New BLRD Parent RFA Requirements to Enhance Real-World Impact of Basic Research

New Format for Project Summary/Abstract & for Translational Stage Reporting

For the BLRD Working Group on Enhancing Clinical Impact of Basic Research on Veteran Health

Arun Sharma, PhD

Agenda

- **Rationale for the Proposed Changes to the RFA**
- **New Requirements for Spring 2024 BX-24-001 RFA Submission**
- **New Formatting Requirement for Abstract/Project Summary**
- **New Appendix to Report Translational Stage(s) of the Proposal**
- **Questions/ Comments**

Rationale for the Proposed Changes

- **To expedite the translational impact of VA research on improving clinical care of Veterans.**
- **To support advancement of basic research findings from early discovery stage to regulatory submissions (IND/IDE), with the eventual goal of expediting the delivery of novel therapeutic approaches for the clinical care of Veterans.**
- **To identify roadblocks in moving discoveries into the clinic.**
- **Encourage investigators initiating and pursuing basic research to envision the path for moving their discoveries into the clinic.**

New Requirements for Spring 2024 BX-24-001 RFA Submission

We are piloting two new requirements for Spring 2024 Submission.

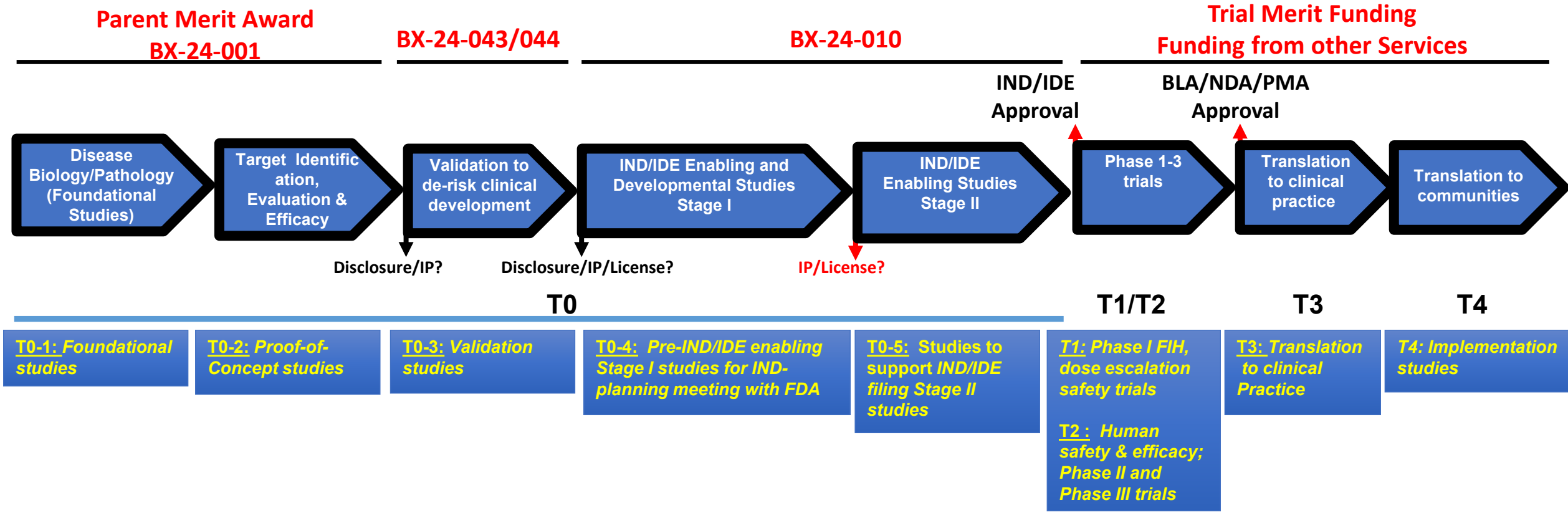
- The required changes are for the BLRD Parent Merit Award (BX-24-001) submission ONLY.
- The format for the Project Summary/Abstract has been modified.
- A new attachment "Appendix 4 - the VA-ORD Translational Pipeline (TP) Stages form" is added to the application process.
- Investigators are required to answer following 3 questions to complete the Appendix 4 and attach it with the application:
  - Please indicate the TP Sub-Categories that best represents the translational stage(s) of your Aims.
  - Will successful completion of the proposed Aims move the projects to another TP Sub-Category?
  - For Renewing applications, please indicate the TP Sub-Categories for the Aims of the previous Award.

Please note that this appendix material will be unscored but is a critical step in tracking the translation of BLRD research findings from bench to bedside.

Changes to Project Summary/Abstract Attachment

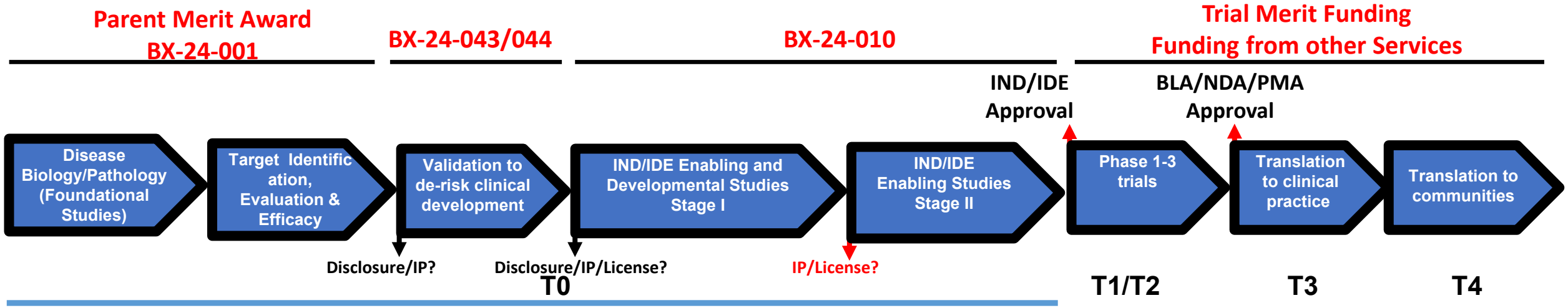
- The Project Summary/Abstract is required in the following format, with the headings as described. 40 lines of text maximum.
- **Background and Innovation:** Briefly describe the project and reasoning behind the proposed work, including a scientific rationale (e.g., based upon a review of relevant Veteran healthcare data or relevance of the animal model to the disease). Summarize the innovative aspects of the project.
- **Significance and Impact to Veterans Healthcare:** Briefly state how the proposed work is directly relevant to Veterans healthcare and Veteran's disease burden, and the gaps in knowledge/healthcare the project will address. Also address how the proposed project addresses VHA/ORD research priorities.
- **Path to translation/implementation:** What will be the next steps to move the research along the translational pathway and/or into practice to improve Veterans healthcare?

A Schematic of Translational Pathway and Current Funding Opportunities



Translational Stages based on the Institute of Medicine and NIH's Clinical Translational Science Award program modified from Surkis et. al., J Transl Med (2016) 14:23

Translational Pipeline (TP) Substages, Subcategories & Definitions



TP Substages	TP Substages Sub-Categories & Definition
T0-1: Disease Biology / pathology (Foundational Studies)	T0-1A: Studying disease/condition to understand pathology and disease progression; biological, social and behavioral mechanisms underlying health or disease.
	T0-1B: Developing / evaluating novel approach/strategy to address unmet clinical need.
	T0-1C: Focused characterization of select pathway, metabolomic-, proteomic-, genomic - data & epidemiologic studies using existing large data sets etc. to identify key approach or target.
T0-2: Target Identification, Evaluation & Efficacy (Proof-of-Concept Studies)	T0-2A: Confirming role of target or approach in disease/condition
	T0-2B: Developing therapeutic approaches based on target/ concept to improve a clinical condition; can include initial studies on lead molecule screening, developing prototype and assessments.
	T0-2C: Proof-of-concept studies in animals to demonstrate feasibility of approach or therapy to address unmet clinical need.

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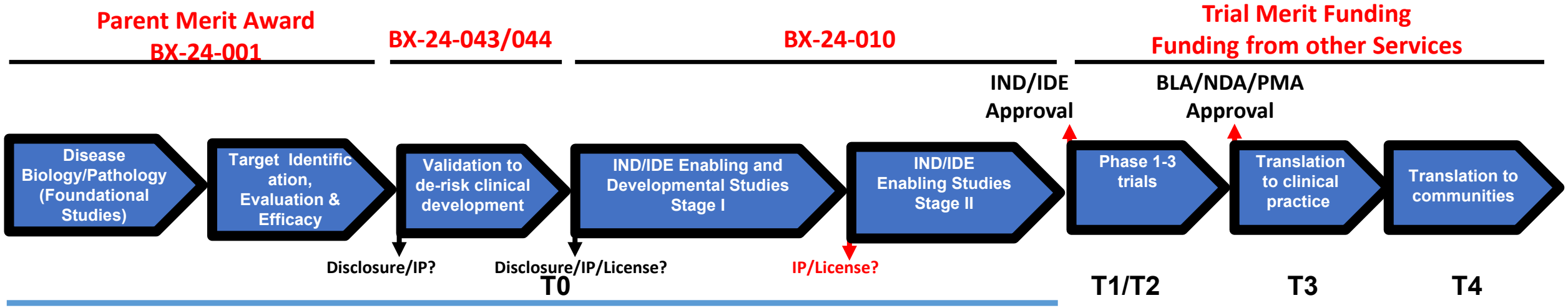

TP Substages	TP Substages Sub-Categories & Definition
T0-3: Validation to de-risk clinical development	T0-3A: Studies in additional disease model(s) to de-risk potential human translational concerns.
	T0-3B: Validation of biomarkers, diagnostics etc. in different (gender, race etc.) populations to determine target group.
	T0-3C: De-risking known FDA-recognized issues with the translational approach.
T0-4: IND/IDE Enabling and Developmental Studies Stage I (Generate Data for FDA INTERACT Meeting)	T0-4A: Lead/device isolation /development, optimization and selection.
	T0-4B: Lead candidate or device selection & profiling manufacturing, stability, solubility, immunogenicity, PK/PD, ADME, preliminary GLP-Toxicology.
	T0-4C: Pre-IND/IDE discussion with FDA. Develop plans for biomarkers, immunogenicity assays, etc. Develop plans for GMP manufacturing, and for clinical evaluation.
T0-5: IND/IDE-Enabling Studies Stage II	T0-5A: GLP-Tox, determine and convert safe animal dose to starting dose for FIH, GMP manufacturing, drug stability, validating biomarkers and assays for clinical trial, etc.
	T0-5B: IND/IDE submission, any additional studies required by FDA for regulatory approval

Responding to Questions in Appendix 4

- Please review the guidance document and associated materials on BLRD/CSRD resources page (BLRD/CSRD Resources For the VA Research Community) and the RFA.
- For specific projects on drugs, biologics, devices or diagnostics the guidance documents provide links to the Translational Readiness Levels (TRLs) used by the VA-TTP's BRAVE funding program.
- The guidance document and Excel file provides correlation between VA-ORD TP subcategories and TRLs used for BRAVE funding.
- Use outcomes of each Aims (new mechanism, new pathway, new target etc.) to determine TP subcategory for that Aim.
- TP subcategory for different Aims can be different.
- For further assistance please reach out to your Scientific Program Manager!

Next Steps

- Please inform all investigators submitting a New, Revised, or Renewal Parent Merit Award (BX-24-001) application about changes to the RFA requirements.
- Please ensure that the Project Summary/Abstract meet the formatting requirements of the revised RFA.
- Complete the Word document “VA-ORD-Translational-PipelineStages-form”by adding the PI’s Name and answering 3 questions.
- Save the Word document as a PDF file and attach document as “14_VA_Appendix_4_Translational Stages.pdf”.
- For questions, please contact the Review Mailbox (vhacoblcsrdrev@va.gov).

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Questions?