TECHNOLOGY READINESS GUIDELINES: **DRUG/BIOLOGICAL**

TRL	Basic Description	Activities	Milestone
1	**Review of Scientific Knowledge Base**	**1.1** Scientific findings are reviewed and assessed as a foundation for characterizing new technologies	
2	**Development of Product Hypothesis**	**2.1** Scientific studies to identify and validate disease target. **2.2** Screen potential compounds (HTS, antibody, etc.) to develop preliminary hits. **2.3** Develop assays to test activities of candidate compounds in vitro. **2.4** Initial intellectual property search for patentability. **2.5** Characterize disease epidemiology.	**2A** Compound series identified
3	**Identification and Characterization of Product Candidate**	**3.1** Decision on which compounds to advance in development. **3.2** Synthesize novel series of compounds, test efficacy and toxicities in vitro. **3.3** Test PK/tox of selected compounds in relevant in vivo models on a non-GLP level. **3.4** Survey relevant patent literature to identify white space and assess patentability of compound series. **3.5** Survey clinical literature to characterize current care patterns and unmet need(s). **3.6** File a provisional patent on the pharmacophore. **3.7** Synthesize and assess several potential lead compounds.	**3A** In vitro efficacy demonstrated. **3B** Preliminary efficacy demonstrated in vivo in appropriate small animal model. **3C** Lead series identified. **3D** Patent application(s) filed
4	**Optimization and Initial Demonstration of Safety and Efficacy**	**4.1** Initiate experiments to identify markers, assays, and endpoints for further non-clinical and clinical studies. **4.2** Assess endpoints for relevant impact in clinical practice. **4.3** Conduct in vivo distribution and elimination studies. **4.4** Non-GLP in vivo toxicity and efficacy of lead compound; pharmacokinetic studies.	**4A** Formulation appropriate for route of administration finalized. **4B** Product Profile drafted. **4C** Regulatory strategy determined. **4D** Current reimbursement mechanisms, economic burden of illness and treatment costs characterized. **4E** Preclinical candidate compound and animal models for GLP tox studies identified.
5	**Advanced Characterization of Product and Initiation of Manufacturing**	**5.1** Develop a scalable and reproducible manufacturing process amenable to GMP. **5.2** Develop assays/analytical methods for product characterization and release (potency, purity, ID, sterility, etc.). **5.3** Perform IND-enabling toxicology studies. Identify KOL's that can help design a clinical trial strategy/sequence, including collection of health economic and longer-term patient outcomes measures. **5.4** Identify clinical sites and begin contract negotiations. **5.5** Begin stability testing on drug substance (i.e., API).	**5A** Candidate identified. **5B** Acceptable ADME characteristics and/or immune responses in GLP animal studies as necessary for regulatory filing demonstrated. **5C** Manufacturing partners identified. **5D** Pre-IND meeting with FDA. **5E** First draft of a target product profile/package insert.
6	**Regulated Production, Regulatory Submission, and Clinical data**	**6.1** Prepare and submit IND. **6.2** Initiate Phase I study.	**6A** GMP-compliant pilot lots manufactured **6B** Regulatory package submitted to FDA. **6C** Conduct Phase 0 and/or 1 clinical trial(s) to determine the safety and pharmacokinetics of the clinical test article.
7	**Scale-up, Initiation of GMP Process Validation, and Phase 2 Clinical Trial(s)**	**7.1** Post Phase 2 meeting with FDA. **7.2** Determine dosing and treatment population for Phase 3 study.	**7A** Scale-up and validate GMP manufacturing process at a scale compatible with USG requirements. **7B** Complete stability studies of the GMP drug product in a formulation, dosage form, and container consistent with Target Product Profile. **7C** Complete Phase 2 clinical trials.
8	**Completion of GMP Validation and Consistency Lot Manufacturing, Clinical Trials Ph3, and FDA Approval or Licensure**		**8A** Finalize GMP manufacturing process. **8B** Complete pivotal clinical efficacy trials (e.g., Phase 3), and/or expanded clinical safety trials as appropriate. **8C** Prepare and submit New Drug Application or Biologics Licensing Application NDA/BLA.

Source: NCAI Technology Readiness Guidelines

TECHNOLOGY READINESS GUIDELINES: **THERAPEUTIC DEVICE**

TRL	Basic Description	Activities	Milestones
1	**Review of Scientific Knowledge Base**	Scientific findings are reviewed and assessed as a foundation for characterizing new technologies	
2	**Development of Product Hypothesis**	**2.1** Scientific "paper studies" to generate research ideas, hypotheses, and experimental designs for addressing the related scientific issues. **2.2** Characterize disease epidemiology. **2.3** Use of computer simulation or other virtual platforms to test hypotheses where possible. **2.4** Initial intellectual property search for patentability and to refine prototype configuration options	
3	**Identification and Characterization of Product Candidate**	**3.1** Explore prototypes, identify and evaluate critical technologies, critical design features needed, and components. **3.2** Survey clinical literature to characterize current care patterns and unmet need(s). **3.3** Initiate user feedback on prototypes.	**3A** Demonstrate in vitro efficacy. **3B** Preliminary efficacy and safety demonstrated ex vivo or in vivo. **3C** Identification of reimbursement and regulatory classification (pathway identification). **3D** File a provisional patent.
4	**Optimization and Initial Demonstration of Safety and Efficacy**	**4.1** Collection of user feedback on prototypes utilized to refine design inputs and identify new ones as needed. **4.2** Iteration and elimination of prototype designs based user feedback, bench testing, ex vivo and non-GLP in vivo testing. **4.3** Integration of critical technologies. **4.4** Initiation of animal model development for desired indication (if necessary). **4.5** Initiation of experiments to identify endpoints for further non-clinical and clinical studies.	**4A** Initiate Design Control activities, establish Design and Development Plan, capture Design Inputs. **4B** Determine IFU, Regulatory & clinical strategy. **4C** Characterize current reimbursement mechanisms, economic burden of illness and treatment costs. **4D** Preliminary FDA meeting. **4E** Non-GLP in vivo efficacy demonstration in accordance with the product's intended use.
5	**Advanced Characterization of Product and Initiation of Manufacturing**	**5.1** Develop test methods for device characterization, performance testing, and product release if relevant. **5.2** Explore potential manufacturing options as well as manufacturability and sustainability of device design, including third-party partners. **5.3** Develop a scalable and reproducible manufacturing process amenable to GMP.	**5A** Demonstrate intended device design addresses. **5B** Design inputs to support regulatory filing (Design freeze). **5C** Preliminary FDA meeting (depending on device type and classification). **5D** First draft of a target product profile/product label and reimbursement strategy.
6	**Regulated Production, Regulatory Submission, and Clinical data**	**6.1** Initiate manufacturing using scalable and reproducible process. **6.2** Integrate Quality. **6.3** Complete testing, bench, in vitro and in vivo GLP study, if necessary, intended to verify and validate the product design (per Design Controls) to support Regulatory submission at design freeze. **6.4** Initiate Shelf Life/Product Stability studies. **6.5** Finalize packaging of the device and sterilization validation.	**6A** Manufacture GMP-compliant devices. Complete **6B** Design Verification and Validation testing. **6C** Prepare and submit regulatory package to FDA (510k, IDE, as needed).
7	**Scale-up, Initiation of GMP Process Validation, and Phase 2 Clinical Trial(s)**	**7.1** Validate manufacturing processes at scale intended to support production. **7.2** Implement CAPA and other Quality requirements. **7.3** Support activities needed to complete clinical trials (for de novo or PMA pathway , if needed).	**7A** Design Transfer activities such as scale-up and validate GMP manufacturing process. **7B** Complete clinical trials (as needed for IDE or EFS). Regulatory submission of results.
8	**Completion of GMP Validation and Consistency Lot Manufacturing, Clinical Trials Ph3, and FDA Approval or Licensure**		**8A** Complete Design Transfer into finalized GMP manufacturing process. **8B** Prepare and submit for market approval: Premarket Approval (PMA), Premarket Notification (510(k)), HUD or Humanitarian Device Exemption (HDE). **8C** Prepare post-market clinical strategy/surveillance plan.

Source: NCAI Technology Readiness Guidelines

TECHNOLOGY READINESS GUIDELINES: **DIAGNOSTIC (ASSAY/TEST)**

TRL	Basic Description	Activities	Milestones
1	**Review of Scientific Knowledge Base**	**1.1** Active monitoring of scientific knowledge base. **1.2** Identify links between disease in humans and animals	
2	**Development of Product Hypothesis**	**2.1** Scientific "paper studies" to generate research ideas, hypotheses, and experimental designs for addressing the related scientific issues. **2.2** Characterize disease epidemiology. **2.3** Initial intellectual property search for patentability.	
3	**Identification and Characterization of Product Candidate**	**3.1** Explore assay components via prototypes and screening; identify and evaluate critical technologies and components, and begin characterization of lead design. **3.2** Survey clinical literature to characterize current care patterns and unmet need(s). Initiate user feedback	**3A** Demonstrate preliminary assay with simplified sample/artificial matrices. **3B** Demonstrate sensitivity and specificity with spike/recovery studies in the appropriate matrices.
4	**Optimization and Initial Demonstration of Safety and Efficacy**	**4.1** Integration of critical technologies and components (including hardware and software). **4.2** Select appropriate candidate reference and QC (quality control) reagents.	**4A** Assay/ test method validation in accordance with the product's intended use (Sample type, volume, assay components). **4B** Establish Draft Product Profile. **4C** Characterize current reimbursement mechanisms, economic burden of illness and treatment costs. **4D** Formulate initial regulatory and reimbursement strategies.
5	**Advanced Characterization of Product and Initiation of Manufacturing**	**5.1** Design freeze. **5.2** Develop a scalable and reproducible manufacturing process aligned with regulatory guidelines (as needed). **5.3** Finalize QC criteria.	**5A** Identify supply chain and/or manufacturing partners. **5B** Demonstrate acceptable performance as necessary for regulatory filing and for impact on clinical care. **5C** Preliminary FDA meeting.
6	**Regulated Production, Regulatory Submission, and Clinical data**		**6A** Manufacture product compliant with quality protocols. **6B** Based on regulatory classification (e.g. CLIA vs IVD route), submit regulatory package
7	**Scale-up, Initiation of GMP Process Validation, and Phase 2 Clinical Trial(s)**		**7A** Assays used to assess product quality are validated. **7B** Assays used to assess critical outcomes in clinical trials and in animal efficacy studies are validated.
8	**Completion of GMP Validation and Consistency Lot Manufacturing, Clinical Trials Ph3, and FDA Approval or Licensure**		

Source: NCAI Technology Readiness Guidelines