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

Special Instructions 020 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-20-100-SOL-0002

The purpose of these Special Instructions are the following:

1) Add Area of Interest (AOI) #14 to the EZ-BAA:

AOI #14: Healing Lungs: Simpler, Safer Lung Support for Severe ARDS Patients

I. INTRODUCTION AND OVERVIEW INFORMATION

A. Development Opportunity Objective:

Under these Special Instructions 020, BARDA is adding **AOI #14** as part of its EZ-BAA (BAA-20-100-SOL-0002). Under this AOI, we are seeking abstract submissions for the following:

AOI #14: Healing Lungs: Simpler, Safer Lung Support for Severe ARDS Patients

Acute respiratory distress syndrome (ARDS) is a serious lung condition caused by multiple factors, including viral and bacterial infections, exposure to toxic radiation or chemicals, smoke inhalation, as well as trauma and severe chest injury. ARDS is characterized by an acute and diffuse lung inflammation associated with alveolar fluid accumulation and surfactant dysfunction, which results in improper lung function, leading to low blood oxygen and, in severe cases, causing lung tissue scarring and permanent respiratory impairment. Mechanical ventilation, which is currently the first-line intervention for ARDS patients, often results in further lung injury. Patients who do not respond to mechanical ventilation are more and more frequently placed on veno-venous extracorporeal membrane oxygenation (VV-ECMO), an intervention that remains labor-intensive, and costly, requiring highly specialized personnel, and prone to risks and complications. The Division of Research, Innovation, and Ventures (DRIVe) is interested in developing alternative options to sustain healthy oxygenation levels in ARDS patients as they heal naturally or await lung transplant, all the while preventing further tissue injury to already damaged lungs, and in advancing solutions for patients refractory to mechanical ventilation. Particularly, DRIVe is seeking innovations that simplify the implementation and operation of VV-ECMO, improve its safety profile, and potentially enhance its availability outside of specialized ECMO centers. BARDA is also interested in non-ECMO methods of oxygen delivery (e.g., synthetic and mammalian cell-derived oxygen carriers) that may offer alternative options to severe ARDS management.

DRIVe is interested in the following focus areas, which cover VV-ECMO and oxygen carrier injectable products:

VV-ECMO:

1. **Maintaining balance between pro- and anticoagulant states in ECMO patients**: DRIVe is pursuing innovative technologies that maintain blood flow inside the circuit, yet prevent pathological thrombosis and hemorrhage and reduce the need for systemic anticoagulation, or allow for ECMO to be administered anticoagulant-free for a minimum of 16 days. Responsive proposals shall include plans to evaluate the biocompatibility and anti-clotting properties of proposed solutions. Applicants should aim to conduct *in vivo* tests for at least 16 days, during which no clots or internal hemorrhage should occur and no embolic complications or adverse events resulting from clot formation should be recorded. The evaluation of proposed solutions will include an assessment of the hemostatic state and coagulation profile using a test panel composed of TEG, ACT, aPTT, PT, antithrombin III, von Willebrand factor, D-dimer, platelet, and fibrinogen concentration. Solutions should aim to maintain tests values within 10% of baseline for a minimum of 16 days. Projects seeking to develop systemic anticoagulant drugs are out of scope. Approaches that focus on dissolving existing clots will not be considered.

Solutions of interest include, but are not limited to:

a) Novel coatings and modifications (e.g., solutions leveraging nitric oxide, tethered liquid perfluorocarbon, novel anticoagulant compound, or combinations of solutions) of the inner surface of circuit tubing and components such as the gas exchanger.
b) Novel design of circuit components (e.g., oxygenator, tubing junction connectors) that improve blood flow path control, limit blood/surface contact, and enhance gas exchange rate, as well as supportive adjunct technologies (e.g., ultrasound-based platforms)
c) Any approach that would combine technical innovations of several circuit components

2. **Approaches that make ECMO more compact and portable, easier to implement and operate:** DRIVe is interested in solutions that would ideally integrate the pump, oxygenator, and heat exchanger into a single miniaturized ECMO circuit component. However, submissions focused on miniaturizing one of these three components alone will also be considered. Responsive proposals shall include comparative studies evaluating the performance of miniaturized components against commercialized components and as part of a complete ECMO circuit. Teams of applicants are welcome to propose collaboration projects and submit their abstract together.

Proposed VV-ECMO solutions should ideally be compatible for use in combination with commercially available circuit components. VV-ECMO submissions shall provide evidence that the technology is ready for large animal testing and include an ovine or porcine ECMO model study using no less than 10 animals. Although large animal studies are preferred for both VV-ECMO topics, small animal studies that may be required for component miniaturization will be considered.

Alternative methods for oxygen delivery and/or carbon dioxide removal:

DRIVe is interested in **injectable compounds** or products that provide sufficient respiratory support to maintain patient oxygen saturation levels at 95% and above, are non-alloimmunizing, and can demonstrate an oxygen-carrying capacity similar to that of human hemoglobin (i.e., ~1.34 ml oxygen per gram). DRIVe seeks technologies that allow repeated administration of oxygen and demonstrate reduced toxicity at effective dosage compared to current generation hemoglobin-based
products and perfluorochemical emulsions. Responsive proposals shall discuss biocompatibility assessment and include an evaluation of the oxygen carrier efficacy and toxicity in an animal model recapitulating severe ARDS presentation in humans (i.e., $PaO_2/FiO_2<100$ mmHg). DRIVe is also interested in injectable compounds or products that provide sufficient respiratory support to maintain arterial carbon dioxide levels at 35-45 mmHg and/or prevent severe hypercarbia.

Solutions of interest include, but are not limited to:

a) Perfluorocarbon (PFC)-based carriers, polymer-based hollow microparticles (PHMs), lipid-coated microbubbles (LOMs), synthetic or cell-based hemoglobin-based oxygen carriers (HBOC), and others
b) Carriers that can be administered intravenously to support respiration without contribution from the lungs to enable lung tissue healing

Additional considerations:
Awardees are encouraged, but not required, to share information and project progress with each other in quarterly meetings, and to consider testing their technology in combination with the innovations of others to assess their synergistic potential. All awarded projects will be reviewed quarterly by an internal review committee comprised of federal staff from BARDA and other federal entities.

Platforms that have not reached, at minimum, a technology readiness level of 3 (TRL 3) and proposals for basic research projects that have not achieved preclinical proof of concept level of development will not be considered. Submissions should address the following points:

- Detailed description of the technology and the innovation
- Preliminary data that demonstrate the proposed approach is scientifically viable, feasible, and suitable for practical applications and product development. Applicants should provide a summary of their preliminary work in the abstract and additional details in attachments to their submission.
- Success metrics and plans to evaluate the safety and efficacy of their proposed solution as part of the project
- Rationale for the choice of selected animal model, including a clear justification and evidence dictating the use of a large animal model rather than other models when appropriate. Applicants shall explain why a particular animal model is required at the stage of development reached by their technology.
- Regulatory and commercial strategies beyond the proposed study are desirable but not required.

Approaches relying on positive or negative air pressure systems and mechanical ventilation, or aerosol or gas inhalation are out of scope and will not be considered.

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.

AOI #14: Healing Lungs: Simpler, Safer Lung Support for Severe ARDS Patients
(HealingLungs@hhs.gov)

AOI #14 will be open for abstract submissions through **12:00 PM ET on 3 Feb 2023,** unless otherwise revised.

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: Interested vendors must submit a request to schedule a market research call to HealingLungs@hhs.gov to be considered for award. This request should include the project title, key project staff, and a brief description of the proposed project. Interested parties that do not submit this request will not be eligible for consideration.

In addition to the "DRIVe Safeguarding of Information" procedures explained in the EZ-BAA, by submitting an abstract to this area of interest the Respondent expressly acknowledges that they are consenting to the disclosure of protected source selection information contained in the abstract to BARDA personnel who may participate in the review and evaluation process. Abstracts not selected for award by BARDA may be shared with other federal agencies for consideration of other funding opportunities.