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

Special Instructions 012 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-20-100-SOL-0002

Revisions to Research Areas of Interest

DRIVe Contracting Office
200 C Street SW
Washington, DC 20201

October 22, 2020

A. OVERVIEW:

BARDA DRIVe issues these special instructions with the intent to:

1. Revise and open Area of Interest (AOI) #1 ENACT (Early Notification to Act, Control and Treat).
2. Revise and open AOI #2: Infection Severity & Solving Sepsis.
3. Revise and rename "AOI #4.3: Alternative Routes of Administration (AROA) for Vaccines" to "AOI #6: Beyond the Needle."

B. STATUS UPDATES FOR RESEARCH AREAS OF INTEREST (AOI):

The following areas of interest (AOI)'s have been established through the original EZ-BAA (BAA-20-100-SOL-0002) or through the current and previous amendments / special instructions. Please be sure to read BAA-20-100-SOL-0002 and all subsequent amendments / special instructions prior to proceeding. In the event of any conflicts, these Special Instructions supersede previous guidance issued under BAA-20-100-SOL-0002.

The following statuses are provided regarding open periods for submissions, specific to each AOI established under the EZ-BAA. Unless otherwise noted below, AOI's are accepting submissions throughout the EZ-BAA open period which, as of the time of this posting, ends 03 February 2023, 1700 HRS ET. BARDA reserves the right to revise the status of submission periods for any of the AOI's or the EZ-BAA itself. Any change to open periods for submissions will be posted in the form of an amendment / special instruction to the EZ-BAA.

1. AOI #1: ENACT (Early Notification to Act, Control and Treat) (ENACT@hhs.gov)

2. AOI #2: Infection Severity & Solving Sepsis (SolvingSepsis@hhs.gov)

3. AOI #3: [Not Currently Accepting Submissions]

4. AOI #4: COVID-19 [Accepting submissions until 31 October 2020, 1700 HRS ET]
    a. AOI #4.1-A: [CLOSED]
    b. AOI #4.1-B: [CLOSED]
    c. AOI #4.1-C: [CLOSED]
    d. AOI #4.1-D: Remote Patient Monitoring/Remote Diagnostic Tools (COVID19DxEzBAA@hhs.gov)
    e. AOI #4.1-E: Pediatric Diagnostic Tools for Severe COVID-19 Disease and MIS-C (COVID19DxEzBAA@hhs.gov)
    f. AOI #4.2: [CLOSED]
    g. AOI #4.3: Alternative Routes of Administration (AROA) for Vaccines is revised and now AOI#6: Beyond the Needle
    h. AOI #4.4: [CLOSED]

5. AOI #5: ReDIRECT (Repurposing Drugs In Response to Chemical Threats)

(chemrepo@hhs.gov) [Accepting submissions through 31 January 2021, 1700 HRS ET)

6. AOI#6: Beyond the Needle (BeyondTheNeedle@hhs.gov)

C. RESEARCH AREAS OF INTEREST:

Below is a list of AOI's revised by these special instructions. See relevant dates above for open periods of submissions. As stated in the EZ-BAA itself, scheduling a call with the relevant Program Manager is strongly encouraged ***prior*** to any submission to better understand the program objectives for each research area. The points of contact for each open AOI are listed above.

AOI #1: Early Notification to Act, Control and Treat (ENACT)

The ability to detect illness and injury early is critical to improving health outcomes and decreasing burden on health care providers and facilities. Through ENACT, DRIVe is seeking technologies and methods to a) identify and characterize biological, behavioral, and physiological signatures that can signal infection or injury before the onset of noticeable symptoms and b) technologies that provide early health status information to medical care providers.
Applications may but do not have to focus on COVID-19 as a potential use case.

To be considered responsive under this topic, technologies should prioritize host-based diagnostics and have one or more of the following desired characteristics:

- Technologies should provide quantitation of host-based biophysical and biochemical health markers through sensors that can be deployed and used by anyone with minimal training. Wearable, continuously operating sensors and sensor suites that monitor an individuals' innate and adaptive immunity are preferred;
- Wearable sensors or sensor suites in form factors that facilitate human use (e.g. microneedle patches, smart band-aids, smart tattoos, eye and oral sensors) are particularly desired;
- Applicants should prioritize sensors or sensor suites that collect and interpret data autonomously, although they can be coupled with cloud-based data reporting and analytics;
- For on-demand sensing, non-invasive or minimally invasive sensors (such as those using a finger stick) are required;
- Technologies that quantify the composition of passive samples (e.g. saliva, interstitial fluid, sweat, breath etc.) are of special interest;
- Technological approaches should include algorithms and smartphone applications for early indication of health status and optimally directing patients and allocating treatment resources in a large-scale health security event;
- Proposals should develop algorithmic and automated approaches to link sensor data to early or presymptomatic disease and injury detection.

Respondents should discuss their approach to obtaining regulatory approval for

their technology and commercialization. All proposed clinical studies must equitably include multiple racial and ethnic groups and all clinical data analyses must include race / ethnicity and biological sex as subject groups.

The ENACT team has retrospective and prospective wearables data including heart rate, heart rate variability, accelerometer, electrocardiogram, and other health signature data sets that may be made available for data analytics, algorithm development, and data mining. The program will support the development and validation of models from prospective partners and can make de-identified clinical data sets available.

The following areas are considered to be out of scope at this time and may not be reviewed:

- Pathogen based detection or technologies – any technologies that are based on the identification of pathogens will not be considered responsive at this time.
- Any technology that is not minimally invasive and simple to use. Specifically, for purposes of this AOI, technologies which require sample preparation and would not be available over-the-counter and cleared / approved by FDA for home use, will be considered non-responsive. (with the exception of app-based solutions).

NOTE: All awarded ENACT partners will be required to share de-identified data collected during the period of performance 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.

AOI #2: Infection Severity & Solving Sepsis

At least 1.7 million Americans develop sepsis each year and nearly 270,000 Americans die annually as a result. Sepsis occurs when an infection leads to a dysregulated host response and organ dysfunction. In addition to the toll on health, sepsis incurs a large economic burden and sepsis survivors also sustain additional chronic illnesses and associated care expenses.

Sepsis can be the endpoint of almost any infection, including SARS-CoV2, and therefore recognition, early detection and mitigation are critical at the first signs of sepsis. We consider sepsis to be a continuum of infection progression that is further complicated by the heterogeneity of the host response and organ dysfunction. Within the program, we are catalyzing the field through a coordinated approach towards development of innovative host-based diagnostics, host-targeted therapeutics, and clinical management approaches that will advance the way we recognize infection severity, combat sepsis, build resiliency in our healthcare system, improve patient outcomes, and ensure that no American life is needlessly cut short by sepsis.

As sepsis can be a complication of any health security threat, as evidenced by the COVID-19 pandemic, in order to fully protect Americans and save lives, the Solving Sepsis program aims to reduce the incidence, morbidity, mortality, and economic burden of sepsis. The program desires to empower both the patient and the

healthcare provider with technologies and approaches that are relevant in a number of care settings, including pre-hospital (e.g., home, nursing homes, outpatient), urgent/emergency care (e.g., EMS transport, Emergency Department), inpatient (e.g., ward, ICU) and post-discharge/recovery (e.g., home, skilled nursing facilities). BARDA is interested in technologies and approaches that apply to adults and special populations, such as neonates and pediatric patients, as all populations are at risk of sepsis.

The program is interested in the following focus areas. Please note that due to the current COVID-19 pandemic, COVID-19 may be an appropriate use case:

1. Host-based diagnostics, monitoring devices and predictive analytics tool:

    a. Diagnostics and monitoring devices that identify sepsis, predict infection severity, or prognosticate outcomes in pre-hospital settings, urgent/emergency care, or post-discharge/recovery settings. We are not interested in tools that can be used exclusively for inpatient settings at this time. The diagnostics must be able to distinguish infection or mild disease alone from severe outcomes, including sepsis, or distinguish from Systemic Inflammatory Response Syndrome (SIRS) in the absence of infection.
    b. Pediatric technologies that improve early detection and diagnosis and/or inform on clinical management of pediatric/neonatal patient progression to sepsis and other severe outcomes, including multisystem inflammatory syndrome in children (MIS-C).
    c. Post-sepsis (or post COVID-19) monitoring technologies (e.g., after hospital discharge) to detect health deterioration or changes in health outcomes, to inform on clinical care. These technologies should not just provide absolute data values but also include approaches to interpret/analyze data and provide actionable information to the healthcare provider or patient.
    d. Patient stratification/endotyping/sub-typing technologies to provide a more tailored approach to improve clinical management in certain subpopulations and potentially correlate with individualized targeted treatment responses (See section 2 below).

2. Host-targeted therapeutics and clinical management approaches:

    a. Novel host-based sepsis therapeutic approaches that can modulate the host response to improve patient outcomes.
    b. Novel clinical management strategies that can be tied to patient stratification approaches (see section 1.d above) to improve patient outcomes.

Submissions should be responsive to the following:

- Medical countermeasures should address infection via any etiology (i.e., bacterial, viral, other) versus approaches that are limited to sepsis induced by a subset of pathogens. However, due the current COVID-19 pandemic, approaches that use COVID-19 as a use case, are appropriate.

- Provide evidence of planned adoption or implementation strategies in relevant settings to improve clinical utility of the proposed technology (pre-hospital (e.g. Home, nursing homes, outpatient), urgent/emergency care (e.g. EMS transport, Emergency Department) and post-discharge/recovery (e.g. home, nursing homes).
- Proposals should include prior demonstration and preliminary data to support use in sepsis or infection severity relevant models (e.g., sepsis patient samples, sepsis [including severe COVID-19] patient clinical data).
- Only technologies focused on host-based approaches or clinical management approaches will be considered. BARDA has existing programs for pathogen-targeted approaches outside of this Area of Interest.
- Research should be considered translational science. There is no interest in early stage or fundamental research projects for this topic at this time.
- Proposals should present a clear FDA regulatory path for approval/clearance (if appropriate) and, if available, evidence of engagement with regulatory authorities.
- Proposals should provide evidence of pre-established agreements with proposed partners for relevant clinical studies, if appropriate.
- Proposals 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 device fabricators/manufacturers; addressing the ability to scale, deploy, and distribute the medical countermeasure; intellectual property; and modeling the cost per unit, reimbursement strategy, etc.
- Clinical studies must be equitable in terms of enrollment, including diversity amongst race, ethnicity, and biological sex.
- Diagnostic approaches may leverage a number of innovative areas including host biomarkers, artificial intelligence/machine learning algorithms, digital health, EHR integration, data interoperability, remote and self-monitoring devices, etc.

The following are considered out of scope at this time:

- Pathogen-based or pathogen targeted approaches, including serology
- Physiological monitoring devices that do not distinguish mild disease or infection alone from severe outcomes, including sepsis, or distinguish from SIRS in the absence of infection
- Devices or technologies that only address prevention or detection of infection and do not address infection severity or sepsis
- Supportive care technologies that do not specifically improve clinical outcomes for sepsis patients
- Sepsis diagnostics that are limited to only the intensive care unit hospital setting
- Exploratory research with no near-term translational application
- Technologies that will require FDA regulatory approval but have not yet engaged or do not have an appropriate regulatory path

AOI #5: ReDIRECT (Repurposing Drugs In Response to Chemical Threats)

The availability of effective medical countermeasures (MCMs) against chemical threats are critical in the treatment of their acute health effects. Necessary attributes of effective MCMs against chemical threats include ease of administration during a mass-casualty situation and rapid efficacy as a post-exposure therapy.

Drug repurposing is a strategy that is used to identify new uses for FDA approved or late-stage investigational therapeutics that are outside of their original clinical indication. The identification of existing compounds for repurposing as MCMs holds the potential to expand current response capabilities to chemical threats, as well as potentially mitigating the costs and risks associated with conventional drug discovery.

BARDA is requesting abstract submissions for projects that repurpose existing therapeutics as MCMs against chemical threats (cyanide, opioids, nerve agents, chlorine, sulfur mustard, etc.). These therapeutics should have a strong mechanistic justification for potential use as MCMs. Ideal candidates for MCMs should have a known safety profile from previous clinical indications or development and be safe and effective for the entire population, including at-risk populations such as pediatrics, geriatrics, pregnant women, and immunocompromised individuals.

MCM candidates should:

(1) Already be approved or in late-stage clinical development for a conventional indication similar to the symptomology associated with exposure to a chemical agent; and
(2) Utilize improved delivery routes or mechanisms that provide ease of administration (including, but not limited to, reformulation of existing products) to large numbers of exposed individuals during mass casualty situations. Priority will be given to products manufactured in the United States.

Therapeutics that are eligible for drug repurposing may target any of the following:

Pulmonary Agents: Development of MCMs to prevent and treat lung damage (including pulmonary edema, pneumonitis, and fibrosis) resulting from exposure to agents such as chlorine, sulfur mustard and phosgene.

Opioids: Development of MCMs to treat life-threatening respiratory depression caused by opioid overdose. These post-exposure treatments should be quick-acting and effective against a variety of opioids, including synthetic opioids such as Fentanyl. Candidates should have a mechanism of action different from existing opioid receptor antagonists.

Vesicants: Development of MCMs that limit harmful aspects of exposure to vesicating agents such as sulfur mustard and Lewisite. Particular preference is given to drugs with potential to ameliorate the long term effects of exposure

including Mustard Gas Keratopathy.

Blood/Metabolic Agents: Development of MCMs to treat acute poisoning from agents such as cyanides. Antidotes should be easily administered by first responders in personal protective equipment. Preference is given to those cyanide antidotes that are also effective against smoke inhalation-related exposure.

Nerve Agents and Organophosphorus (OP) Pesticides: Development of MCMs to treat life-threatening and long-term effects of nerve agents and OP pesticides. Antidotes should be easily administered by first responders in personal protective equipment.

Computational approaches to identify candidates for drug repurposing: Development of improved methods to rapidly identify FDA approved or late stage candidate compounds that can be repurposed against any of the aforementioned chemical threats.

To be considered responsive under this AOI, respondents should have:

(1) A drug that is a candidate for repurposing as a MCM against pulmonary agents, opioids, vesicants, blood/metabolic agents, nerve agents, or organophosphate pesticides; and
(2) A FDA approved drug, or one that has completed Phase 2 trials as evidenced by a clinical study report; and
(3) A clear rationale as to why the candidate would be efficacious as a chemical MCM.

Priority will be given to MCMs developed in the United States.

AOI #6: Beyond the Needle

The administration of therapeutics, such as vaccines, biologics, or other medications, can be markedly enhanced by utilizing alternative routes of administration that rely less on a needle and syringe approach used in traditional intravenous (IV), intramuscular (IM), or subcutaneous (SC) administrations. These traditional routes via a needle and syringe are often logistically challenging, rely on cold-chain storage that hinders distribution, and almost exclusively require experienced personnel for administration. The DRIVe **Beyond the Needle** program seeks to develop technologies that (1) utilize alternative routes of administration for administering therapeutics, such as but not limited to: oral, intranasal, transdermal patches, sublingual, and buccal mechanisms of administration, (2) involve simplified logistics that enable easier deployment and uptake, and (3) able to be administered without a trained health-care professional.

As a consequence to reduce production costs, the medical supply industry has evolved to “just-in-time” supply chain models that involve sourcing and manufacturing raw materials outside the United States. As a result, the domestic availability of needle and syringes is limited and poses as a bottleneck for therapies requiring their use on a large scale. In recent months, the pandemic has highlighted opportunities to strengthen and bolster the United States medical supply chain. The Beyond the Needle program seeks to develop therapeutics that can be administered

in a broad range of care settings including within the home and do not rely on skilled medical personnel for administration. A successful alternative technology for administration would reduce the demand placed on qualified personnel, particularly in communities that are underserved and have reduced access to care.

BARDA is seeking abstracts for the development of technology that features an alternative route of administration for any type of payload, including vaccines, drugs (biologics, small molecules, nucleic acids), as well as adjuvants against CBRN threats, Influenza (seasonal/pandemic), coronaviruses (SARS-CoV-2), and other emerging infectious diseases that is of pandemic concern as outlined on www.medicalcountermeasures.gov.

The ideal attributes for therapeutics or adjuvants delivered via alternative routes of administration would be single dose (although additional dosing is acceptable), room temperature-stable without the need for cold-chain storage, and indicated for all populations. Therapeutics delivered via alternate routes of administration should have similar or superior performance characteristics as traditional routes administered via a needle and syringe (i.e. safety and efficacy).

Emphasis will be placed on proposals that focus on the delivery and not on the discovery of payloads.

In some cases, alignment with a proven therapeutic provider might be beneficial, although it is not required for consideration.

All submissions must include:

1. A proposed technology or platform for administering a therapeutic (can include vaccines, biologics, small molecules, nucleic acids etc.) candidate via an alternative route of administration. Therapeutics may target CBRN threats, Influenza (seasonal/pandemic), SARS-CoV-1 / 2, as seen on (www.medicalcountermeasures.gov) but are not required.
2. Plans for IND enabling pre-clinical studies or provide existing supporting data.
3. Product development plan and a target product profile is desired.
4. Any regulatory communication with US FDA (pre-IND/IND).
5. Any pre-clinical or clinical data using this platform.
6. Potential for use or implementation in underserved communities.

D. Eligible Respondents & Scope Parameters:

These Special Instructions are open to all responsible sources as described in the EZ-BAA and subsequent amendments / special instructions. Abstract submissions that do not conform to those outlined requirements may be considered non-responsive and will not be reviewed. As a reminder, an entity must have an active registration with www.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 www.SAM.gov.

E. Application Process:

All submissions will follow the same submission process and review procedures as established under the EZ-BAA as published on. For complete details, please read the EZ-BAA (i.e. BAA-20-100-SOL-0002) document in its entirety, along with all previous amendments / special instructions.