



# TBI Endpoints Development Initiative

*A collaborative for advancing diagnosis and treatment of TBI*

## Research Collaboration Policy

June 16, 2015

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# TED Research Collaboration Policy

## 1. OBJECTIVES

The objective of the TBI Endpoints Development (*TED*) *Research Collaboration Policy* is to establish a framework to support the conduct of collaborative research projects involving the TED Investigators, the TED Metadataset, and external parties.

### 1.1 TED STUDY DESCRIPTION

The TED study will directly impact public health by creating a Metadataset of integrated clinical, imaging, proteomic, genomic, and outcome biomarkers, contributed by numerous individual studies across civilian, military, and sports cohorts, which will permit more precise TBI diagnosis, prognosis, and treatment, and which will accelerate the validation and regulatory readiness of candidate clinical outcome assessments (COAs), biomarkers, and devices for use in the U.S. Food and Drug Administration (FDA) Qualification Process for Drug and Medical Device Development Tools and other regulatory processes. Creating a range of validated COAs, biomarkers, and devices will: 1) permit more accurate disease/condition diagnosis, 2) identify patient subpopulations likely to benefit from therapy/intervention, and 3) provide refined outcome assessments to confirm efficacy. With the support of the Department of Defense, and the unique private-public partnership model of the TED Initiative, over the 5-year duration of the TED Initiative, we will create the TED Metadataset, and identify (Stage I) and validate (Stage II) candidate COAs and biomarkers that could enter the regulatory pipeline, and/or be qualified by FDA as DDTs or MDDTs for future TBI trials to benefit military and civilian populations.

Detailed data from numerous clinical studies enrolling subjects across the TBI injury spectrum, along with CT/MRI imaging, blood biospecimens, and outcomes measures, will be curated and analyzed, permitting the identification/validation of COAs and biomarkers, and identification of structural abnormalities that may be predictive of outcomes, making strides toward a new taxonomy for TBI. The infrastructure of integrated databases and imaging and biospecimen repositories will create a high quality, legacy database for current and future generations of international researchers.

### 1.2 TED LEADERSHIP (EXECUTIVE and STEERING COMMITTEES)

TED is a large and complex project. Its institutional and public-private partnership is comprised of numerous study sites, managed through 7 Cores (Administrative, Clinical/Rehabilitation, Emerging Technologies, Informatics, Neuroimaging, Outcomes, Biostatistics), totaling nearly 50 collaborating institutions, corporations, and philanthropies. Governance is implemented by the Executive Committee, consisting of leaders of the Cores. The Executive Committee receives input from a Steering Committee, consultants, and participating organizations as to strategic research participation and planning, and dissemination of TED scientific findings, as well as oversight from its Government Steering Committee.

Oversight of Research Collaborations will be performed by the TED Executive Committee, which meets bi-weekly with few exceptions, and the Steering Committee. Submitted Research Collaboration Request forms will be screened by the Executive Committee, and reviewed, and approved/rejected by the Steering Committee.

TED Executive Committee		
Name	Role	Institution
Geoffrey Manley, MD, PhD	Contact PI, Admin Core Leader	UCSF
Harvey Levin, PhD	PI, Outcomes Core Leader	Baylor Institute of Medicine
Joseph Giacino, PhD	PI, Clinical/Rehab Core Leader	Spaulding Rehabilitation Center
Michael McCrea, PhD	PI, Outcomes Core Leader	Medical College of Wisconsin
Murray Stein, MD MPH	PI, Outcomes Core Leader	University of California, San Diego

Nancy Temkin, PhD	PI, Biostatistics Core Leader	University of Washington
Ramon Diaz-Arrastia, MD	PI, Emerging Tech Core Leader	Center for Neuroscience and
Steven Wisniewski, PhD	PI, Biostatistics Core Leader	University of Pittsburgh
Sureyya Dikmen, PhD	PI, Outcomes Core Leader	University of Washington

TED Steering Committee		
Name	Role	Institution
Geoffrey Manley, MD PhD	Contact PI, Admin Core Leader	UCSF
Arthur Toga, PhD	Informatics Core	University of Southern California
Claudia Robertson, MD	Clinical & Rehabilitation Core	Baylor College of Medicine
David Cifu, MD	Clinical & Rehabilitation Core	Virginia Commonwealth University
David Okonkwo, MD PhD	Clinical & Rehabilitation Core	University of Pittsburgh
David W. Wright, MD	Clinical & Rehabilitation Core	Emory University
Harvey Levin, MD	Outcomes Core	Baylor College of Medicine
James Kelly, MD	Outcomes Core	National Intrepid Center of Excellence
John Whyte, MD PhD	Clinical & Rehabilitation Core	Moss Rehabilitation Research Inst.
Joseph Giacino, PhD	Clinical & Rehabilitation Core	Spaulding Rehabilitation Center
Kevin Guskiewicz, PhD	Outcomes Core	University of North Carolina
Michael McCrea, PhD	Outcomes Core	Medical College of Wisconsin
Michael Weiner, MD	Neuroimaging Core	UCSF
Murray Stein, MD MPH	Outcomes Core	University of California, San Diego
Nancy Temkin, PhD	Biostatistics Core	University of Washington
Pratik Mukherjee, MD PhD	Neuroimaging Core	UCSF
Ramon Diaz-Arrastia, MD PhD	Emerging Technologies Core	Uniformed Services University of the Health Sciences
Rick Williams, PhD	Biostatistics Core	RTI International
Robert Knight, MD	Emerging Technologies Core	University of California, Berkeley
Stephen Wisniewski, PhD	Biostatistics Core	University of Pittsburgh
Sureyya Dikmen, PhD	Outcomes Core	University of Washington
William Jagust, MD	Emerging Technologies Core	University of California, Berkeley

## 2. PROCESS FOR RESEARCH COLLABORATION REQUESTS

Access to study data, materials sharing, and mutual collaboration among research teams in order to accelerate research in TBI are fundamental tenets of the TED project and are core beliefs of its investigators. The TED Metadataset and repositories can only serve their intended purposes as a current and legacy resource for further research with a robust, transparent, and open-access collaboration policy. To ensure optimal use and to limit possible misuse of the data and materials derived from an effort of this magnitude, the TED Executive Committee will monitor all ongoing Research Collaborations.

The TED Executive and Steering Committees will not entertain unfunded collaborations that increase cost to the TED study. Furthermore, all potential collaborations must not interfere with or otherwise compromise the specific aims, outcomes, follow-up rates, or integrity of the parent TED study objectives and mandates.

### 2.1 Research Collaboration Requests

All Research Collaborations with TED will begin with a written request submitted to the TED Executive Committee. The Research Collaboration Proposal form is attached here as Appendix 1. Completed Research Collaboration Proposal forms are to be submitted to Dr. Geoffrey Manley, Contact PI for TED, in care of Brian Fabian (Brian.Fabian@ucsf.edu).

Research Collaboration Requests will include notation of the TED PI who will serve as a sponsor of the proposal, a table of authors and their affiliations, as well as the study aims and sub-aims, and a description of the methodologies and approaches to be used to address the scientific questions involved.

The Research Collaboration Request will also provide a proposed budget (see Section 6 below).

Research Collaboration Requests will be screened by the TED Executive Committee, and sent for review, and approval/rejection/request for revision by the TED Steering Committee.

## **2.2 Data Use Agreements**

The Data Use Agreement for TED Research Collaborations is attached as Appendix 2. This Agreement is for the use of clinical and experimental data collected by the TED investigators.

The Data Use Agreement must be endorsed by the Organization Principal Investigator for the collaborating entity, and UCSF via the TED Contact PI (Dr. Manley).

## **3. INTELLECTUAL PROPERTY**

Management of intellectual property rights, including copyright, will be handled by the Office of Technology Management at the University of California, San Francisco, in accordance with applicable University of California policies governing intellectual property rights.

## **4. AUTHORSHIP AND PUBLICATIONS**

Any publications that emerge from use of TED data and material are subject to the review and authorship acknowledgments set forth in the TED Data Use Agreement (Appendix 2) and Publication and Authorship Guideline (Appendix 3).

In the spirit of collaboration, all publications will be joint publications with Data Contributors, Collaborators, and TED Investigators.

All efforts will be made to protect proprietary information or intellectual property that might be disclosed by the manuscript or abstract.

Failure to comply with authorship and publication expectations will result in termination of the Research Collaboration Agreement(s).

## **5. CONFLICT OF INTEREST**

Researchers involved in collaborative research projects must disclose and manage any actual or apparent conflicts of interest relating to any aspect of the research collaboration with the TED study in accordance with the Conflict of Interest Policy of the University of California, San Francisco.

## **6. BUDGET**

The goal of research collaboration with TED is to build intellectual synergism that will enhance the objectives of the TED study and serve public health. TED on its own, does not have adequate funding, resources, or intellectual capacity to maximize its potential impact on traumatic brain injury and public health. Forming strategic collaborations can be an effective and economical way of accessing resources and may lead to longer-term partnerships.

Nevertheless, the scope of work for any and all collaborations with external parties must be accounted for with appropriate resources. The budget must be an accurate reflection of the amount and the timing of the resources required for the collaborative project, as included in the Research Collaboration Request Form.

There must be enough funding to undertake the proposed collaboration without detracting from other efforts and core deliverables already underway. Staff time in managing and executing the collaboration must be reflected in the budget. In-kind contributions from corporate collaborators will be taken into consideration in the overall budget assessment.

The budget provided in the Research Collaboration Request must specify when payments will be made and clearly indicate when the contributed in-kind resources, if any, will be provided. Failure to adhere to the specified, agreed-upon budget will result in termination of the Research Collaboration Agreement and any and all attendant Data Use or Material Transfer Agreements.

## **7. TERMINATION OF RESEARCH COLLABORATION AGREEMENTS**

All Research Collaboration Agreements with TED will have a specified date upon which the research collaboration project must end. The end date may be extended through the amendment process, if both parties agree.

The TED Leadership reserves the right to terminate a Research Collaboration Agreement or Data Use Agreement before the end date at the discretion of the Executive Committee with a 30-day written notice.

## Appendix 1: Research Collaboration Proposal Request Form

Instructions: A completed and approved Research Collaboration Proposal Request is required to be submitted to the TED Executive Committee (care of [brian.fabian@ucsf.edu](mailto:brian.fabian@ucsf.edu)) and should be no more than 2 pages long. Authors are encouraged to contact the Biostatistics Core to receive assistance with the statistical analysis plan. Clinical site statisticians are also encouraged to participate in these consultations. Proposals will be reviewed by the TED Executive Committee. All aspects of manuscript development will be governed by this Guideline. Proposals should contain the following elements:

Date:

Investigator's Name:

Clinical Center:

E-mail:

Telephone:

TED Sponsor (if not a TED investigator):

Other investigators who will be working on this analysis:

Analysis Plan Title:

TED Metadataset studies to be used:

Please attach a 2-page description of your analysis plan. Please include the following:

- 1) Short background/rationale for addressing the research question
- 2) Primary variables to be used in the analysis (please provide mock tables)
- 3) Brief description of methods and statistical analysis plan
- 4) What is the impact if successful?

**Appendix 2: Data Use Agreement THIS WILL BE THE DATA “OUT” AGREEMENT – IN PREPARATION BY UCSF  
TECH TRANSFER LAWYERS**

### Appendix 3: TED Publication and Authorship Guideline

This **Publication and Authorship Guideline** has been established by the TED Executive Committee for the publication of data collected under the protocol entitled: Traumatic Brain Injury Endpoints Development Initiative (TED). TED is governed by data use guidelines, as described in the TED Data Contribution and Use Agreement, the Data Use Agreement, and the TED Research Collaboration Policy. This Publication and Authorship Guideline will be in effect until such time as the data may become publically accessible, and is subject to amendment by the TED Executive Committee.

This guideline addresses three major types of manuscripts. **Primary manuscripts** are those that report the conduct and outcome of the major objectives of the trial (i.e., the major results of the collaboration). **Secondary manuscripts** refer to secondary hypotheses and ancillary analyses that come from data that were collected for this study. **Tertiary manuscripts** are those in which data collected are used as an illustrative example of a proposed preferred methodology or studies for which ancillary data, unrelated to the primary study hypotheses, are collected, sometimes on only a subset of study sites. All data presentations, including abstracts, oral presentations, and posters, are encompassed by the term “manuscript.”

#### General Principles

1. This guideline may be subject to ongoing interpretation by the Executive Committee. Experience and new insights from this trial may necessitate periodic modification by consensus of the Executive Committee.
2. No TED data shall be presented, submitted or published in any way without the express prior written approval of the Executive Committee.
3. Primary Authorship, denoted as those on the first line(s) of the authorship attribution in a journal and in indexing services, should be based on appropriate effort as defined in the guidelines published by the International Committee of Medical Journal Editors (ICMJE, [http://www.icmje.org/roles\\_a.html](http://www.icmje.org/roles_a.html)). Primary authors should meet all four of the following criteria:
  - 1) Substantial contributions to the conception or design of the work; or the acquisition, analysis or interpretation of data for the work; AND
  - 2) Drafting the work or revising it critically for important intellectual content; AND
  - 3) Final approval of the version to be published; AND
  - 4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
4. Authorship credit will be granted to the primary authors *with the TED Study Investigators as an author*. Following the list of primary authors, all publications using TED data will bear the following attribution: “and the TED Study Investigators” listed in alphabetic order. Including the TED Study Investigators allows for all members to be indexed as authors (not contributors) in PubMed.
5. Responsibilities and tasks for production of primary manuscripts will be determined by the Executive Committee and the Biostatistical Core. The results to be included in the primary manuscript will be presented to the Executive and Steering Committees for review and response. Twenty-one days prior to submission, a complete draft will be circulated to the Executive Committee for review and comment.
6. Secondary and tertiary manuscripts are strongly encouraged and may be initiated by any participating



TED investigator. Two-page proposals for secondary and tertiary manuscripts must include a tentative title, primary author(s), background/rationale, and statistical analysis plan (NOTE: see Appendix 1 to Research Collaboration Agreement) and must be submitted to the Executive Committee in care of Contact Principal Investigator, Geoffrey T. Manley, MD PhD via the Project Administrator ([brian.fabian@ucsf.edu](mailto:brian.fabian@ucsf.edu)). Consultations with the Biostatistical Core are essential to developing adequate statistical plans prior to final submission to the Executive Committee. Clinical site statisticians and epidemiologists are encouraged to participate in these consultations, which should take place after proposal submission to the Executive Committee and acceptance by the TED Steering Committee, and before posting on the One Mind Portal. All submitted and finalized proposals will be posted on the One Mind Portal for review and comment by all TED PIs and co-Is. All eligible proposals will be presented, discussed, reviewed, and voted on either during Steering Committee meetings, or via email ballot within 14 days following the meeting. Approval will be determined by simple majority.

7. Each secondary and tertiary manuscript proposal will identify a primary author/writing group leader, who will be responsible for assigning tasks to members of the writing group. To uphold the authorship criteria presented in General Principle 3, it is expected that primary authors will delegate writing responsibilities early enough so that all members of the writing group are given the opportunity to contribute substantively. The primary author will have sole responsibility for ensuring that authorship order has been discussed and confirmed by co-authors. There is no prescribed limit of authors from each institution; however, each named author must have contributed significantly to the manuscript as described above. If there is a disagreement among the potential co-authors, the Executive Committee will determine inclusion of an author and/or order. If agreement cannot be reached by the Executive Committee, Michael Weiner, MD PhD, of the TED Scientific Advisory Board will be the tie-breaker and serve as mediator. For secondary (and possibly tertiary) manuscripts, the author list will include the named authors followed by “and the TED Study Investigators.”
8. Before submission of an abstract to a scientific meeting, it is expected that the associated data analyses and interpretation will be completed. The abstract, data tables, and text of the interpretation will be submitted to the Executive Committee and posted on the One Mind Portal for comment and the designated author(s) will present their data and interpretation (10-minute presentation) to the Executive Committee for discussion and review during an Executive Committee telephone meeting. The Executive Committee will discuss the presentation and approve submission by simple majority vote. It is expected that the resultant manuscript will be submitted to a journal by or before 3 months following presentation of the abstract at the scientific meeting. The same process is required before submitting a manuscript to a journal if no associated abstract has been previously approved.
9. If preparation and submission of manuscripts is not accomplished in a timely manner (within six months following the receipt of data), the Executive Committee reserves the right to delegate manuscript-writing responsibility to another investigator. These requirements are in place to ensure the timely publication and dissemination of study results to the public and the scientific community.
10. Using TED data as preliminary data for grant submission by investigators at participating institutions is encouraged. However, any data tables included in a grant proposal must be approved by the Steering Committee before submission.
11. Proposals for single-site analyses of TED data will be handled the same way as multi-site analyses.
12. The Steering Committee will consider requests from unrelated third parties for access to study data for research and publication purposes *prior* to the data becoming available publically. All parties obtaining

access to the data will agree to abide by the obligations of the TED Data Use Agreement and as set forth in this Guideline.

13. All authors are responsible for notifying the Executive Committee (via email to Brian Fabian brian.fabian@ucsf.edu) of all accepted manuscripts, abstracts, and oral and poster presentations, as well as the journal, date of publication, page number(s) and other information necessary to reference the publication/presentation. The TED Administrative Core will maintain a central list of all accepted abstracts, presentations and publications relating to TED, which will be posted on the TED Web site.

### Acknowledgements

1. As this study was sponsored by external sources an acknowledgement is required on all publications.

“Sponsored by the U.S. Department of Defense (Grant #W81XWH-14-2-0176), and our public and private partners. The opinions or assertions contained here are the private views of the authors and are not to be construed as official or as reflecting the views of any sponsor.”

2. Contributions from other collaborators, including laboratory, economists, scientists, consultants or other individuals providing expertise during the trial design, conduct and manuscript processes but not members of the official TED Study Investigators and not meeting the prescribed authorship criteria should also be listed in the acknowledgments.

TED Executive Committee		
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James Kelly, MD	Outcomes Core	National Intrepid Center of Excellence
John Whyte, MD PhD	Clinical & Rehabilitation Core	Moss Rehabilitation Research Inst.
Joseph Giacino, PhD	Clinical & Rehabilitation Core	Spaulding Rehabilitation Center
Kevin Guskiewicz, PhD	Outcomes Core	University of North Carolina

Michael McCrea, PhD	Outcomes Core	Medical College of Wisconsin
Michael Weiner, MD	Neuroimaging Core	UCSF
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