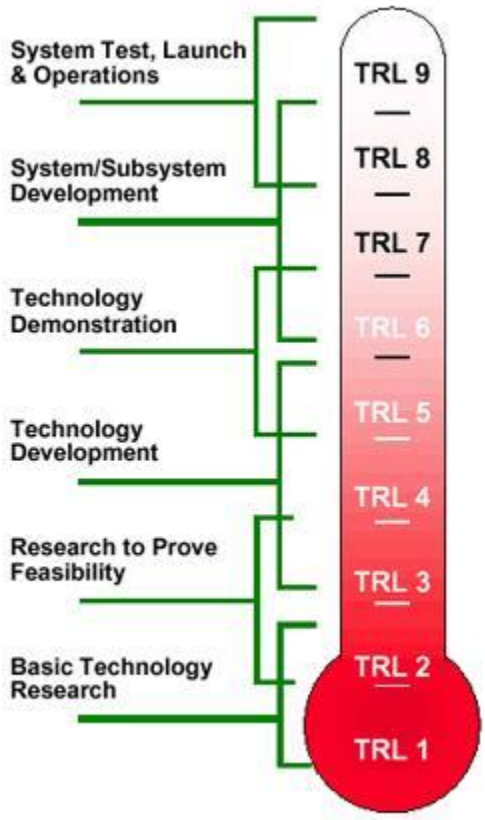
TECHNOLOGY READINESS LEVELS (TRLs)

Technology readiness levels (TRLs) is a measure of estimating technology maturity of core technologies in a program during the selection process and in subsequent monitoring and evaluation phases until these technologies, or products utilizing them, attain market readiness. Originally introduced by NASA, the TRL scale is a metric with nine technology readiness levels for describing the maturity of a technology from ideation stage (TRL-1) to highest degree of application/commercial readiness (TRL-9). Levels in between covers establishment of proof of concepts, prototype developments, functional validations from models to real operational environments and clearances of mandatory regulatory barriers between levels towards market introduction of these technologies/products.



NASA Technology Readiness Levels

References:

a.) Gustav Notander, EIT Health, European Union (Technology Readiness Levels – TRL-NASA's contribution to Horizon 2020.

b.) Technology Readiness Assessment (TRA) Guidance. U.S. Department of Defense, (2011).

c.) Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India (2016), Department of Biotechnology, India.
d.) The TRL Scale as a Research & Innovation Policy Tool-EARTO Recommendations (2014).
e.) TRL-NASA ESTO (https://www.nasa.gov/pdf/458490main_TRL_Definitions.pdf).
f.) Banke, J., August 20, 2010, Technology Readiness Levels Demystified, NASA.
g.) Crop Research Technology Readiness Level (TRL)(2016)-United State Department of Agriculture National Institute of Food and Agriculture Institute of Food Production and Sustainability.

Technology Readiness Levels Required for Applications

Sl. No	Thematic Area	Stage	Required TRL	Definition
1	Drugs (including Drug Delivery)	Proof of Concept Established	TRL-4	Efficacy,& safety of candidate drug formulation is demonstrated in a defined animal model (Results of formulation studies, pharmacokinetic studies & ADME , PD , safety of candidate formulations at preliminary level and efficacy in *in-vivo* disease model)
2	Regenerative Medicine	Proof of Concept Established	TRL-4	Candidate Optimization and Non-GLP *in vivo* Demonstration of Activity and Efficacy **Animal Models:** Initiate development of appropriate and relevant animal models(s) for the desired indications and perform non-GLP *in vivo* toxicity and efficacy. **Assays:** Initiate development of appropriate and relevant assays and associated reagents for the desired indications. **Manufacturing:** Manufacture laboratory scale (non-GMP) quantities of bulk product and proposed formulated product. Demonstrate non-GLP in

				vivo activity and potential for efficacy consistent with the product's intended use (i.e., dose, schedule, duration, route of administration and route). Conduct initial non-GLP toxicity studies and determine pharmacodynamics and pharmacokinetics and/or immune response in appropriate animal models (as applicable). Initiate experiments to determine assays, parameters, surrogate markers, correlates of protection and endpoints to be used during non-clinical and clinical studies to further evaluate and characterize candidate(s).
3	Vaccines	Proof of Concept Established	TRL-4	Efficacy & safety of vaccine candidate is demonstrated in a defined animal model (Results of serological studies in different animals at preliminary level and efficacy in defined *in vivo* model, Manufacturing and QC release of vaccine for Studies, Scale up Development).
4	Clinical Trials	Early Stage Validation	TRL-5	Pre-clinical studies including GLP efficacy, acute and chronic toxicity, all the studies mandatory for safe exposure to humans such as repeat dose toxicity (RDT) and safety in animal model producing sufficient data for DCGI application for clinical trials.
5	Devices & Diagnostics	Proof of Concept Established	TRL-4	<u>Medical Devices/Diagnostic Devices:</u> Functional Prototype developed by integration of different

				modules and safety, efficacy and performance of candidate device or system demonstrated in a defined laboratory, Simulated Environment or animal model (with Institutional Animal Ethics Committee approvals). Diagnostic Kits: Optimized core components integrated into the kit or platform (Microfluidics/ filter paper/ LFA etc) along with the reagents to come up with a functional prototype of the kit. Integrated system tested in house with metabolite, serial dilution or ELISA or spiked biological samples. Biomedical Implants: Material safety and or imaging compatibility proven in *in vivo* small animal model study (with Institutional Animal Ethics Committee approvals). Functional Prototype implant device developed as per the design in a near GMP condition. Sterilization and packaging established.
6	Bioinformatics	Early Stage Validation	TRL-5	Developed software technologies to integrate with different aspects of existing system; Developed software technologies implementations conform to target environment interfaces; experiments with realistic problems; rigorous alpha testing.
7	Industrial Biotechnology/Secondary Agriculture	Proof of Concept Established	TRL-4	Concept proven from lab scale to Bioreactor level experiments under optimized conditions at less than 100L.

				Necessary approvals to be obtained for using GMOs (RCGM/GEAC).
8	Agriculture	Late Stage Research	TRL 5	Marker Assisted Selection**:** Development of homozygous lines for gene of interest through marker assisted foreground and background selection. Transgenics/ Gene Edits: Integration and the expression analysis of the trans/cis- gene in the T1 generation. Bio control: *In vitro* evaluation and screening of local strains against target pathogens or insects. Tissue Culture**:** Optimization of conditions for hardening and establishment of plants inside greenhouse/ net house.
9	Aqua Culture and Fisheries	Early Stage Validation	TRL 5	Component and or basic subsystem technology tested /validated in controlled conditions in smaller tanks in laboratory/hatchery with proper control following statistically designed protocols.
10	Veterinary	Early Stage Validation	TRL 5	Drugs/vaccines: Demonstration of proof of concept (PoC) in limited number of animals (by serological studies). Working on feasible formulation development and conducting safety and efficacy studies). Devices "High-fidelity" laboratory integration of components. The basic technological components are integrated with reasonably realistic supporting elements so they can be tested in a simulated environment.

				Diagnostics Establish all the diagnostic kits to have desired specificity & sensitivity based on the data generated.
11	Clean Energy & Environmental Solutions	Proof of Concept Established	TRL-4	Demonstrated technology at pilot stage.