

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

Special Instructions 014 Issuance for Easy Broad Agency
Announcement (EZ-BAA) BAA-20-100-SOL-0002



The purpose of these Special Instructions is the following:

- 1) Close Area of Interest (AOI) #1 supporting the Early Notification to Act, Control, and Treat (ENACT) program.
- 2) Pause AOI #7 supporting the ImmuneChip+ program until further notice.
- 3) Add AOIs #8 #9, #10, and #11a and #11b to the EZ-BAA:

AOI #8: Bringing Laboratory Testing to the Home

AOI #9: Digital Health Tools for Pandemic Preparedness

AOI #10: Next Generation Sequencing (NGS)-based Agnostic Diagnostic for Respiratory RNA Virus Pathogens

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

I. INTRODUCTION AND OVERVIEW INFORMATION

A. Development Opportunity Objective:

Under these Special Instructions, DRIVe is doing the following:

- 1) Closing Area of Interest (AOI) #1 supporting the Early Notification to Act, Control, and Treat (ENACT) program.
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- 3) Adding AOIs #8, #9, #10, and #11a and #11b to the EZ-BAA (BAA-20-100-SOL-0002):

AOI #8: Bringing Laboratory Testing to the Home

AOI #9: Digital health Tools for Pandemic Preparedness

AOI #10: Next Generation Sequencing (NGS)-based Agnostic Diagnostic for Respiratory RNA Virus Pathogens

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

Under these 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 obtain quantitative information about patients' health status rapidly and in a CLIA-waived environment without going through traditional central laboratory testing, which is cumbersome, time-consuming, and can 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.

Submissions should include a demonstration of the platform technology in detecting **at least four different biochemical markers in a multiplexed assay, utilizing clinical samples**. Biochemical markers of interest include, but are not limited to: host lipids, proteins, nucleic acids, small molecules, such as bilirubin, creatinine, CRP, uric acid, triglycerides, glucose, hemoglobin, Iron, Calcium, Potassium, IP10, TRAIL, cortisol, etc. Submissions should also include a plan for assay validation and comparison to FDA-approved laboratory tests, if available.

Examples of desired use cases include detection of biochemical markers relevant to infectious diseases, rapid results of critical cardiac functions, complete blood counts, wellness testing such as lipids, hormones and metabolics. If specific interest lies with informing on infection severity, you 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 that can provide quantitative biomarker data/detection of biomarkers when used by untrained personnel in the home. The platform technology must be designed for operation in a CLIA-waived environment.
- 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 to inform on care. The purpose of this topic is to make laboratory assays a commodity at-home to facilitate rapid and easy access to additional health data.
- 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 known samples (e.g. venous blood) - preferably measured through a qualified and validated laboratory test or FDA-regulated assay.
- 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.
- Sample preparation should include no more than a single manual step.
- Any visual readouts confirming proper use of the system should be easy to interpret by lay individuals.
- The test cartridges and any ancillary reagents should be shelf-stable for at least six months at 4 deg C and at least 24 hours at room temperature (15 deg C – 30 deg C) and at a relative humidity of 50% - 100%.
- Analytical performance of the test should be commensurate with up-to-date regulatory and public health guidance.
- Priority will be given to products manufactured in the United States.

Other Characteristics:

- Analytical performance of the test should be commensurate with up-to-date regulatory and public health guidance.
- Priority will be given to products manufactured in the United States.
- The system may include a smartphone, mobile device, portable desktop device, or instrument for data collection and transfer to a medical care provider.
- 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.
- While plans for product commercialization, including a regulatory pathway, are desired, they are not required. Note the emphasis of this topic, however, is on technology and assay development, not seeking regulatory approval, unless all can be addressed under a single submission. Projects are not required to interpret any biochemical marker results for diagnostic purposes.

Out-of-Scope Topics:

- Platform technologies that detect pathogens are out of scope for this AOI.

- Technologies requiring blood draws or other invasive samples will not be considered for this AOI.
- Submissions combining at-home sample collection with testing at another location will be considered non-responsive.
- 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. Applicants may consult AOI #2 instead.

AOI #9: Digital Health Tools for Pandemic Preparedness

To prepare for and to accelerate the public health response in the event of a future infectious disease epidemic or pandemic, DRIVE is interested in supporting the development of novel digital technologies that can serve as the first line of defense and augment existing medical countermeasures. Such digital health tools, including smartphone apps, social networks, telehealth, or other web applications, are intended to provide broadly available nowcasting and rapid response solutions, e.g. tools for 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 (data and analytics-based) health tools and applications with stringent privacy and data security safeguards. Submissions for digital solutions should focus on one or more of the following topics and include relevant data analytics approaches:

1. **Prediction:** Submissions should 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.
2. **Detection:** Proposed solutions should serve as early warning, nowcasting, and epidemiological tools by collecting, accessing, and/or interpreting population-wide health data.
3. **Prevention and Safeguarding:** Submissions should 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, and/or augmenting existing medical countermeasures to equitably increase awareness and improve education, outreach, and distribution.
4. **Other Topics:** Any other novel and innovative digital health tools that support pandemic preparedness and align with BARDA's mission of developing medical countermeasures against communicable infectious diseases.

Submissions may focus on respiratory pandemic pathogens such as SARS-CoV-2 as a test case and, if relevant, demonstrate rapid adaptability to other infectious disease pathogens.

Respondents must address in their EZ BAA abstract the following characteristics of their solution: innovation, efficacy, equity, ease of use, adaptability to a new disease, affordability, and broad and rapid availability. Preliminary data as a proof-of-concept is desirable.

Submissions describing any digital solutions that rely on additional hardware components, beyond a smartphone, (for example wearable sensors, diagnostic platforms and assays, other medical and remote monitoring devices, etc.) for implementation will be considered non-

responsive, however, any existing data may be used under appropriate privacy safeguards.

Submissions focusing on the clinical utility of existing technologies, infection severity/sepsis, or interpretation of quantitative biochemical results for diagnostic or triage purposes are not responsive, and Respondents may consult AOI #2 (Solving Sepsis) instead.

AOI #10: NGS-based Agnostic Diagnostic for Respiratory RNA Virus Pathogens

To accelerate the public health response in the event of an epidemic or pandemic, a move from an observational and reactive posture to a more preemptive stance in detecting pathogenic respiratory RNA viruses is warranted. An agnostic test that can detect any and every respiratory RNA virus including new, emerging, and existing, and can be implemented rapidly without the need for additional future regulatory approvals could help reshape the public health response and also aid in tailoring interventions to improve patient outcomes. Next-generation sequencing (NGS) technology can detect and analyze viral genomes but the translation of this technology as an FDA-cleared diagnostic for the agnostic detection of any novel or known pathogenic respiratory virus has not occurred due to multiple challenges associated with sample preparation, distinguishing viral RNA from the host background RNA, and the bioinformatics analysis.

DRIVE is interested in advancing existing NGS-based platforms in terms of the development, clinical validation, and regulatory clearance for an agnostic diagnostic for respiratory RNA viruses. Submissions should address the following:

- Demonstrate a standardized non-targeted NGS assay using existing sequencing platforms that can agnostically detect any known and emerging respiratory RNA virus.
- Must provide feasibility data in support of existing non-targeted NGS diagnostic assay for detection of RNA viruses. Standardized assays that require no or minimal research and development effort are preferred.
- Must provide a regulatory strategy for engaging with the FDA for agnostic diagnostic approval based on draft guidance from the FDA (<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/infectious-disease-next-generation-sequencing-based-diagnostic-devices-microbial-identification-and>).
- Demonstrate ability to deplete host nucleic acids and/or enrich viral RNAs, thereby enabling detection at the same sensitivity as existing molecular diagnostics assays.
- The diagnostic platform should offer a complete solution including sample preparation, enrichment (if needed), sequencing, and data analysis. Medium- to high-throughput assays with automated sample preparation, library preparation, sequencing, and analysis, and minimum hands-on time are preferred.
- The diagnostic platform should be able to determine the viral load based on the number of sequencing reads or other similar metrics equivalent to existing molecular assays.
- The total time from sample collection to results (including sample preparation) should be no more than 24 hours; a sample-to-result time of less than 12 hours is preferred.
- The platform should be able to use samples of any type, including but not limited to lower nasal swabs, mid-turbinate nasal swabs, oral swabs, saliva, and nasopharyngeal wash. Submissions should include a demonstration that RNA can be adequately extracted and analyzed from multiple sample types.
- Applicants should provide data as evidence that the platform can adequately detect

different RNA respiratory samples (contrived samples are acceptable).

- All submissions must include a pressure test utilizing blinded contrived samples and clinical samples to validate the diagnostic platform. Respondents shall submit a clear plan for creating contrived specimens (with diverse RNA viruses and varying viral loads) and obtaining clinical specimens.
- Access to regulatory-grade reference target sequences of respiratory RNA viruses and near neighbors is required per FDA guidelines.

Out-of-Scope Topics:

- Submissions for targeted NGS-based diagnostic platforms that are pursuing pathogen-specific indications and aim to expand them for broader indications in the future.
- Agnostic pathogen detection platforms that are not based on NGS.
- Research and development activities for research use only (RUO) NGS-assay development that do not support regulatory path or FDA engagement.

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 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 exiting 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 in less than 6 months after contract start
- 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 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 shelf stability at room temperature and humidity for 1 year or more.
- Diagnostic tests with a market price point in the range of 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 during evaluation.

- The entire test process – sample collection, sample application to the test, test readout – must all be performed in the home by untrained personnel.
- 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 start.
- 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 (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 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, 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 personnel.
- Submissions leveraging small, easy to use devices are sought. 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 for assay platforms is desirable.
- The technology readiness level (TRL) for adapting existing approved assays is 4 and for novel platforms 3. Refer to Appendix 1 for a definition of TRLs.

Examples of innovations sought include, but are not limited to:

- Work that demonstrates proof of concept of the application of the enhanced technology (assay reagents, format/design and detection modalities) to an existing device with EUA
- A novel platform that results in improved assay sensitivity and equivalent or improved specificity will likewise be acceptable.
- Demonstration of these improvements on clinical samples must be a component of the proposed work
- Automation technologies and/or novel materials that demonstrate cost-savings directly applicable for home use as compared to currently authorized assays are highly desired.

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. To clarify, an entity must have an active registration with <https://sam.gov> at the time of submission to be reviewed. If not, submissions 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 submit a request to schedule a market research call. 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 #8: Bringing Laboratory Testing to the Home (homediagnostics@hhs.gov)

AOI #9: Digital Health Tools for Pandemic Preparedness (digitalhealth@hhs.gov)

AOI #10: NGS-based Agnostic Diagnostic for Respiratory RNA Virus Pathogens (NGS@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)

AOIs #8 and #9 will be open for abstract submissions through **5:00 PM ET on 03 February 2023**, unless otherwise extended.

AOI #10 will be open for abstract submissions through **5:00 PM ET on 30 November 2021**, unless otherwise extended.

AOIs #11a and #11b will be open for abstract submissions through **5:00 PM ET on 15 January 2022**, unless otherwise extended.

C. Number of Awards:

Multiple awards are anticipated and are dependent upon the program priorities, scientific/technical merit of submissions, how well 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, award(s) expected to be made under these Special Instructions 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 solicitation 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: Awarded partners 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 partners 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 <i>A product can be described as achieving a TRL only if all relevant activities identified in that TRL have been completed.</i>
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.