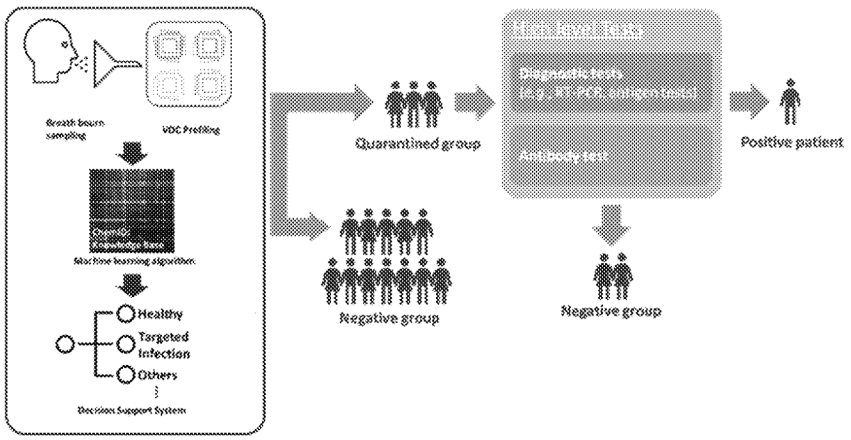
DEPARTMENT OF HOMELAND SECURITY (DHS)

STATEMENT OF WORK (SOW)
FOR
Rapid Infection Screening *via* Exhalation (RISE)

1.0 BACKGROUND



Highly contagious respiratory diseases (such as COVID-19) cause significant disruption to social and economic systems if the spread is uncontrolled. Many countries are suffering from the scarcity of rapid and reliable COVID-19 testing kits and the lack of reliable testing may contribute to continued community viral transmission. Currently, real-time reverse transcription-polymerase chain reaction (RT-PCR) is the primary means of COVID-19 diagnosis. This method requires a long diagnostic duration (> 3 hours, including preparation of viral RNA), as well as specialized laboratories and skilled technicians to perform the test and analyze the resulting data. There is on-going research to apply breath analysis for direct detection of SARS virus, such as COVID-19, but this capability is still immature.

The overall goal of this project is to devise a breathalyzer platform for early detection of viral respiratory infection for realizing initial screening at key check points such as port of entry, building check points, school entry, and many others. The **R**apid **I**nfection **S**creening *via* **E**xhalation **(RISE)** is a breathalyzer device that would rapidly detect viral infection and distinguish symptomatic patients from a healthy group. This is aligned with DHS's objective to develop a non-invasive device for identifying individuals who may be infected with a communicable disease. Further, this device should be re-configurable to address the need for widespread, rapid screening in a future pandemic. The rapid and precise identification of viral infection before entering crowded or vulnerable areas is essential for suppressing transmission effectively.

2.0 SPECIFIC REQUIREMENTS/TASKS

The system will have breath sampling capability, N5's patented multiple VOC sensors array, and wireless connectivity toward cloud-based analytic engine. The multiple VOC sensors array will profile exhaled breath rapidly, and the system connected to a back-end server designed for real-time data aggregation and analysis will provide the profiled results to decision support system and knowledge base programmed with machine learning algorithms. The decision support system will take all sorts of decisions according to the knowledge acquired with the analysis of the stored information, and provide the 1st stage screening results to check point center. N5 are proposing the following 9 major tasks for the Phase II of this project: 1) Select VOC Biomarkers and Interferents, 2) Breath Sensors Design, Fabrication and Testing, 3) Initial Prototype Design Development, 4) Downselect and Development of RISE Prototype, 5) Develop Machine Learning Algorithms, 6) Prototype Testing with Simulated Breath Samples, 7) Prototype Refinement and Ruggedization, 8) Conduct Feasibility Study, and 9) Final Report.

Table 1: Key milestones for each task

Task	Key milestones
1. Select VOC Biomarkers and Interferents	• Down-select to 6 ~ 10 breath biomarkers • Indicate 2 ~ 3 Interferents to demonstrate feasibility of the RISE system
2. Breath Sensors Design, Fabrication and Testing	• Select photocatalytic materials for targeted analytes • Demonstrate performance for sensor arrays with targeted chemical analytes • Improve sensor performance
3. Initial Prototype Design Development	• Test VOC sensors with ✓ CONOPS I: Blow-N-Know ✓ CONOPS II: Blow-N-Plug ✓ CONOPS III: Blow-N-Plug+ (Blow-N-Plug with compact separation column installed) • Refine the data processing and drift compensation
4. Downselect and Development of RISE Prototype	• Evaludate and downselecte RISE Prototype
5. Develop Machine Learning Algorithms	• Collect data at the various environmental condition • Evaludating and Implementing machine learing algorithms • Preprocessing data (Standardization and dimensionality reduction) • Selecting proper machine learning algorithm
6. Prototype Testing with Simulated Breath Samples	• Preparing simulated breath based on collected information • Performing in-house bench test
7. Prototype Refinement and Ruggedization	• Refining sensor module and prototype • Improving firmware, integrating and testing the refined prototype • Reruggedizing prototype and improving firmware
8. Conduct Feasibility Study	• Screnning and recruiting testee • Data and statistical analyses
9. Final Report	• Providing test results summary for detailed CONOPs • Providing the information Operational, Reliability, and Maintenance • Delivering an at-scale cost model for commercial deployment

2.1 TASK ONE. *Select VOC Biomarkers and Interferents (N5 90 %, LEVL 10 %)*

In Phase I, we selected 31 breath VOC biomarker candidates. In Phase II, we will down select to 6 ~ 10 breath biomarkers and 2 ~ 3 Interferents to demonstrate feasibility of the RISE system. We will collaborate with LEVL to draw from their expertise in breath analyses. The team at LEVL possess extensive experience in the breath analysis field and their commercial product (breath acetone collection and measurement) is an FDA registered instrument. N5 and LEVL will work to develop the select list of biomarkers indicative of infection and identify potential interferents. We anticipate that at least one VOC analyte per unique chemical functional groups (*e.g.,* acetone for ketone group) will be selected as a potential biomarker based on the Phase I literature survey. Biomarker chemicals, such as those produced from oxidative stress associated with lung inflammation, are high priority candidates.

2.2 TASK TWO. *Breath Sensors Design, Fabrication and Testing (N5: 100 %)*

N5 will utilize its existing materials science toolbox to design an initial array of SPH sensors suitable for detection of VOCs or other biomarkers (as determined in Task 1). Sensor architecture design involves optimization of parameters including doping, thickness, width, length, orientation, and the impact these have on power consumption, signal to noise ratio, response magnitude, minimum detection limit and range. Based on the proposed sensor design, N5 will fabricate VOC

sensors using our well-established process protocol. The process entails: 1) GaN backbone etching, 2) deposition of ohmic contact, 3) deposition of functional layers (*i.e.*, metal oxide semiconductor and metal cocatalyst, and 4) deposition of bond-pad. These sensors will be tested in the laboratory for detection of target VOCs.

2.3 TASK THREE. *Initial Prototype Development (N5 80%, LEVL 20 %)*

Three initial concepts for the RISE breath analyzer are shown in **Figure 1.** The first concept, referred to as "Blow-N-Know", is a handheld device which would only require the user to blow into the device once or twice. This action would then deliver the breath sample directly to the N5 VOC sensor array. This device would be the simplest to operate, and likely the least expensive in production. The second design, referred to as "Blow-N-Plug" is based in part on existing commercial instruments designed for detection of certain metabolites expressed in breath, and relevant to weight control. The center picture in **Figure 1** is a unit developed by the Phase II partner, LEVL. The system operates by the user blowing into a breath sampler, or pod, which is then inserted into the instrument for analysis. Based on intial discussions with LEVL, we believe that breadboard integration of this unit with the N5 sensor array is feasible, and this will be tested in Phase II. This would be a relatively inexpensive and low-risk way to evaluate an alternative CONOPS. The third concept is based on the simple "Blow-N-Know" approach but adds a compact gas separation column similar to those used in gas chromatography. This approach would provide some chemical and temporal separation of the breath components possibly improving the selectivity by reducing interferent effects.

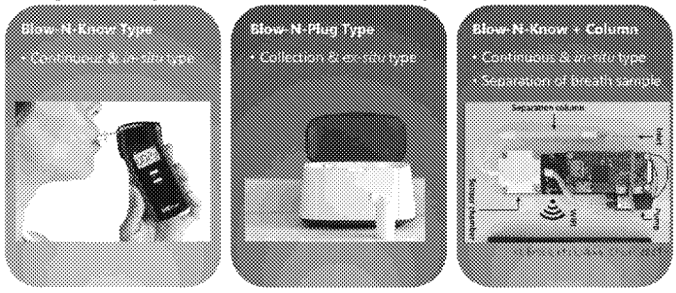


Figure 1. Three design and operational concepts for the RISE breath analyzer.

2.4. TASK FOUR. *Downselect and Development of RISE Prototype (N5: 100 %)*

N5 will down select and specify the final prototype based on evaluation of the three candidates in Task 3 and on the criteria in **Tables 2**. These criteria cover technical, implementation, and commercial adoption considerations. N5 will evaluate the prototype candidates' sensor design, battery life, ability to collect and analyze breath samples, speed of analysis, reliability of outcomes. N5 will also evaluate the commercial viability of each design which would include affordability (*i.e.*, bill of materials), usability by end customers, and ability to detect a wide variety of infections.

Table 2. Feature comparison for three RISE design concepts developed in Phase I. Note, the Estimated Price is based on low volume, pre-production units.

	Blow-N-Know	Blow-N-Plug	Blow-N-Know + Column
Sensor	High-Plex Sensor Array (>10)	High-Plex Sensor Array (>10)	Multi-Plex Sensor Array (2<x<10)
Power supply	Battery	AC 110 V	Battery
Estimated Price/System	500 USD	600 USD	700 USD
Pros	• Hand-held and mobile • Low cost	• Able to control breath sample • More expansion • Larger Computation Power	• Hand-held and mobile • Less computing required • High humidity resistance
Cons	• Loss of sample (dead space stream)	• Pseudo-mobile • High cost	• Loss of sample (dead space stream)

	• Low humidity resistance • Limit of MCU memory		• Longer response time • Additional consumable
Operational Logistics	• Disposable mouthpiece • Stable under ambient condition • Slow turning-over	• Disposable mouthpiece • Stable under ambient condition • Fast turning-over	• Disposable mouthpiece • Need to be regenerated regularly • Slow turning-over
Time to Market	Medium	Fast	Slow

2.5. TASK FIVE. *Develop Machine Learning Algorithms (N5: 100 %)*

N5 Sensors will build upon the results achieved in Phase I by evaluating, implementing, and deploying a robust machine learning algorithm that can efficiently run on a handheld device and accurately predict the presence of VOC markers for infection screening. Two fundamental components are needed to achieve this goal: sensor array testing data sets with VOCs and interferents; and a machine algorithm that can efficiently run in a low-power microcontroller platform. Proven designs exist for the microcontroller platform. The sensor array module will include integrated electronics for the signal processing and classifier stages. Our unique sensor array design combined with a smart machine algorithm will be capable of detecting VOCs in the part per billions (ppb) levels.

2.6. TASK SIX. *Prototype Testing with Simulated Breath Samples (N5: 100 %)*

A comprehensive system test plan will be developed for testing the selected prototype design. The test plan will be used to evaluate the RISE prototypes against performance parameters and system attributes establish in the previous tasks. N5 will work on development of in-house and the external test plans. Most of the prototype testing will be performed at N5 using representative VOC mixtures, and VOCs with interferants. **Table 3** lists the target performance parameters for the prototype RISE system.

Table 3. Target performance of prototype RISE system

Parameters	Performance goal
Key Output	Alert (Positive or negative) with VOC profiles
Response time	< 30 s
Recovery time	< 1 min
Size & Weight	Blow-N-Know: 3 in × 5 in × 1 in (200 g including battery) Blow-N-Plug: 20 in × 10 in × 12 in (4 kg) Blow-N-Know+: 4 in × 5 in × 1 in (300 g including battery)
Power	Lithium ion battery for Blow-N-Know and Blow-N-Know+ AC power supply for Blow-N-Plug
Cost	Blow-N-Know: 500 USD Blow-N-Plug: 600 USD Blow-N-Know+: 700 USD
Maintenance Frequency	Lifetime on the system 10 years, sensor module calibration and replacement per year
Installation Requirements	No special equipment needed, self-sustained devices, self-guided gateway installation

2.7. TASK SEVEN. *Prototype Refinement and Ruggedization (N5: 100 %)*

The purpose of this task is to address sensor and system performance shortcomings prior to the extramural testing with actual breath samples. This will not be a full optimization of all parameters but will be functional modifications consistent with an alpha level prototype.

2.8. TASK EIGHT. *Small-Scale Feasibility Study with Human Breath (N5: 50 %, LEVL: 50 %)*

Based on our initial analysis and after talking to various breath experts, we decided to pursue human breath sample testing. The diagnostic performance of the device will be evaluated using breath samples from human volunteers. With LEVL, N5 proposes to conduct a feasibility study with 35 COVID-19 positive and 15 COVID-19 negative subjects (~2-to-1 ratio). Aligned to DHS's objectives, the goal of this feasibility study is to confirm and validate RISE's performance with human breath samples to prove our concept. Completion of this goal will result in a proof-of-concept prototype and design which DHS can use to detect viral infections (*e.g.*, COVID-19) in public areas, such as airports. We anticipate RISE will offer a faster, more reliable, and affordable method to identify infected individual in public areas. Thus, N5 will also perform an analysis to evaluate the time and costs of diagnostic performance and evaluation between the RISE device and standard methods (e.g., PCR testing). Prior to recruitment of volunteers, the study will be approved by an Institutional Review Board (IRB; TBD) to meet the requirements detailed in Federal Policy for the Protection of Human Subjects and in accordance with DHS Management Directive Number 026-04, as set forth in 45 C.F.R. Part 46 (Subparts A-D). Dr. Anderson (LEVL) will design the human-breath study, and the location will be determined after Phase II award. LEVL has relationships with a number of hospitals across the US such as University of Washington, University of Maryland, and Providence North West. This is a minimal risk study with the outcomes not benefiting nor harming participants in any way. No adverse events are expected due to the nature of the study. All participation is voluntary, and participants may drop out at any time. We will do our best to recruit participants based on a variety of ages and cultural backgrounds to be representative of the targeted population group.

2.9. TASK NINE. *Final Report Production (N5: 100 %)*

N5 will deliver a final report that will summarize the following for the down-selected design (**Table 4**).

Table 4. N5's Phase II final report with key items.

Design and Performance Benchmarks	Sensor design specifications; design selection
Test Results Summary	Results of internal and external testing
Detailed CONOPs	Detailed, updated CONOPs for the down selected design Document system design (sensor/hardware/firmware/software) for technology transition
Operational, Reliability, and Maintenance	Full report describing the issues and risks of the design in full commercial deployment

N5 will also deliver an at-scale cost model for commercial deployment that will include the major items listed in the table and projected cost breaks at production volumes (**Table 5**).

Table 5. Cost Model Parameters

Unit Volume / Cost Breakdown	1 - 100	100 - 1000	1000 – 10,000	10,000 – 50,000	> 50,000
Unit Cost	Working with production and assembly to develop price breaks				
Add-On Battery Module	Working with a supplier to estimate price breaks				
Replacement Sensor Module	Based on replacement frequency determined during the program				
Maintenance and Calibration (per year, per unit)	Based on replacement frequency determined during the program				
Training	Training per user and maintenance				
Storage	Standard storage in room conditions				

3.0 DELIVERABLES

Task#	Task Description	Deliverables	Specific Due Date	Payment upon Delivery
1	Monthly Status Report	Monthly Status Report	10th of every Month	
2	Monthly Meeting	Monthly Status Meeting	15th of every Month	
3	Select VOC Biomarkers and Interferents	Report detailing our downselecting final biomarkers and interferents	4/20/2022	250,000 $
4	Breath Sensors Design, Fabrication and Testing	Report explaining N5's sensor modules development and their testing results. The report will highlight the sensor performance for each selected VOC analyte	11/20/2022	50,000 $
5	Initial Prototype Design Development	Report detailing initial prototype design development and testing results of each CONOPs device	12/20/2022	50,000 $
6	Downselect and Development of RISE Prototype	Report detailing breath analyzer types selected for feasibility demonstration in phase II. The report will highlight the performance and evaludation for conducting feasibility study	3/20/2023	150,000 $
7	Develop Machine Learning Algorithms	Report containing the test results for machine learning algorithm based on performance metric, computational requirements, and cost of implementations	9/20/2022	100,000 $
8	Prototype Testing with Simulated Breath Samples	Report containing the testing results of selected prototype with simulated breath samples	6/20/2023	100,000 $
9	Prototype Refinement and Ruggedization	Report detailing the prototype refinement and ruggedization	9/20/2023	100,000 $
10	Conduct Feasibility Study	Report containing the demonstration of feasibility with actual breath samples.	2/20/2024	100,000 $
11	Final Report	Report detailing our finding and research strategy for Phase III. It includes the original purpose, approach, results, and conclusions of the work performed under this Agreement	3/20/2024	99,991.32 $