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

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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

Disease Biology/Pathology (Foundational Studies) → Target Identification, Evaluation & Efficacy → Validation to de-risk clinical development → IND/IDE Enabling and Developmental Studies Stage I → IND/IDE Enabling Studies Stage II

IND/IDE Approval → BLA/NDA/PMA Approval

Phase 1-3 trials → Translation to clinical practice → Translation to communities

T0: Disclosure/IP? Disclosure/IP-License?
T0-1: Foundational studies
T0-2: Proof-of-Concept studies
T0-3: Validation studies
T0-4: Pre-IND/IDE enabling Stage I studies for IND-planning meeting with FDA
T0-5: Studies to support IND/IDE filing Stage II studies
T1: Phase I FIH, dose escalation safety trials
T2: Human safety & efficacy: Phase II and Phase III trials
T3: Translation to clinical Practice
T4: Implementation studies

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**

<table>
<thead>
<tr>
<th>TP Substages</th>
<th>TP Substages Sub-Categories &amp; Definition</th>
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</thead>
</table>
| 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. |
## Translational Pipeline (TP) Substages, Subcategories & Definitions

### TP Substages

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

### TP Substages (Stage I) (Generate Data for FDA INTERACT Meeting)

- **T0**:
  - Disclosure/IP?

### TP Substages (Stage II)

- **T0**:
  - Disclosure/IP-License?

### TP Substages (Stage III)

- **T0**:
  - IP-License?

### TP Substages (Stage IV)

- **T1/T2**
  - BLA/NDA/PMA Approval
- **T3**
  - Phase 1-3 trials
- **T4**
  - Translation to clinical practice
  - Translation to communities

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**Parent Merit Award**
BX-24-001

**Trial Merit Funding**
Funding from other Services

**Parent Merit Award**
BX-24-043/044

**Trial Merit Funding**
BX-24-010

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**Disease Biology/Pathology (Foundational Studies)**

**Target Identification, Evaluation & Efficacy**

**Validation to de-risk clinical development**

**IND/IDE Enabling and Developmental Studies Stage I**

**IND/IDE Enabling Studies Stage II**

**Phase 1-3 trials**

**Translation to clinical practice**

**Translation to communities**

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**Choose VA**

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**U.S. Department of Veterans Affairs**
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).
Acknowledgment

• Dr. Holly Krull     Acting Director BLR&D Service

• Members BLRD Working Group
  
  Dr. Michael Burgio     Sara Clark
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  Natalie Washington
Questions?