



*i*Diagnostics® for all

A SAFETY NET FOR HUMANITY

Precision Molecular Diagnostics for Home Use
Altruistic Project

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Efficient Infrastructure for Biological Safety Is Necessary to Prevent Pandemics



Rapid Precision Diagnostics and Proactive Intelligence Are Front Lines of Biological Safety

Current COVID-19 pandemic has demonstrated the necessity of infrastructure that would prevent and localize outbreaks of infections. In 2008-2016, many scientists foresaw the pandemics and stimulated the US Government to create such infrastructure with proactive intelligence and advanced diagnostics as its critical frontlines [see 2016 PCAST letter to US President, Ref. 1, www.i-diagnostics.net]. However, the Government disregarded this necessity. Not surprisingly, Bill Gates, who invested millions of dollars in diagnostics, recently stated that “... *most COVID-19 tests in the US are 'completely garbage' because it takes too long to get results*” [1, 2].

The pandemic showed that the world needs new paradigm of biological safety. Fast, accurate, home-use tests are of great necessity and importance for biological safety. However, it is too difficult, if not impossible to create such diagnostics at the avenue of for-profit endeavors.



Natural and Artificial Pandemics

Biotechnology challenge: The power of biotechnologies (e.g. DNA manipulation, synthetic biology, etc.) is sufficient for self-eradication of humanity. Production and weaponizing of biotech products will be soon available to millions. Turchin et al. (2018) published a paper with the harrowing title “*Artificial Multipandemic as the Most Plausible and Dangerous Global Catastrophic Risk Connected with Bioweapons and Synthetic Biology.*” (see [3] and Ref. 11 at www.i-diagnostics.net). They suggest that biohackers is the most likely source of a bacterial or viral pathogens capable of rapid and global biological catastrophe.

In recent years, naturally occurring infectious diseases have also become far more resilient to treatment and prevention as they develop resistance to standard antibiotic medications. The best way to stop natural and artificially-born pandemics is through proactive steps that include early and accurate diagnostics and isolation of exposed individuals. However, the current diagnostic tests for diseases are too slow, inaccurate, and require “off-line” analysis at centralized settings. By the time the lab results are ready, the disease could have spread to thousands of others.

Problems with the Current Diagnostics



Tests are expensive
E.g. PCR test for COVID-19 costs \$1,800.



Tests are slow
In the US, average turnaround time is 1-3 days.



Tests are inaccurate
Too high rate of false negative and false positive results.

iDiagnostics – Critically Necessary Safety Net for Humanity Revolutionary New Approach for Biological Safety



TIRF Labs, founded by an internationally recognized expert in biological technologies and biodefense, Dr. Alexander Asanov, has invented and prototyped a platform technology, iDiagnostics, which is exceptionally well-suited for the envisioned biosafety infrastructure. In 1999-2018, Alexander served as the Principal Investigator on BAA and SBIR grants awarded by the US Government totaling \$4.3M. He assembled a team of scientists and engineers, who developed unique analytical techniques for molecular diagnostics, a family of advanced Total Internal Reflection Fluorescence (TIRF) instruments [www.tirf-labs.com]. TIRF Labs pioneered several ground breaking discoveries and accumulated a unique experience in using the TIRF technique for life science applications. Over 200 research groups worldwide acquired TIRF products, generated unique research data and published articles in leading scientific journals.

We inquire your help for special funding of our iDiagnostics project, or/and for promoting the project to The Giving Pledge members or similarly situated individuals. This project does not pursue a for-profit objective. Our goal is to make rapid and accurate home-use diagnostics available and affordable to everyone.

Along with the uniquely advantageous platform technology, the project offers revolutionary new approach of Open Innovation Business Model, which will combine the collective knowledge and innovations of the entire diagnostics community. Global efforts on iDiagnostics project will lay the foundation for several lines of biological defense, the necessary infrastructure, technologies and networks to prevent and combat existing and emerging infections.

*i*Diagnosics - Accurate and Rapid Tests for Home-use to Prevent and Combat Natural and Man-made Epidemics



Our goal is to make *i*Diagnosics devices available and affordable to every family on the globe. Accurate, rapid, personalized, yet affordable molecular diagnostics for home use will improve many aspects of healthcare and enable a multitude of related applications. *i*Diagnosics unsurpassed accuracy comes from its ability to detect a panel of biomarkers of several classes simultaneously, including proteins, nucleic acids, and metabolites with ultimate sensitivity *down to single molecules*. *i*Diagnosics[®] is robust, inexpensive (~\$100/\$1-5) and user-friendly for home-use, similar to the pregnancy strip test.

- *i*Diagnosics[®] provides a unique solution that allows citizens worldwide to test themselves at home for pathogens and diseases.
- Our open-source innovation business model allows for the rapid development of new testing kits in the event of novel, natural or artificial pathogens.





Powerful Combination of High Sensitivity, Accuracy, Speed, and Affordability

iDiagnostics is a platform technology, where the information about new pathogen can be “dropped in” to start volume manufacturing of diagnostic tests in a matter of several hours.

Distinctive Features of iDiagnostics Project

- *Super-sensitive detection of proteins, DNA/RNA, metabolites, and selected chemical agents.*
- *Simultaneous multiplexed detection of up to thousands of molecular markers in a small sample of biological fluids, including saliva, sputum, urine, and whole blood.*
- *Many important biomarkers do not endure shipping and certain sample preparation procedures. iDiagnostics[®] allows to perform analyses at the point-of-care.*
- *No or minimal sample preparation is necessary to perform the test.*
- *iDiagnostics development tools are available to the entire diagnostic and R&D community.*
- *Open Innovation Business Model will involve up to 40,000 research groups.*
- *Several thousands of healthcare, agricultural, environmental, and other applications.*



How *i*Diagnosics Works?

The underlying technology of *i*Diagnosics uses the principles of real-time TIRF microarrays to simultaneously detect four classes of molecular markers – DNA, RNA, proteins, and metabolites in bodily fluids such as saliva, urine, sweat, blood, and other fluids.

Preparation

A biological fluid, e.g. blood, urine, saliva flows over the microarray of bioassays. Each bioassay contains an affinity molecule or complex, which specifically binds only a specific target biomarker, which results in de-quenching or emerging of fluorescence.

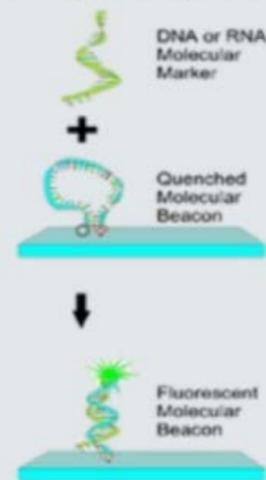
Detection

Excitation light propagates inside the TIRF slide reflecting from the top and the bottom. A microarray of bioassays is printed. If a biomarker is present, respective spot of the microarrays fluoresces, and the fluorescence is detected by low-light cellphone camera.

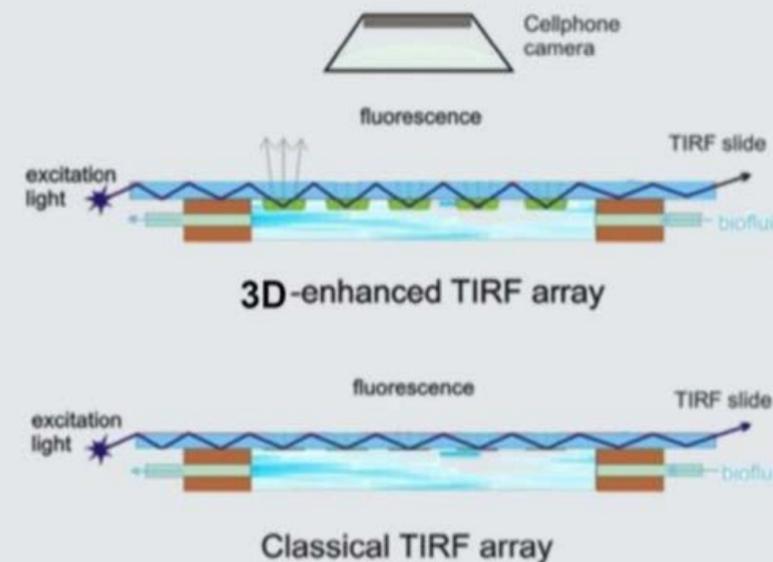
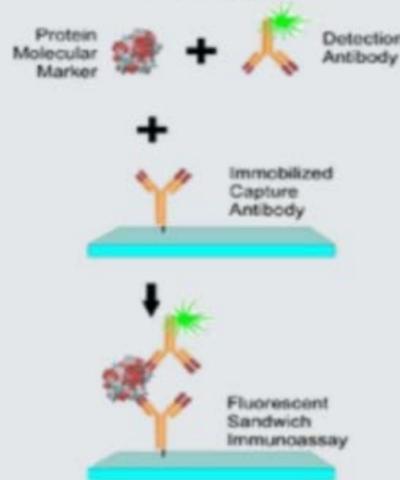
Analysis

The kinetics of fluorescence response is analyzed by *i*Diagnosics app; concentrations of multiple bio-markers are derived; the data are combined with clinical symptoms entered into the app; and in 5-10 minutes after applying the sample, test results are reported.

Molecular Beacon Assay



Immunoassay



Principles of *i*Diagnosics are described at the URL http://www.i-diagnostics.net/tirf_technology.html



Why is *iDiagnostics* so Uniquely Advantageous?

The answer lies in the phenomena of Total Internal Reflection and the Evanescent Wave, the main actors in real-time TIRF microarrays, the underlying technology of *iDiagnostics*.

- *These phenomena provide exceptional surface selectivity and enable TIRF with the ultimate limit of detection - down to single molecules.*
- *TIRF is capable of detecting a multitude of molecular markers of four classes simultaneously, a feature not found in any other technology.*
- *TIRF microarrays require minimal-to-no sample preparation.*
- *Results are obtained in a matter of 5-10 minutes.*
- *This supersensitive, accurate and rapid technology, can be downsized to an inexpensive handheld device for home-use. The projected cost of the *iDiagnostics* cradle is \$100, while disposable cartridges are anticipated to cost \$1-5.*
- *We are not aware of other technology that could be as sensitive, accurate, and rapid, can detect all four major classes of biomarkers, and yet be affordable.*



- Our progress in TIRF microarray biosensor development spanned from large bench-top instrument through portable sensors to small handheld devices.
- In 2013, we discovered that silk fibroin enhances the fluorescence of TIRF microarrays so that we can use a cellphone camera instead of expensive cameras. This patent-pending discovery has been incorporated into *iDiagnostics*.

*i*Diagnosics Applications

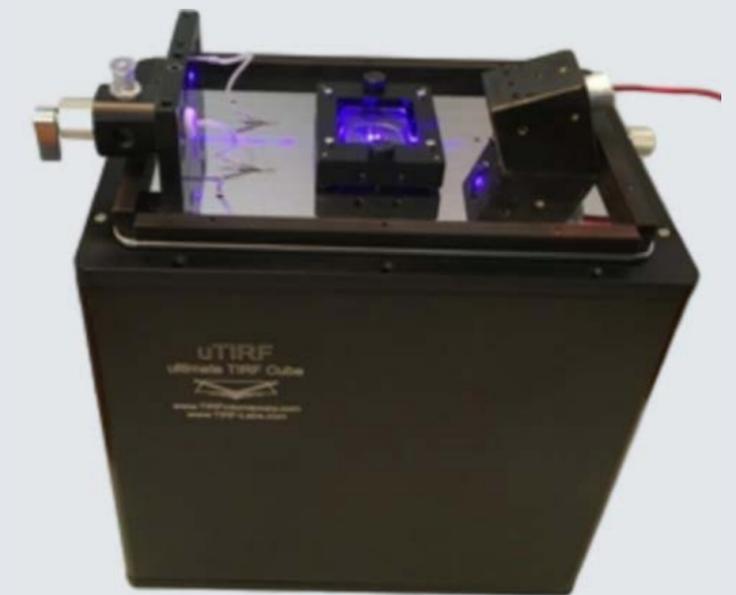
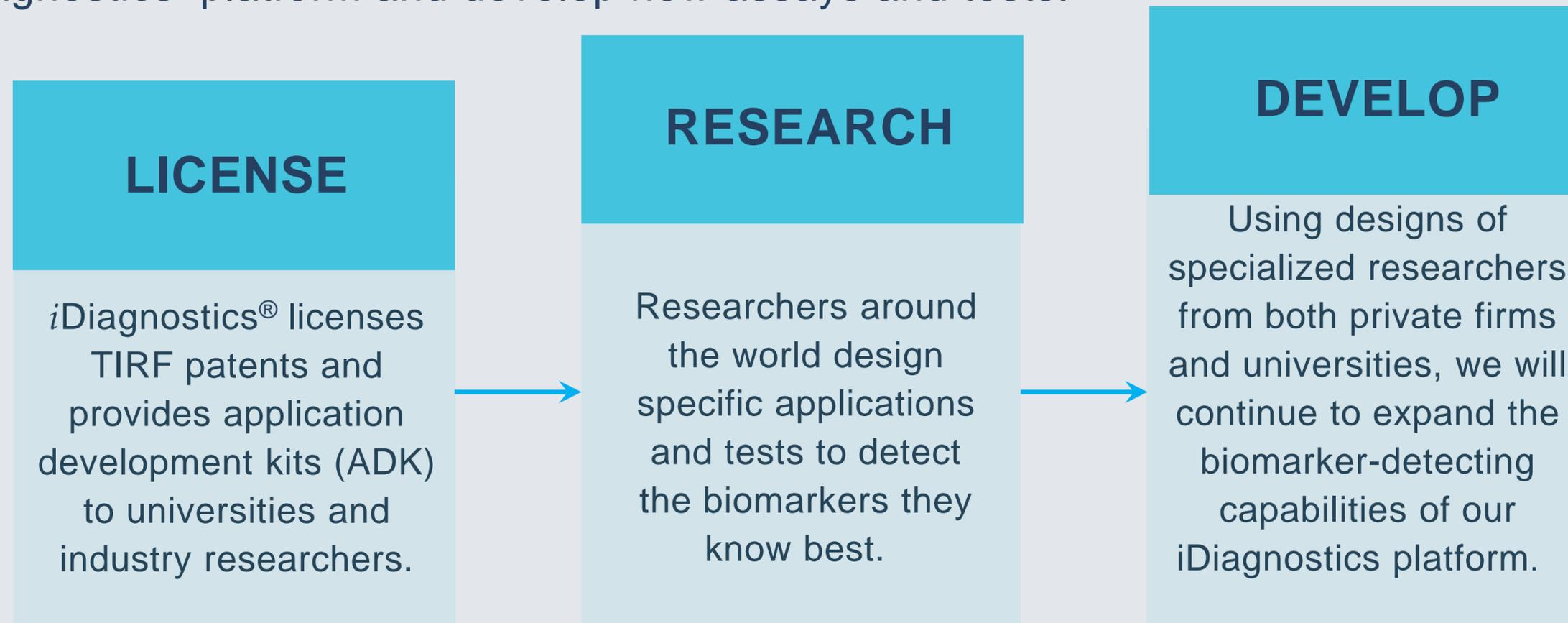


- ✓ *Prevention of pandemics and epidemics*
 - ✓ *Diagnostics of infection diseases: SARS, influenza, Ebola, HIV, Zika, STDs, etc.*
 - ✓ *Diagnostics and prognosis of cancer*
 - ✓ *Diagnostics and prognosis of cardio-vascular diseases*
 - ✓ *Diagnostics and prognosis of Alzheimer's and other neurological disorders*
 - ✓ *Drug development studies*
 - ✓ *Longevity studies and popular efforts*
 - ✓ *Food and water safety applications*
 - ✓ *Military and civil biodefense applications*
 - ✓ *Forensic applications*
 - ✓ *Environmental applications*
 - ✓ *Agricultural analyses and studies*
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- As soon as *i*Diagnosics becomes popular, many routine analyses of blood, urine and other bodily fluids that currently are performed in clinical labs, will migrate to the *i*Diagnosics device.
 - Along with the main goal of home-use, family doctors, cardiologists, dentists, first responders, pharmaceutical companies, food safety, agriculture, and environment protection specialists have expressed their interest in using *i*Diagnosics for their applications.
 - There are thousands of new applications that can be developed for the *i*Diagnosics platform.



Open Innovation Business Model

Open Innovation Business Model will be used in this project to stimulate the exchange of Intellectual Property (IP) between collaborators. TIRF Labs is an integral part of diagnostics research community. We have supplied our advanced TIRF instruments to over a hundred of research groups worldwide and have created the prototype of the network which will lay the foundation for an extended biological safety network, which is of paramount importance for the envisioned infrastructure. TIRF Labs has already practiced OIBM, supplied the iDiagnostics development tools to several research groups and received enthusiastic responses from them. We will supply to R&D community patented technologies, unique hardware, software, cartridge blanks, development tools, reagent kits, methods and protocols to help to interface existing bioassays with the iDiagnostics platform and develop new assays and tests.



Development tool: uTIRF station



Funding, Research Network Expansion, and R&D Goals

In 2014, the US DOD performed an exhaustive survey of molecular diagnostic methods and ranked high an earlier prototype of iDiagnostics for both biological and chemical detection. To date, we believe iDiagnostics holds a unique combination of features that keeps the technology unrivaled.

To further develop the applications of *iDiagnostics*, to refine the prototype for home use, and to lay the foundation for the biological safety network, TIRF Labs is seeking \$24 million. This project does not pursue a commercial goal. We envision a large social impact of our endeavor and address our request for funding to The Giving Pledge members and similarly positioned individuals. We also address our appeal to the US government. The mission of this project is to create diagnostic tools for biological safety infrastructure by making the handheld precision diagnostics available to everyone. It is essential for combating current and preventing future pandemics.

The significance of this project goes beyond the scope of medical diagnostics. Together with the envisioned handheld diagnostics, we are already offering to the research community the entire line of instruments, development tools, methods, protocols and suppliers that facilitate all stages of diagnostics development. If funded, this project will create not only a network of scientists and engineers, consolidating efforts of international teams in the framework of the Open Innovation Business Model. The project will also unite medical doctors, other healthcare professionals, administrators, businessmen, and grassroots enthusiasts, creating the powerful infrastructure for biological safety.

Business Plan Outline



Phase 1

Phase 2

Project launch

Manufacture Application Development Kit (ADK)

Design and prototype *i*Diagnostics cradle and cartridge

Raise \$18 million for Phase 1 efforts

18-24 months

Distribute ADKs

License patents and facilitate IP exchange

Finalize design for *i*Diagnostics cradle and cartridge

36 months

Integration of new arrays and diagnostics panels

Raise \$6 million for Phase 2 – manufacturing and integration

48 months

Large-scale manufacturing and distribution of *i*Diagnostics cradle and cartridges for 12-20 applications including SARS, other infectious diseases.

Panel of ~30-40 assays for personalized treatment of COVID-19

Phase 1 Deliverables: TIRF Labs will supply the uTIRF station and *i*Diagnostics Application Development Kit (ADK), supplies, manuals, protocols, reagent kits, cartridge blanks, sample prep modules to other research groups that are developing molecular diagnostic applications. The ADK and uTIRF will facilitate assay development, creating panels of biomarkers, and pre-clinical testing.

Phase 2 Deliverables: TIRF Labs will start manufacturing hand-held *i*Diagnostics devices and begin supplying them to all interested parties, including general public.

Deliverables and Costs



Home Use

Laboratory Use

~ \$100



iDiagnostics® Cradle

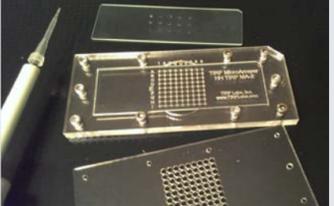
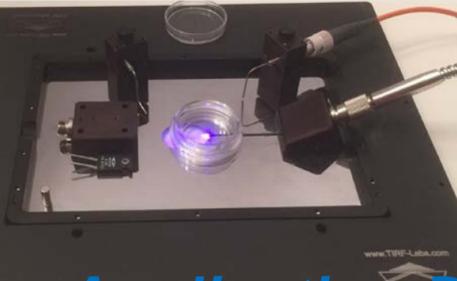


uTIRF mini-station

\$1-5



Disposable microarray cartridges



Application Development Tools

TIRF Labs' Team and Principal Investigator



TIRF Labs' team is described at URL: www.i-diagnostics.net/about.html.

The Principal Investigator, Dr. Alexander Asanov, held academic positions at the Institute of Chemical Physics, Russian Academy of Sciences (RAS), the University of Alabama at Birmingham, and Mississippi State University. He received an M.S. degree in Biophysics from the Moscow Institute for Physics and Technology, and a Ph.D. degree in Chemical Physics from the Institute of Chemical Physics, RAS. His Ph.D. advisor was a Nobel Prize laureate academician N. N. Semenov.

Dr. Alexander Asanov has a broad background in spectroscopy, electrochemistry, molecular biology, cell biology, nanoengineering, chemistry and optics, which represent the key areas for the *i*Diagnosics project. He has led successful R&D projects in the field of molecular diagnostics, and believes he is well suited to lead the proposed project. He endeavors to give back to society and believes that this altruistic project is the way of demonstrating his gratitude to America and to the world.

Dr. Asanov's scientific biosketch URL: www.i-diagnostics.net/Biosketch_Alexander_Asanov2020.pdf

PUBLICATIONS AND AWARDS

50+ articles published in scientific journals.

\$4M+ US Government awards in BAA and SBIR R&D grants.

RESEARCH AREAS

TIRF Spectroscopy, TIRF Microscopy, Electrochemistry, Molecular Engineering, Nanotechnology, Optical Engineering.

FDA Compliance, Literature, Contact Us



TIRF Labs complies with all FDA guidelines for medical device manufacturers.

We adhere to the following FDA guidance:

- Medical Device Software Guidance and Requirements
- Design Considerations for Devices Intended for Home Use
- Guidance for Molecular Diagnostic Instruments with Combined Diagnostic and Research Functions.

LITERATURE:

1. Wired, Science, Bill Gates on COVID: Most US Tests Are 'Completely Garbage', Retrieved 2020, August, from <https://www.wired.com/story/bill-gates-on-covid-most-us-tests-are-completely-garbage/>
2. Business Insider, Bill Gates says most COVID-19 tests in the US are 'completely garbage' because it takes too long to get results, Retrieved 2020, August, from <https://www.businessinsider.com/bill-gates-covid-tests-us-completely-garbage-2020-8>
3. Turchin A., Green B.P., Denkenberger D., "Artificial Multipandemic as the Most Plausible and Dangerous Global Catastrophic Risk Connected with Bioweapons and Synthetic Biology", Foundation for Longer Life, Moscow, Global Catastrophic Risk Institute, Tennessee State University, Santa Clara University, 2018, Retrieved 2020, August, from <https://philpapers.org/rec/TURAMA-3>

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