
- Platforms not providing single time point measurements.
- Abstract submissions combining at-home sample collection with testing at another location.
- Abstract submissions focusing on clinical validation or clinical utility of existing technologies, infection severity/sepsis, or interpretation of quantitative biochemical results for diagnostic or triage purposes are not responsive. If applicable, Respondents may instead consider AOI #2 Infection Severity and Solving Sepsis.

NOTE: All awarded Respondents will be required to share any collected, de-identified data during the performance of their project in an effort to advance the field and knowledge. Interested Respondents are encouraged to commercialize their technology and algorithms, but data collected through the use of Government funding will be made available through full Government purpose rights.

AOI #9: Digital Health Tools for Pandemic Preparedness

DRIVe is interested in supporting the development of novel digital health tools that can be the first line of defense and augment existing medical countermeasures in the event of a future infectious disease epidemic or pandemic. Digital health tools may include smartphone/web applications, data analytics approaches (AI/ML-based or other approaches), or novel data sources (e.g., social network, telehealth, diagnostic testing, vaccination, or environmental data). These tools are intended to provide broadly available nowcasting and rapid response solutions, including monitoring the spread of an epidemic or pandemic, illness detection, risk assessment, clinical intervention support, and public health guideline dissemination, among others.

Specifically, DRIVe is seeking innovative, effective, equitable, affordable, easy-to-use, and broadly and rapidly available digital health tools, data sources, and analytics approaches that demonstrably mitigate the immediate effects of a pandemic. Proposed solutions must integrate stringent privacy and data security safeguards. Abstract submissions should incorporate metrics for tool adoption (e.g., surveys that determine users' behavior changes) and must discuss the impact on the pandemic.

Abstract submissions should focus on one or more of the following topics and include relevant data analytics approaches:

Prediction: Demonstrate an assessment of the risk of contracting a pathogen and/or developing the disease, to enable individuals as well as organizations to make appropriate behavior adjustments and recommendations. Abstract submissions could also be for novel mathematical models that provide predictive capabilities, e.g., with respect to viral evolution (validated by historical events), the geographic and demographic pattern of a disease spread, etc.

Detection: Contain solutions that serve as early warning, nowcasting, and epidemiological tools by collecting, accessing, or interpreting population-wide health-related data. Solutions based on novel data sources (e.g., infection case rates, hospitalizations, vaccinations, environmental data) and data mining approaches are preferred.

Prevention and Safeguarding: Focus on innovative digital health solutions for reducing infection rates and improving patient outcomes, including providing a real-world assessment of relevant public health measures, safeguarding vulnerable populations, or augmenting existing medical countermeasures to equitably increase awareness and improve education, outreach, and distribution. Real-world studies of medical countermeasure effectiveness will be considered under this topic.

Other Topics: Any other innovative digital health tools that support pandemic preparedness and align with BARDA's mission of developing medical countermeasures against communicable infectious diseases, with demonstrable and measurable mitigation of the direct effects of an epidemic or pandemic.

Abstract submissions may focus on respiratory pathogens such as SARS-CoV-2 as a test case but should also demonstrate rapid adaptability to other infectious disease pathogens, where appropriate.

Respondents must address in their abstract submission the following characteristics of their solution: innovation, efficacy (contribution to reducing the direct impact of a pandemic), equity, ease of use, adaptability to a new disease, affordability, and broad and rapid availability. Respondents must include appropriate metrics for assessing tool adoption and the impact of the solution. Preliminary data as a proof-of-concept is desirable.

Abstract submissions describing any digital solutions that rely on hardware components beyond a smartphone or computer (e.g., wearable sensors, diagnostic platforms and assays, other medical and remote monitoring devices) for implementation will be considered non-responsive, however, any existing private or public data sources (including social network, telehealth, diagnostic testing, vaccination, and/or environmental data) may be used under appropriate privacy safeguards.

Abstract submissions focusing on the clinical utility of existing technologies, infection severity and sepsis, or interpretation of quantitative biochemical results for diagnostic or triage purposes are not responsive. If applicable, Respondents may instead consider AOI #2 Infection Severity and Solving Sepsis.

AOI #11a: Home-based, Over-the-Counter Diagnostics for the Detection of SARS CoV-2

The development of rapid and affordable home-based diagnostics to detect SARS-CoV-2 acute infection is critical for empowering individuals with actionable information to promote adequate social distancing and isolation, thus preventing pathogen transmission. Critical features of home-based diagnostics for SARS-CoV-2 include low cost, over-the-counter (OTC) availability, high accuracy, ease of use for both the sampling and testing method, and straightforward interpretation of results.

DRIVe is seeking abstract submissions for the development of Emergency Use Authorized (EUA), home-based in-vitro diagnostic assays that can detect SARS-CoV-2 in samples collected in a home setting. These rapid, low-cost, easy-to-use tests must be submitted for FDA EUA for home use within 6 months of contract start. The ideal candidates would be a diagnostic test (antigen detection or molecular) based on an existing FDA cleared platform using existing manufacturing capability that can support the OTC market.

Responsiveness Criteria:

- Ability to rapidly develop and submit for FDA EUA of a home-use acute infection test within 6 months after contract award
- The test should use specimens that can be effectively and efficiently collected at home by an untrained non-medical person, preferably 18 years of age or older.
- Acceptable samples include lower nasal swabs, mid-turbinate nasal swabs, oral swabs, saliva, breath, and nasopharyngeal wash.
- Serology based Abstract submissions and use of moderately invasive sample types (nasopharyngeal and oropharyngeal swabs, nasopharyngeal aspirate, bronchoalveolar lavage, tracheal aspirate, sputum, blood) will be considered non-responsive.
- Test should demonstrate storage stability at room temperature and humidity for 1 year or more.
- Diagnostic tests with a market price point similar to glucose test strips, including amortized reader if required, will be given priority.
- Acceptable test formats include but are not limited to lateral flow and cartridge-based technologies. The assay system may include (but does not require) a read-out instrument. If one is utilized and requires purchase of a new device by the user, its amortized market price will be included in the market price per test for purposes of evaluation.
- The entire test process – sample collection, sample application to the test, test readout – must all be performed in the home by untrained persons.
- Tests that require samples to be collected at home and shipped for testing will be deemed non-responsive.
- Sample to answer time should be less than 30 minutes.
- The minimum technology readiness level (TRL) for this assay is 4. Refer to Appendix 1 for a definition of TRLs.
- Analytical performance, including but not limited to LOD, inclusivity, cross reactivity, interference, should be commensurate with up to date regulatory and Public Health guidance.
- Funded projects will be expected to submit an application for FDA EUA OTC home testing within 6 months of contract award.
- Technologies that support future multiplex of multiple analyte tests are preferred.
- Priority will be given to products manufactured in the United States.

AOI #11b: Enabling Technologies to Support Home-Based Diagnostics for SARS-CoV-2 Acute Infection

The standard pathogen testing paradigm involves samples to be run in centralized laboratories, requires many steps, and has supply chain and logistical constraints. A push to a decentralized testing model is necessary to provide patients and users with actionable health information when symptoms first occur so that they can self-isolate and seek medical care. Reducing the barrier to testing is critical to suppressing the pandemic curve. Innovation is greatly needed to help enable more wide-spread decentralized testing, namely inside the home. DRIVe is seeking abstract submissions for (1) technologies that can enable more wide-spread adoption of at-home testing, and (2) improvements on current technological limitations of diagnostic sensitivity/specificity and performance.

Desirable characteristics of enabling technologies include, but are not limited to:

- Simple sample collection and processing that maximizes viral recovery and minimizes dilution effects.
- Translation of laboratory detection methods to systems designed for non-expert users.
- Assay reagents, formats/designs, and detection modalities that can provide superior limits of detection (e.g., on the order of 10^2 cp/ml), sensitivity and specificity, with shorter time to result and simplified workflow, compared to currently available systems.
- Novel use of communication technology to assist in assay interpretation and HIPAA compliant transmission of results to medical and non-medical authorized personnel.
- Abstract submissions leveraging small, easy to use devices are sought. Abstract submissions seeking incremental size and energy use reductions to existing benchtop laboratory equipment will be deemed non-responsive.
- Capitalization of novel materials and high-volume manufacturing processes adapted for assay platforms is desirable.

NOTE: The technology readiness level (TRL) for adapting existing approved assays is 4 and for novel platforms 3. Please refer to Appendix 1 for a definition of TRLs.

AOI #13: Endotyping for Host-Directed Therapeutics

Severe outcomes from infectious diseases are often rooted in the host response to the pathogen, and pathogen–targeted mitigation efforts (e.g. antivirals, antibiotics) may not sufficiently restore homeostasis and improve clinical outcomes. There are currently no approved host-directed therapeutics for the treatment of severe infections that lead to multi-organ dysfunction (sepsis) or acute respiratory distress syndrome (ARDS). And such approaches are necessary for improving the myriad of severe clinical outcomes that can occur for infectious disease. Although there has been some success from promising candidates in early clinical evaluation, no Phase 3 clinical studies have succeeded in improving clinical outcomes for infections that progress to severe states of disease. Clinical trials traditionally focus on a specific indication related to the pathogen, i.e COVID-19, flu, or bacterial pneumonia, versus targeting common clinical pathophysiology across multiple indications/primary diagnosis. However, review of some clinical trials for sepsis or ARDS suggest there may be evidence for common clinical characteristics or underlying biomarkers that could be used to sub-type patients most likely to benefit from a particular therapeutic. DRIVe is interested in further de-risking the development of host-directed therapeutics by validating targeted enrollment strategies based on individual patient characteristics, including immune profiling, biomarker analysis, or other methods of patient stratification (i.e, Endotyping for Host-Directed Therapeutics). Ultimately the goal is to increase the likelihood of meeting therapeutic efficacy endpoints by evaluating the drug specifically in the sub-population for which that therapeutic will most benefit.

This AOI is intended to support clinical development of host-directed therapeutics for infectious disease while simultaneously validating a means to sub-type patients that will benefit from the therapeutic in development. The mechanism to stratify patients should previously have been identified within a specific disease clinical phenotype (e.g., sepsis, ARDS, AKI, endotheliopathies) or across multiple etiologies (e.g. flu, COVID-19, pneumococcus) with a common clinical profile (e.g. lung dysfunction) that are likely to respond to a specific therapeutic. Endotyping for Host-Directed Therapeutics strategies should present scientific rationale to support use of the specific biomarker(s) or clinical characteristic(s) to identify patient populations that may respond to the specific mechanism of action of the therapeutic under development. Therapeutic candidates must have successfully completed a Phase I clinical trial, have an open IND with the FDA and have

data to support that a specific sub-type of patients is likely to respond to treatment. In addition, if a companion diagnostic will be necessary to support the stratification approach, then engagements with FDA on the diagnostic should also have occurred. Although the focus of this AOI is on conducting clinical trials to show improved clinical efficacy of therapeutic candidates through Endotyping for Host-Directed Therapeutics approaches, abstract submissions that focus primarily on the advancement of a specific companion diagnostic, device or assay needed to rapidly obtain patient data to stratify patients will also be considered, as long as the clinical data is from a therapeutic candidate already in advanced development (Phase 2/3 efficacy trial).

Abstract submissions should consider the following:

- Include a clear and feasible strategy for identifying eligible patients for the therapeutic clinical study based on previously identified biomarker(s), clinical characteristics, or other method of identifying the appropriate sub-population.
- Include a rationale to demonstrate the sub-population identified (i.e. by patient characteristic being used for patient stratification) can benefit from the mechanism of action of the therapeutic under development.
- Provide an intended use statement for the investigational therapeutic candidate including the definition of the sub-population that will be targeted for treatment.
- Include the patient characteristic(s) or biomarker(s) that will identify the appropriate sub-population and a clear strategy for identifying these patients for enrollment in a clinically relevant timeframe.
- Describe any past, current, or planned engagement with FDA for the proposed clinical study of the therapeutic as well as companion diagnostic, if relevant.
- Describe how the proposed scope of work advances development of the host-directed therapeutic and is distinct from previous and/or existing clinical trials of the candidate therapeutic. Note the intent of this topic is to advance stratification approaches that can be utilized to support regulatory path for the therapeutic in development, not just to conduct investigational research of the stratification approach.
- Describe the intended route(s) of administration and dosing regimen of the candidate therapeutic.
- Only technologies focused on host-directed approaches or clinical management approaches will be considered. BARDA has existing programs for pathogen-targeted approaches outside this AOI.
- Research should be considered translational science. Early stage or fundamental research will not be considered at this time. Sponsors should already have submitted an IND to the FDA.
- The investigational drug must be on a clear path to achieving regulatory NDA or BLA for the therapeutic candidate as well as PMA or 510(k) for the companion diagnostic, if relevant, and information on regulatory approach and guidance to date should be provided.
- Abstract submissions should provide evidence of pre-established agreements with proposed partners for relevant clinical studies (e.g. clinical site or partnership with a pre-existing clinical network), GMP manufacturers of product, etc.
- Abstract submissions should include consideration of commercialization strategy outside the work proposed to this announcement. This may include other ongoing relevant research; establishment of partnerships with appropriate manufacturers; addressing the ability to scale, deploy, and distribute the product; intellectual property; and modeling the cost per unit, reimbursement strategy.
- Clinical studies must be equitable in terms of enrollment, including diversity amongst race, ethnicity, and biological sex.

Out of Scope Topics:

- Pathogen targeted products.
- Supportive care technologies that do not specifically improve clinical outcomes for patients.
- Exploratory research with no near-term translational application.
- Exploratory efforts to identify potential biomarkers /clinical characteristics to delineate patient sub-populations (i.e., biomarker discovery efforts).
- No IND established with FDA for therapeutic candidate in development.

B. Eligible Respondents & Scope Parameters:

These Special Instructions are open to all responsible sources as described in the EZ-BAA. Abstract submissions that do not conform to the requirements outlined in the EZ-BAA may be considered non-responsive and will not be reviewed. In particular, an entity must have an active registration with https://sam.gov at the time of submission to be reviewed. If not, the abstract submission will not be reviewed and will be rejected. Please do not attempt to submit an abstract if your registration is not active in https://sam.gov.

IMPORTANT NOTE: Interested vendors are strongly encouraged to request and schedule a market research call before submitting an abstract. This request should include the project title, key project staff, and a brief description of the proposed project. Please submit the requests to the following:

AOI #2: Infection Severity and Solving Sepsis (solvingsepsis@hhs.gov)
AOI #5: ReDirect (chemrepo@hhs.gov)
AOI #8: Bringing Laboratory Testing to the Home (homediagnostics@hhs.gov)
AOI #9: Digital Health Tools for Pandemic Preparedness (digitalhealth@hhs.gov)
AOI #11a: Home-based, Over-the-Counter Diagnostics for the Detection of SARS-CoV-2 (COVID19_homeDx@hhs.gov)
AOI #11b: Enabling Technologies to Support Home-Based Diagnostics for SARS-CoV-2 Acute Infection (COVID19_homeDx@hhs.gov)
AOI #12: Mitigating Long-term Effects (MILE) of Respiratory Distress (HostTx@hhs.gov)
AOI #13: Endotyping for Host-Directed Therapeutics (HostTx@hhs.gov)

The table below indicates the closing dates for abstract submissions for each AOI, unless otherwise extended:

Area of Interest	Closing Date for Abstract Submissions
#5	12:00pm ET on 31 March 2022
#2, #11a, #11b, and #12	12:00pm ET on 29 April 2022
#13	12:00pm ET on 29 July 2022
#8 and #9	12:00pm ET on 03 February 2023

C. Number of Awards:

Multiple awards are anticipated and are dependent upon the program priorities, scientific/technical merit of abstract submissions, how well the abstract submissions fit within the goals of the AOI, and the availability of funding. The program funding is subject to change based on the Government's discretion.

Additionally, awarded contracts expected to be made under the EZ-BAA will be less than $750,000 in total Government funding. Funding is limited, so we encourage any interested vendors to reach out to the respective program as soon as possible before submitting an abstract.

D. Special Instructions Application Process:

These Special Instructions will follow the same submission process and review procedures as those established under the EZ-BAA. For complete details, please read the EZ-BAA in its entirety. DRIVe takes the protection of Respondent information very seriously to ensure that information is safeguarded in full compliance with all applicable regulations and law.

IMPORTANT NOTE: Respondents who are awarded a contract under each of these AOIs will be required to share any collected, de-identified data in an effort to advance the field and knowledge. Interested Respondents are encouraged to commercialize their technology and algorithms but data collected through the use of Government funding will be made available through full Government purpose rights.

Appendix 1: Diagnostics and Medical Devices TRLs adapted from Q-TRLs

TRL Level	**TRL Description** *A product can be described as achieving a TRL only if all relevant activities identified in that TRL have been completed.*
1	**Review of Scientific Knowledge.** Active monitoring of scientific knowledge base to identify clinical pathological markers for diagnostic countermeasure candidates. Scientific findings are reviewed and assessed as a foundation for characterizing approaches to intervene in disease. Basic research needs identified.
2	**Concept Generation and Development of Experimental Designs** Develop research plans to answer specific questions and experimental designs for addressing the related scientific issues and to establish feasibility. Focus on practical applications based on basic principles.
3	**Characterization of Preliminary Candidates(s) and Feasibility Demonstration** Begin R&D, data collection, and analysis in order to verify feasibility. Explore alternative concepts, identify and evaluate critical technologies and components, and begin characterizing specifications required. Demonstrate the performance of candidate diagnostic targets and high risk components. Develop a business case for the proposed product.
4	**Optimization and Preparation for Assay, Component, and Instrument Development** Prepare for test system development. Finalize diagnostic target(s) and methods for detecting or quantitating target(s). Develop detailed plans and finalize critical design requirements. Execute commercial agreements with key external development partners. Identify manufacturing resources, vendor sourcing, and experimental designs
5	**Product Development – Reagents, components, subsystems and modules** Develop reagents and buffers. Build and test non-GLP prototypes of components and subsystems. Code and unit test software. Begin pilot scale manufacturing preparations. Develop protocols for assay and integration testing. Initiate reagent stability testing. Hold pre-IDE meeting with FDA. Initiate Design History file.
6	**System integration & testing** Integrate and test alpha and beta instruments/devices, software and assays, evaluating performance and updating specifications. Implement design improvements to address defects discovered during testing. Produce and evaluate pilot lots of reagents and beta (pilot) instruments. Increase the maturity of software. Prepare for clinical testing. Complete short term stability testing of reagents.
7	**Analytical Verification and Preparation for Clinical Studies** Evaluate assay and integrated diagnostic system performance utilizing contrived, retrospective human and animal samples. Make preparations for clinical evaluation. Begin preparation for full scale production of instruments and assays.
8	**Clinical Studies and/or evaluation with Animal Studies, FDA Clearance or Approval, Finalize GMP manufacturing preparations.** Complete clinical evaluations. Prepare and submit FDA filing. **End of TRL8:** Acquire FDA approval, or clearance.