ANNEXURE B: DESCRIPTION OF TECHNOLOGY READINESS LEVELS (TRL)

Different definitions are used to assess the maturity of evolving technologies in different technology fields, namely Biomedical (medical devices, drug development and biologics/vaccines) and engineering projects. Although TRLs are conceptually similar, differences exist in terms of maturity at a given technology readiness level. The TRLs provided below have been adapted to align with TIA funded projects.

Relative Technology Development Level	TRL	Level Definition	Description (Biomedical & Engineering Projects)	Key Question for Stage Pass	TIA Approach
Basic technology research	1	Basic research	Basic science research Not focused on a specific application Principles observed and reported (published papers) to characterise new technologies	Have basic principles been observed and reported/published?	Not funded by TIA
	2	Concept formulation	Some practical applications identified Materials or processes required confirmed Technology concept/ hypothesis formulated Research plans and protocols are developed, peer reviewed and approved	Has a concept application been formulated? Analytical models or simulations developed?	Activities that are pre-TRL3 may be funded or supported in collaboration with other stakeholders
Feasibility research	3	Critical function or proof of concept established	Laboratory measurements validate analytical predictions of separate technology elements Hypothesis tested, alternative concepts explored and critical technologies and components supporting biological/vaccines/ drug candidate constructs been identified and evaluated for eventual development of candidate countermeasure. Agent challenge studies are conducted to support models based on presumed disease conditions.	Has analytical and experimental and/or characteristic proof of concept been demonstrated? Have Biologicals/vaccines/drug construct candidates been demonstrated in limited in vitro and in vivo research models (product development component)?	All activities within this level are eligible for funding.

			Research scale process initiated and evaluated under limited studies to identify sites and mechanism of action Potential correlates of protection for vaccines have been identified and initial physical/chemical characterisation of constructs Initial drug candidates have been characterised in pre-clinical studies.		
Technology development	4	Validation in the laboratory environment	Design and development of laboratory components Test results confirm design and meet technical performance criteria Hypothesis refined under non-GLP formulation using rigorous experimental design. Exploratory study of critical technologies performed to integrate into candidate biologic/vaccine constructs such as environmental milieu, route/methods of administration, proposed production/ purification methods, further physical/chemical characterisation. Candidate biologic/vaccine constructs are evaluated in animal model(s) to identify and assess safety and toxicity, biological effects, adverse effects and side effects. Assays, surrogate markers, and endpoints to be used during non-clinical and clinical studies are identified to evaluate and characterise candidate biologic/vaccine constructs.	Has a “breadboard unit” or “test tube model” been demonstrated in a laboratory environment/controlled conditions? Have non-GLP formulation, dose, pharmacokinetic, safety and efficacy studies been demonstrated in defined laboratory/animal model (product development component)?	All activities within this level are eligible for funding.

	5	Laboratory scale, validation in relevant environment	Validation under relevant operational conditions, mimicked in the laboratory (non-clinical). Non-clinical and preclinical research studies involving well-defined data collection and analysis systems with pilot lots of candidate biologics/vaccines produced under clinical Good Laboratory Practice (cGLP) conditions. Research results with pilot lots provide a basis to propose a potency assay, develop a manufacturing process amenable to clinical Good Manufacturing Practice (cGMP) - compliant pilot lot production, identifying and demonstrating proof of concept for a surrogate efficacy marker in an animal model(s) applicable to predicting protective immunity in humans, and demonstrating preliminary safety and efficacy against an aerosol challenge in a relevant animal model. Conduct cGLP safety and toxicity studies in animal model systems. Identify endpoints of clinical efficacy or its surrogate in animal models that may be applicable to predicting protective immunity in humans. Conduct studies to evaluate immunogenicity, as well as pharmacokinetics and pharmacodynamics when appropriate stability studies are initiated. The resultant draft data package will form the basis of a Food and Drug Administration Investigational New Drug (FDA IND) application Resultant documentation in the draft technical data package contains data from animal pharmacology and toxicology studies, proposed manufacturing	Has a “breadboard unit” or” test tube model” performance been demonstrated in a relevant environment or context? Have candidate vaccine/biological batches been produced under cGLP conditions? (cGLP conditions must be achieved by developing the process and product behind the process.) Have research results of pilot lots conveyed a draft technical data pack confirmed by reviewers? Is there sufficient data on candidate drug, biologic, vaccine to compile an IND application?	All activities within this level are eligible for funding.

			information, and clinical protocols suitable for Phase 1 clinical testing.		
Technology demonstration	6	Integrated prototype system verified in operational environment	Prototype demonstration in an operational environment.	Has a prototype been demonstrated in a relevant environment or context? Is the Phase 1 data compliant with safety requirements to proceed to Phase 2 clinical studies?	All activities within this level are eligible for funding.
			cGMP pilot lot batches must be produced for Phase 1 clinical testing. The process and product must be robust and repeatable.		
			Phase 1 clinical trials are conducted to demonstrate safety of candidates in a small number of human subjects under carefully controlled and intensely monitored clinical conditions. Evaluation of immunogenicity and/or pharmacokinetics and Pharmacodynamics data to support design of Phase 2 clinical trials. Surrogate efficacy models are validated.	Do conclusions thus far show any requirements for further product development? Are there any requirements for further process development?	
System commissioning	7	Integrated pilot system demonstrated in operational environment	Integrated full-scale pilot system demonstrated in an operational environment or site.	Has a prototype unit been demonstrated in the operational environment? Is there an approved Phase 3 clinical study plan?	All activities within this level are eligible for funding. Funding level for clinical trials will be subject to limits per project.
			Phase 2 safety and immunogenicity trials are conducted. Product immunogenicity and biological activity (e.g. preliminary evidence of efficacy) are determined. Product final dose, dose range, schedule, and route of administration are established from vaccine immunogenicity and biologic activity and, when necessary, from clinical pharmacokinetics and pharmacodynamics data.		
			Phase 2 clinical trials completed. Data are collected, presented, and discussed with appropriate regulatory		

			body at pre-Phase 3 in support of continued development of the biologics/vaccines. Clinical endpoints and/or surrogate efficacy markers and test plans agreed on.		
	8	System incorporated in commercial design	Actual product completed and qualified through certifications, tests and demonstrations (pre-commercial demonstration). Implementation of expanded Phase 3 clinical trials or surrogate tests to gather information relative to the safety and effectiveness of the candidate biologic/vaccine. Trials are conducted to evaluate the overall risk-benefit of administering the candidate product and to provide an adequate basis for product labelling. Production capability has been ramped up to capacity that will provide operational sustainability. Process validation is completed and followed by lot consistency/reproducibility studies. Clinical trial feedback used to validate manufacturing product process. Pre-BLA (Biologics License Application) meeting with respective regulatory body for BLA preparation and submission.	Has an identical system been demonstrated on an operational environment in a different configuration? Can the means of production support the production of unit levels required to provide operational sustainability? Has clinical safety and efficacy been demonstrated? Have manufacturing/production processes been validated? (Reiterations on the product and process development components are revisited.)	The type of funding is largely from the pre-commercialisation Support Fund and meant to support pre-commercialisation activities. The funding is also meant to support activities that are geared at facilitating follow-on funding.

				Has the BLA been submitted and received regulatory body approval?	
System operations	9	Proven system and ready for full commercial deployment	Product proven ready through successful operations in operating environment and ready for full commercial deployment. Actual system operated over the full range of expected conditions.	Has an identical unit been successful on an operational environment in an identical configuration? Has unit been completed and qualified through test and demonstration?	Activities that are post-TRL8 may be funded or supported in collaboration with other stakeholders
			The pharmaceutical (i.e. biologic or vaccine) or medical device can be distributed/marketed. Post-marketing studies (non-clinical or clinical) maybe required and are designed after agreement with the appropriate regulatory body and post-marketing surveillance commences.	Has the post market surveillance commenced according to regulatory body requirements?	

ANNEXURE C: DESCRIPTION OF BUSINESS READINESS LEVELS (BRL)

BRL	Description	Business Maturity Milestone/Readiness Level
1	Inventor(s) with an idea	Discovery/Invention Proven (e.g. in Research Environment)
2	Documented analysis of how the idea can be developed into a self-sustaining business	

3	Demonstrated capability and capacity to conduct experimentations to prove key functions of the idea	
4	Demonstrated capability and capacity to perform research and development activities in order to validate prototypes in a laboratory environment	Discovery/Invention Functional (e.g. in Technology Development Environment)
5	Demonstrated capability and capacity to engineer the deployment of laboratory validated prototypes in a relevant operational environment	Business Feasibility Validated (e.g. in a Technology Piloting Environment)
6	Demonstrated capability and capacity to design and develop a market-oriented product or service	
7	Business team in place, with capability to produce product or deliver service at limited scale	New Firm/Company/Business Division established
8	Business team scaled up to full production or service delivery and appropriate business model(s) validated	
9.	Fully established business with appropriate infrastructure and staffing	Self-Sustaining Business Operating (i.e. Viable Business)

ANNEXURE D: DESCRIPTION OF MARKETING READINESS LEVELS (MRL)

MRL	DESCRIPTION	DETAIL
1	Unsatisfied need identified	Documented idea of something that is missing in the market (identification of market gap)
2	Assessment of the need	Documented idea of functionalities that can be offered to address the identified market gap
3	Identified business opportunity	Documented analysis and quantification of the potential market and demand therefrom
4	Market research	Gathering of information about the external environment in order to formulate strategies for market entry.
5	Value proposition	Translation of the market strategy into product or service delivery capabilities and functionalities
6	Market segmentation, targeting and positioning	Potential market is divided into subsets of customers, industries or countries to determine the 'right' customers who are most likely to use the technology and whom the commercialisation efforts will be directed towards.
7	Promotion/Advertising	Documented strategies of how the technology will be communicated to the target market in order to improve uptake
8	Market testing	Test the technology in the market to confirm if assumptions made about market size, demand and uptake were correct. Depending on the results of market testing, MRL 5, 6 and 7 may need to be repeated
9	Market uptake	Usage of product or service by the market, resulting in sustainable sales revenue