DMTC Guideline - Technology Readiness Levels

MEDICAL COUNTERMEASURES

Technology Readiness Levels (TRLs) are a numerical classification on the status of the development of a technology. TRLs provide a common language whereby the status of a technology can be described without the need to have an understanding of the technology itself.

1. Steps to Track TRLs within DMTC projects

    i. Prepare a Technology Readiness Assessment (see following Technology Readiness Levels Guide).

    ii. Define the current TRL levels of the technology and the target TRL levels at project completion (see following Technology Readiness Levels Guide).

    iii. Review status and progress of TRL advancement in project reviews.

    iv. Ensure that the TRLs fit with the technology trajectories described in the Impact Tool.

    v. Document TRL status in project completion statement.

Technology Readiness Levels

Technology Readiness Levels (TRLs) are used as standardised numerical indicators of the level of maturity of a technology. The standard TRL definitions are given in Table 1. The descriptions given in the following table are generic and should be used to guide the compilation of a technical description of each TRL for every technology being developed. Additional terms and definitions are given in the example case studies provided at the end of this Guideline.

Table 1: TRL definitions

Phase	TRL	Description	Key indicators	Examples
Research phase	1 Review of Scientific Knowledge Base	Lowest level of technical readiness. Active monitoring of scientific knowledge base to identify countermeasure candidates. Scientific findings are reviewed and assessed as a foundation for characterizing approaches to intervene in disease. References to who, where, when.	Basic identification of opportunity.	**1A** Identify threat agent challenge agent and make link. **1B** Perform natural/case history studies of threat agent. **1C** Pathogenesis, and pathophysiology studies to relate to humans. **1D** Review the pathology of human disease.
Research phase	2 Development of Hypotheses and Experimental Designs	Invention begins. Scientific "paper studies" to generate research ideas, hypotheses, and experimental designs for addressing the related scientific issues. Focus on practical applications based on basic principles observed. Use of computer simulation or other virtual platforms to test hypotheses.	Concept formulation. Technology review leading to understand market position of technology	**2A** Identify and characterize threat agent. **2B** Generate hypotheses for types of animal models. **2C** Perform exploratory studies. **2D** Summarize the description of the human disease.

Phase	TRL	Description	Key indicators	Examples
Research phase	3 Target/Candidate Identification and Characterization of Preliminary Candidate(s)	R&D underway. Begin research, data collection, and analysis in order to test hypothesis. Explore alternative concepts, identify and evaluate critical technologies and components, and begin characterization of candidate(s).	Research results support concept.	Preliminaryefficacy demonstrated in vivo. **3A** Identify target and/or candidate. **3B** Demonstrate in vitro activity of candidate(s) to counteract the effects of the threat agent. **3C** Generate preliminary in vivo proof-of-concept efficacy data (non-GLP (Good Laboratory Practice)).

Phase	TRL	Description	Key indicators	Examples
Development phase	4 Candidate Optimization and Non-GLP In Vivo Demonstration of Activity and Efficacy	Initiation of animal model development. Non-GLP in vivo toxicity and efficacy demonstration in accordance with the product's intended use. Initiation of experiments to identify markers, correlates of protection, assays, and endpoints for further non-clinical and clinical studies. **Animal Models**: Initiate development of appropriate and relevant animal model(s) for the desired indications. **Assays**: Initiate development of appropriate and relevant assays and associated reagents for the desired indications. **Manufacturing**: Manufacture laboratory-scale (i.e. non-GMP (Good Manufacturing Practice)) quantities of bulk product and proposed formulated product. **Devices**: Laboratory testing of critical components and processes. Proof of concept of device demonstrated in relevant laboratory and animal models.	Industry engagement in project. Integration of critical technologies for candidate development. Value proposition stated.	**4A** 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 of threat agent challenge). **4B** Conduct initial non-GLP toxicity studies and determine pharmacodynamics and pharmacokinetics and/or immune response in appropriate animal models (as applicable). **4C** 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).

Phase	TRL	Description	Key indicators	Examples
Development phase	5 Advanced Characterization of Candidate and Initiation of GMP Process Development	Continue non-GLP in vivo studies, and animal model and assay development Develop a scalable and reproducible manufacturing process amenable to GMP. **Animal Models:** Continue development of animal models for efficacy and dose-ranging studies. **Assays**: Initiate development of in-process assays and analytical methods for product characterization and release, including assessments of potency, purity, identity, strength, sterility, and quality as appropriate. **Manufacturing**: Initiate process development for small-scale manufacturing amenable to GMP. **Target Product Profile**: Draft preliminary Target Product Profile. Questions of shelf life, storage conditions, and packaging should be considered to ensure that anticipated use of the product is consistent with the intended use for which approval will be sought from FDA/TGA. **Devices**: Further development of device candidates and system solutions. Validation of system components and processes in relevant laboratory environment. Classification of device by appropriate regulatory body and, when appropriate, an Investigational Device Exemption (IDE) prepared and submitted for review.	Industry provides specifications and/or materials. Establish draft Target Product Profiles. Competitive advantages of technology specified.	**5A** Demonstrate acceptable Absorption, Distribution, Metabolism and Elimination characteristics and/or immune responses in non-GLP animal studies as necessary for IND filing. **5B** Continue establishing correlates of protection, endpoints, and/or surrogate markers for efficacy for use in future GLP studies in animal models. Identify minimally effective dose to facilitate determination of "humanized" dose once clinical data are obtained**.**

Phase	TRL	Description	Key indicators	Examples
Development phase	6 GMP Pilot Lot Production, IND Submission, and Phase 1 Clinical Trial(s)	Manufacture GMP-compliant pilot lots. Prepare and submit Investigational New Drug (IND) package to FDA/TGA and conduct Phase 1 clinical trial(s). **Animal Models**: Continue animal model development via toxicology, pharmacology, and immunogenicity studies. **Assays**: Qualify assays for manufacturing quality control and immunogenicity, if applicable. **Manufacturing**: Manufacture, release and conduct stability testing of GMP-compliant bulk and formulated product in support of the IND and clinical trial(s). **Target Product Profile**: Update Target Product Profile as appropriate. **Devices**: System/device prototype demonstrated in an operating environment. Clinical testing to demonstrate safety may be required. Depending on the device classification, Premarket approval or Premarket notification may apply	Candidate meets industry expectations. Determine the safety and pharmacokinetics of the clinical test article. Candidate meets external stakeholder requirements.	**6A** Conduct GLP non-clinical studies for toxicology, pharmacology, and immunogenicity as appropriate**.** **6B** Prepare and submit full IND package to FDA/TGA to support initial clinical trial(s). **6C** Complete Phase 1 clinical trial(s) that establish an initial safety, pharmacokinetics and immunogenicity assessment as appropriate.

Phase	TRL	Description	Key indicators	Examples
Industry utilisation phase	7 Scale-up, Initiation of GMP Process Validation, and Phase 2 Clinical Trial(s)	Conduct animal efficacy studies as appropriate. Conduct Phase 2 clinical trial(s). **Animal Models**: Refine animal model development in preparation for pivotal GLP animal efficacy studies. **Assays**: Validate assays for manufacturing quality control and immunogenicity if applicable. **Manufacturing**: Scale-up and validate GMP manufacturing process at a scale compatible with USG requirements. Begin stability studies of the GMP product in a formulation, dosage form, and container consistent with Target Product Profile. Initiate manufacturing process validation and consistency lot production. **Target Product Profile**: Update Target Product Profile as appropriate. **Devices**: Clinical safety and effectiveness trials conducted using a fully-integrated prototype version of the medical device in an operating environment. Data evaluated to support further development. The final product design is validated and the final prototype and/or device intended for commercial use produced and tested.	Industry undertakes testing. Scale-up and initiate validation of GMP manufacturing process.	**7A** Conduct GLP animal efficacy studies as appropriate for the product at this stage **7B** Complete expanded clinical safety trials as appropriate for the product (e.g., Phase 2)

Phase	TRL	Description	Key indicators	Examples
Industry utilisation phase	8 Completion of GMP Validation and Consistency Lot Manufacturing, Pivotal Animal Efficacy Studies or Clinical Trials3, and FDA/TGA Approval or Licensure	Finalize GMP manufacturing process. Complete pivotal animal efficacy studies or clinical trials (e.g., Phase 3), and/or expanded clinical safety trials as appropriate. Prepare and submit NDA/BLA. **Manufacturing**: Complete validation and manufacturing of consistency lots at a scale compatible with Regulator requirements. Complete stability studies in support of label expiry dating. **Target Product Profile**: Finalize Target Product Profile in preparation for FDA/TGA approval. **Devices**: Premarket application or premarket notification submitted and approved.	Certification by external regulator. Customer acceptance. R&D ceased.	**8A** Complete pivotal GLP animal efficacy studies or pivotal clinical trials (e.g., Phase 3), and any additional expanded clinical safety trials as appropriate for the product. **8B** Prepare and submit New Drug Application (NDA) or Biologics Licensing Application (BLA) to the FDA/TGA. **8C** Obtain FDA/TGA approval or licensure.
Industry utilisation phase	9 Post-Licensure and Post-Approval Activities	Actual application of the technology in its final form and under mission conditions, such as those encountered in operational test and evaluation (OT&E). Examples include using the system under operational mission conditions. Product launched. Post-marketing studies and surveillance	Industry controls technology. Customer controls technology. Regulator approved/licensed labelling. Product for sale.	**9A** Commence post-licensure/post-approval and Phase 4 studies (post-marketing commitments), such as safety surveillance, studies to support use in special populations, and clinical trials to confirm safety and efficacy as feasible and appropriate. **9B** Maintain manufacturing capability as appropriate.