MTEC-20-12-COVID-19_Diagnostics
Diomics Corporation

Statement of Work

Proposal Number: MTEC-20-12-Diagnostics-001

Organization: Diomics Corporation

Title: (b) (4) [redacted]

ACURO and/or HRPO approval needed: ACURO Approvals Needed.

Introduction/Background

The COVID -19 pandemic has shattered our beliefs about the type and scope of health information captured and compiled. The lack of volume test data and the corresponding analytics has left decision makers in a tough place, making decisions without ideal tools or data. Data requirements go way beyond traditional medical practitioner health info and should include a wider variety of real time data about the health state of that individual as well as other user activities. The pandemic has proved a) that healthcare is not local, regional, national or global - it is all of the above and b) in an environment like today, the ability to capture and hyper analyze individual data and distribute that data to resource allocation planners is beyond necessary.

According to the Annals of Internal Medicine, the median incubation period for the COVID -19 virus is estimated to be 5.1 days with 97.5% of patients developing symptoms within 11.5 days post infection. These estimates imply that 101 out of every 10,000 cases will develop symptoms after 14 days. The lack of real time monitoring during this base incubation period creates issues for small and large groups alike; a) we are only testing based upon presented symptoms, we are missing asymptomatic shedders of the virus with limited testing and b) since we discover the presence of the virus in an individual late in the incubation sequence, others are being infected and viral control capabilities are reactive as opposed to proactive.

But a more important number surrounds the statistical the belief that up to 50% of infected individuals are asymptomatic.

This truly affects all group orientations including first responder health care workers and patients, members of the military, high risk groups like the aged in elder care facilities, prison staff and inmates, apartment dwellers, meat packers and individual members of a single family. The results of a lack of pre-symptom data and real time auditing during the incubation process, creates mass inefficiencies for the targeted use of therapeutic equipment resources, inventory of personal protection equipment and the potential for an increased loss of life. The use of a reactive PPD has been used in some form since 1890 for the monitoring and detection of *Mycobacterium tuberculosis*. A small drop of filtered tuberculin liquid containing some components of heat-killed TB bacteria is injected 3mm under the top layer of the forearm skin.

(b) (4) [redacted]

(b) (4)

One of key issue of the pandemic today is the development and validation of methods to rapidly monitor and identify contagion infections in large segments of our American society. (b) (4)

(b) (4)

(b) (4), is an FDA approved (b) (4) which has been widely used in human tissue repair & surgical applications. (b) (4)

(b) (4)

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(b) (4) haracteristics are well suited for (b) (4)

(b) (4) can be (b) (4)

(b) (4) which will sequester the reactive antigens and provide for accurate depth & precise delivery for optimal display of epitopes for elicitation of an immune response.

(b) (4)

(b) (4) tips allow for the presentation of the reactive antigen under the surface of the skin to a prescribed depth (2-3mm).

(b) (4), would be useful as an over the counter, easy to apply product filling a large product and technology gap in the diagnostic system today and in the future. In the second version, (b) (4)

(b) (4)

The COVID -19 recombinant antigens (e.g. spike protein, etc.) are commercially available and will be used for alpha versions of the product; improved fusion COVID -19 antigens have been expressed in mammalian systems and will also be investigated (b) (4)

(b) (4)

The lack of real-time viral monitoring during the incubation period creates issues for small and large groups alike. The results from a lack of pre-symptom data and real time auditing during the incubation process, creates mass inefficiencies for the targeted use of therapeutic equipment resources, inventories of personal protection equipment and the potential for an increased loss of life.

(b) (4)

(b) (4) This technology is a (b) (4)

(b) (4) which has utility when combined with a suite of contagion monitoring methods in a triage approach to control the contagion. We believe the

(b) (4)

These diagnostic medical devices have immediate applicability to many groups including first responder health care workers and patients, members of the military, high risk groups, e.g. the aged in elder care facilities, prison staff and inmates, apartment dwellers, meat packers and

(b) (4)

Scope/Project Objective

We propose to create a (b) (4)

(b) (4) developed over 100 years ago, the Mantoux tuberculin test is still used today to determine if an individual has been exposed to tuberculosis (TB). (b) (4)

(b) (4)

We propose to develop, test & manufacture both the (b) (4)

(b) (4) with plans to bring the most promising application to marketplace first. (b) (4)

(b) (4) and testing the products reliability, stability and efficacy in several animals studies and early human clinical trials for a EUA development sprint over the next 6 months (June 1 project start date).

Milestones include initial specification and testing data for the (b) (4) we also will define the scalable processes for production of the final medical devices and based on testing, trial data and project specific operating procedures, we will begin the process towards final product approvals and commercialization in support of the MTEC project requirements.

Requirements

(b) (4)

(b) (4) ; the devices will generate a localized immune reaction to circulating antibodies directed against the antigen, if an individual has been infected with COVID-19.

During (b) (4)
(b) (4)
(b) (4) and in Phase One animal studies.

In Phase Two, our focus will be on moving towards commercialization with validation of scaled-up manufacturing, production SOPs. The products developed will subjected to extensive *in-vitro* immunological analysis, Phase Two animal studies and early human clinical trials employing patients who have cleared Covid-19 which possess circulating antibodies directed against COVID-19.

PHASE ONE

Task 1– Project Initiation

1.1 Form Fashioning of Transdermal and Implantable (b) (4) Polymer, Antigen Coupling

(b) (4)
(b) (4) . PCL has been widely used in 3-D printing, electrospinning and compression molding and is well suited for this application (b) (4)
(b) (4)
(b) (4) the subject of our first animal study outlined below.

1.2 (b) (4) to reactive Covid-19 antigens

In this task, the reactive (b) (4)

(b) (4)
(b) (4) However, antigen loading and microweb structuring may require optimization for efficient antigen display and epitope presentation.

1.2 Efficacy testing of prototype (b) (4)

Once the finalized prototype (b) (4) have been produced, (b) (4) will be evaluated and quantified with comprehensive *in vitro* immunological and molecular diagnostic studies using the reagents produced in Task 1

for both *in vitro* and *in vivo* small animal models. The first animal studies (*in progress*), involve an(b) (4)
(b) (4)
Avian Infectious Bronchitis is a single stranded RNA gamma-coronavirus, closely related to the Covid-19, a beta-coronavirus; we believe the IB model will serve as an immediate proof of concept, with detection of a related viral pathogen.

(b) (4)
(b) (4)

1.4 Development and Initial Testing of Transdermal Patch System

(b) (4)
(b) (4) Task also involves adapting research-level production methods to large-scale manufacturing and refinement of SOPs.

1.5 Production of Prototype (b) (4) PPDs & Scale Plan

Vetting has begun on potential production vendors for production of materials needed in the volumes that will be required. The providers of Antigens are known to the Company and their background and history will be part of the reports generated during the project. Part of our discovery discussions with the various governmental partners will be defining manufacturing requirements, vendor approvals and the development of a production plan to support the volume requirements of the US Governmental Programs.

1.6 Application of In Vivo Research and Integration to Device Project

One of the primary objectives of the initial stages of the development cycle is the production of data supporting the (b) (4) . These early material tests and animal associated tests using various Antigens themselves and their interactions with mice, will form the basis on the initial first article form factors. Guidelines for the research will be developed early in the project by a PhD member of our staff with a research background at UCI. The level of initial testing rigor in the individual studies will be based on the predetermined outcomes that we believe are necessary for early assumptions of a successful production level product. Early information derived will take those early assumptions and evolve the product level requirements forward towards a successful efficacy based result and the ability to manufacture at scale.

PHASE TWO:

Task 2 – Efficacy Study

2.1 Product Efficacy

In the second phase of this program, we will evaluate production ready(b) (4)
(b) (4)
(b) (4) we will also(b) (4)
(b) (4)
(b) (4) previously immunized with COVID-19 antigens. (b) (4)
(b) (4) . Control animals will not

have ben inoculated with the COVID-19 antigen, and thus do not contain anti-Covid19 circulating antibodies. The control animals will also be tested in long term, high antigen load studies to confirm no systemic immune response can be elicited by this diagnostic biopolymer.

2.2 Stability Study

The recombinant COVID-19 antigens covalently coupled to th (b) (4)

(b) (4)

2.3 Toxicity Study

Toxicological analysis will be performed at (b) (4) under the supervision of (b) (4) (b) (4). Initially in vitro studies will provide insight on the material capabilities and effectiveness as an immunoreagent; subsequent in vivo animal testing under his approved animal protocols (UCI AUP 17-241). From our internal review and previous lab work, we do not believe that the FDA-approved polymer covalently coupled to a recombinant Covid19 antigen will pose much threat from the toxicology to regulatory data. Numerous publications on the old-school Mantoux tuberculin test also support the safety of this approach.

Task 3 – In Vivo Testing (Phase One and Phase Two)

3.1 Animal testing

All *in vivo* animal studies of the (b) (4) test will be conducted at the University of California, Irvine campus facilities under the guidance of (b) (6). Initially in vitro studies will provide insight on the material capabilities and effectiveness as an immunoreagent; subsequent in vivo animal testing under his approved animal protocols (UCI AUP 17-241) will be conducted in experimental mice models and egg-laying hens to evaluate the biocompatibility and function in transdermal and subdermal delivery followed by histological evaluation using specific immune-histological assays.

(b) (4)

(b) (4) a NIH funded program which coordinated trial design and full implementation of clinical outcomes.

3.2 Human Clinical Trials

Initial safety studies will be coordinated through the UC Irvine ICTS which will assist with patient selection, inclusion/exclusion criteria and provide nursing and medical support for the study. They have assisted with UC Irvine IRB submission, and all regulatory aspects of the clinical trial.

Prospective statistical review of protocols will determine the appropriate statistical measures, outcomes and sample size required for these studies.

Task 4 - FDA Evaluation, Compliance, EUA

4.0 - FDA Phase 1 Clinical Safety Study Approval Process

A Phase One safety study will be conducted to evaluate safety, tolerability and compliance.

Task 5 – Submit Report

Primary Outcome Measures:

- Safe product with no negative outcomes
- Defined and appropriate and consistent localized immune response reactivity.
- No detectable cross-reactivity with related viral strains
- Proven product stability, efficacy, reliability of diagnostic output
- Development of scalable standard operating procedures.

Deliverables:

- Commercialization for pre-production hand off to approved contract manufacturer
- Acute toxicology animal study report
- Phase 1 safety study report
- Monthly, Quarterly and Final Technical & Business Reports
- Phase 2 FDA compliance and approvals

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Milestone Payment Schedule

MTEC Milestone Number	Task Number	Task Description	Start Date	Finish Date	Government Funds	Cost Share	Total
1	1	Project Initiation		6/22/2020	$(b) (4)	(b) (4)	$(b) (4)
2	1.1	Form fashioning of transdermal & implant (b) (4) polymer, antigen coupling studies	6/22/2020	7/22/2020	$(b) (4)	(b) (4)	$(b) (4)
3	1.2	Optimize coupling of form factored (b) (4) reactive Covid-19 antigens	6/22/2020	9/28/2020	$(b) (4)	(b) (4)	$(b) (4)
4	1.3	Efficacy testing of prototype DIOTEST PPD C19 (Phase One)	7/22/2020	10/27/2020	$(b) (4)	(b) (4)	$(b) (4)
5	1.4	Development and Initial Testing of Transdermal Patch System	7/22/2020	11/27/2020	$(b) (4)	(b) (4)	$(b) (4)
6	1.5	Production of prototype (b) (4) PPDs & scale up plan	6/22/2020	9/18/2020	$(b) (4)	(b) (4)	$(b) (4)
7	1.6	Application of In Vivo Research and Integration to Device Project	6/22/2020	10/30/2020	$(b) (4)	(b) (4)	$(b) (4)
8	2	Efficacy Study (Phase Two)	8/22/2020	11/27/20	$(b) (4)	(b) (4)	$(b) (4)
9	N/A	Bimonthly Report # 1		9/25/2020	(b) (4)	(b) (4)	(b) (4)
10	2.1	Commcialization of Platform Requirements	7/15/2020	10/30/2020	$(b) (4)	(b) (4)	$(b) (4)
11	2.2	Stability Study (Phase Two)	8/22/2020	11/21/2020	$(b) (4)	(b) (4)	$(b) (4)
12	2.3	Toxicity Study (Phase Two)	8/22/2020	2/10/2021	$(b) (4)	(b) (4)	$(b) (4)
13	3	Animal Testing (Phase One and Phase Two)	6/22/2020	3/12/2021	$(b) (4)	(b) (4)	$(b) (4)
14	3.1	~~Human Testing (Phase One and Phase Two)~~Clinical Trials Phase 1 and Phase 2/3 Studies	8/22/2020	5/30/2021	$(b) (4)	(b) (4)	$(b) (4)
15	N/A	Bimonthly Report # 2		11/25/2020	(b) (4)	(b) (4)	(b) (4)
16	4	FDA Phase 1 Clinical Safety Study (Phase Two) Approval Process	8/22/2020	5/30/2021	$(b) (4)	(b) (4)	$(b) (4)
17	N/A	Bimonthly Report # 3		1/25/2021	(b) (4)	(b) (4)	(b) (4)
18	N/A	Bimonthly Report # 4		3/25/2021	(b) (4)	(b) (4)	(b) (4)
19	5	Submit Final Reports (Business and Technical)		6/9/2021	$(b) (4)		
		Total			$(b) (4)		$2,317,165.00

Note: The In-Kind Contribution is a 45% discount off labor and functions as a credit against the overall cost of the project and is included in the

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$2,113,146 net project cost. TTL cost represents the net required funding for the project development and commercialization.