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| **TRL-0** | A perceived need or possible desired outcomes has been broadly described and a possible approach to satisfying the need or achieving the desired outcomes is conceived. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | The need to develop vaccines faster without having to grow weakened forms of a virus and the possibility that mRNA can be used to accomplish the objective. |  | The need to detect hemorrhages earlier than the current standard of care to enable faster intervention and the possibility that an approach based on monitoring peripheral blood flow and blood content can accomplish the objective. |  | The need to address drinking water scarcity and the possibility that water can be extracted from the air to accomplish this objective. The need to make cleaning water filtration membranes easier and the possibility that a different water filtration membrane could achieve this objective. |
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| **TRL-1** | How one or more phenomena might be applied to achieve a specified end are broadly described but it is not entirely clear that the approach will work. Basic principles are identified. Efforts are started to translate basic principles into a technology solution to satisfy the need and achieve the desired outcomes. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | Review of the related literature and drugs currently available in the market or in clinical trial provide evidence to suggest that the solution approach is worth pursuing. As an example, research discussed in the literature suggesting that modified mRNA could be used to create vaccines against various viruses and bacteria without concern about low stability or strong immunogenicity. |  | Review of the related literature as well as devices and methods currently in use or in clinical trials provide evidence to suggest the solution approach is worth pursuing. As an example, research discussed in the literature that suggests hemodilution can be detected noninvasively. |  | Review of the related literature and solutions currently available on the market or in development provide evidence that the solution approach is worth pursuing. As an example, literature that suggests that graphene oxide nanocomposites could be applied to water filtration. Another example is literature suggesting that heat exchange principles could be scaled and used to extract clean drinking water from air. |
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| **TRL-2** | The technology has been formulated in some detail and there is *prima facie* evidence to suggest that it might work. However, the proposed technology is still speculative. There is not yet sufficient experimental proof or detailed analysis to support the conjecture that there is a better than random chance that the proposed technology will work. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | A target indication is identified, and preliminary conceptual analysis has been conducted. As an example, identification of COVID-19 as a target indication and development of the basic approach for using mRNA to create a vaccine against the virus that causes it. |  | A target indication is identified, and preliminary conceptual analysis has been conducted. As an example, identification of postpartum hemorrhage as a target indication and a conceptual design of a device for identifying postpartum hemorrhage based on monitoring peripheral blood flow and blood content. |  | Preliminary conceptual analysis has been conducted. As an example, sketching of a working scheme for a crumpled graphene-based reactive filtration membrane. Another example is a conceptual sketch of a heat exchange system for extracting clean drinking water from air. |
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| **TRL-3** | Theoretical analyses or small-scale experiments on key aspects of the solution approach have been conducted to provide insight into whether the technology might work, and results are promising. Analytical studies setting the technology into an appropriate context and laboratory-based studies to demonstrate that the analytical predictions regarding the technology are correct have been done. These studies and experiments constitute “proof-of-concept” validation of the proposed technology solution. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | *In silico* analysis, laboratory experiments, or Fermi estimates. As an example, an *in silico* immune simulation of a potential vaccine against Mycobacterium tuberculosis. Another example is experiments showing that PI3K/phosphate and fungi homology deleted on chromosome 10 (PTEN)/AKT/TSC pathway (a signaling pathway in which gene mutations can lead to malignant tumors) is the main activator of mammalian target of rapamycin complex one (mTORC1), which regulates cell growth and metabolism. |  | *In silico* analysis, laboratory experiments, or Fermi estimates. As an example, laboratory experiments that demonstrate the available optical technologies can be used to noninvasively measure blood flow and blood content to detect postpartum hemorrhage. As another example, in the course of developing nerve stimulation technology to manage various diseases by excitation or inhibition of the sympathetic nervous system, experiments are conducted on rats to demonstrate that the sympathetic nerve can be stimulated from at least 4 mm away, but the experiment does not demonstrate treatment of a specific disease. |  | *In silico* analysis, laboratory experiments, Fermi estimates, or conceptual designs as necessary. As an example, experiments demonstrating that a single-step aerosol method can be used to synthesize crumpled nanocomposites of crumpled graphene oxide (CGO) and that a variety of functional materials can be incorporated via encapsulation. Another example is calculations that show the performance requirements of a heat exchange system for extracting clean drinking water from air are attainable. |
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| **TRL-4** | A low fidelity prototype or demonstration of the technology comprising the main components has been sufficiently tested in a laboratory environment with promising results, but the prototype contains imperfections that are unwanted or unacceptable in a final technology solution. The basic technological elements are integrated to establish that the “pieces” will work together to achieve concept-enabling levels of performance. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | In vitro studies conducted. As an example, an in vitro study showing that the antibodies from people who have received the Pfizer-BioNTech COVID-19 vaccine effectively neutralize SARS-CoV-2 with a key mutation that is also found in two highly transmissible strains. Another example is an in vitro study demonstrating that alpha nucleotidyl transferase (HT) enzymes have high potential as anti-Cryptococcus neoformans agents. |  | Laboratory proof-of-concept prototype constructed and sufficiently tested. As an example, a rudimentary hemodilution detection device for noninvasively detecting postpartum hemorrhage that is fabricated from off-the-shelf components and demonstrates the key functionality of noninvasively measuring blood flow and blood content but lacks the desired form of the envisioned device and certain functionality such as remote monitoring. |  | The problem or need and desired outcomes have been validated with a clearly specified target user and a laboratory proof-of-concept prototype has been constructed and sufficiently tested. As an example, a benchtop demonstration system that shows crumpled graphene oxide nanocomposites encapsulating titanium dioxide (TiO2) and silver (Ag) can exclude a model organic and a model protein and maintain the minimum required water flux for a commercial application. Another example is a prototype heat exchange water extraction system constructed from off-the-shelf components that demonstrates the desired functionality but is not in the envisioned final form. |
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| **TRL-5** | A sub-scale research prototype of the solution comprising the key features, basic form, and desired functionality of the envisioned technology has been sufficiently tested in a simulated environment and results are promising. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | Drug targets, hit compounds, and lead compounds have been identified and the delivery mechanism has been designed. As an example, a study for developing a vaccine for Mycobacterium tuberculosis (Mtb) that shows the compound 4-Aminoquinolone piperidine amides targets DprE1 and has good solubility, strong activity against replicating Mtb, and an acceptable secondary pharmacological profile. |  | The risk classification and the approval pathway are determined, and a preclinical research prototype has been constructed and sufficiently tested in simulated environment. As an example, a refined prototype of a hemodilution detection device for noninvasively measuring blood flow and blood content to detect postpartum hemorrhage that is in the form of the envisioned device and demonstrates all the functionality of the envisioned device. |  | The solution has been validated with target users and a research prototype has been constructed and sufficiently tested in a simulated environment. As an example, a commercial grade crumpled graphene oxide nanocomposite water filtration membrane is produced in a one-off batch process and tested in the laboratory. Another example is a one-off prototype heat exchange water extraction system that is in essentially the envisioned form and exhibits all intended functionality is constructed and tested in the laboratory. |
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| **TRL-6** | A high-fidelity full-scale research prototype close to the final form and functionality of the envisioned technology has been sufficiently tested in a relevant environment under stringent controls and results are promising. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | *In vivo,* *ex vivo,* or *in situ* study with a small number of subjects or multiple comparative studies. As an example, a study in which new lipid nanoparticle mRNA COVID-19 vaccine candidate protected 70 percent of mice expressing the human angiotensin-converting enzyme 2 (ACE2), while all the non-vaccinated mice died. |  | Preclinical research prototype constructed and sufficiently tested on suitable models or in a simulated environment. As an example, a refined prototype of a hemodilution detection device for noninvasively measuring blood flow and blood content to detect postpartum hemorrhage that is in the form of the envisioned device, demonstrates all the functionality of the envisioned device, and is tested in a swine model of hemorrhage. |  | A refined research prototype has been constructed and sufficiently tested in a simulated environment. As an example, in developing a crumpled graphene oxide nanocomposite water filtration membrane a demonstration of in situ synthesis of nanoscale silver (nAg) particles by crumpled graphene oxide titanium dioxide (GO–TiO2 or GOTI) nanocomposites as an approach to generate and regenerate enhanced antimicrobial activity over extended operation times. |
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| **TRL-7** | A high-fidelity pre-production prototype with the complete form and functionality of the envisioned technology has been sufficiently tested in an intended environment under necessary controls and the results are promising. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | Phase I and Phase II clinical trials in process. As an example, a Phase I trial of a compound for the potential treatment of obesity that comprised 41 subjects and demonstrated the safety, tolerability, and clinical effect of single and multiple doses as well as escalating doses of the compound. Another example is a Phase II trial of an adenosine triphosphate-competitive and reversible inhibitor of aurora kinase A that comprised 91 subjects with endocrine-resistant, HER2-negative metastatic breast cancer who were previously treated with fulvestrant, which demonstrated the efficacy, response rate, and optimal dosing regimen of the treatment. |  | Manufacturing processes and practices defined and tested. A preproduction prototype has been refined as necessary, undergone design verification, and constructed using defined manufacturing processes and practices. |  | A pre-production prototype with the complete form and functionality has been constructed and sufficiently tested in an intended environment. As an example, manufacturing processes for a crumpled graphene oxide nanocomposite water filtration membrane is defined and pre-production units are produced, and field tested. Another example is the manufacture of pre-production units of a heat exchange water extraction system using the specified production processes and field testing of the system in an arid location. |
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| **TRL-8** | A production unit with the complete form and function of the envisioned technology has been sufficiently tested in an intended environment and results are promising. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | Phase III clinical trials in process. As an example, a Phase III trial of a prostate cancer treatment that targets androgen receptor signaling which comprised 1,311 subjects with metastatic castration-resistant prostate cancer (mCRPC) and demonstrated the radiographic progression-free survival (rPFS) and overall survival (OS) improved to a statistically significant degree. |  | The medical device validation plan is completed. Validation testing of a production prototype is being performed to provide the necessary evidence to evaluate the safety and effectiveness of the device required for the approval pathway. |  | A production unit has been produced using the manufacturing processes and practices and sufficiently tested in an intended environment. As an example, a production unit of a heat exchange water extraction system is field tested at a camp in the Mojave Desert. |
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| **TRL-9** | The technology is ready to be implemented in an intended environment or introduced to the market. | | | | |
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|  | **Examples – Medical Drugs** |  | **Examples – Medical Devices** |  | **Examples – Non-Medical** |
|  | Ready to prepare and submit new drug application (NDA) to the U.S. Food and Drug Administration (FDA). |  | Ready to prepare and submit application to market medical device to the public to the U.S. Food and Drug Administration (FDA). |  | A production model is ready to be implemented in an intended environment. Only minor fixes or changes to address small, non-critical problems identified following market introduction. |