TBI Endpoints Development Initiative

A collaborative for advancing diagnosis and treatment of TBI

Research Collaboration Policy

March 23, 2018

Table of Contents

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	University of Pennsylvania
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	University of Pennsylvania
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 Committee 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).

Upon receipt, research collaboration requests will be screened by the TED Initiative Ombudsperson to identify and/or mitigate circumstances in which an overlap may occur in research aims, proposed methods, or analytical design with other TED Initiative work whether currently proposed or previously approved. Once vetted and cleared by the Ombudsperson, the collaboration request will then be circulated to the TED Executive Committee for review, and approval/rejection/request for revision. Please allow 4-6 weeks for this process.

2.2 Data Use Agreements

The Data Use Agreement/Human Materials Transfer 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) 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: Investigator's Title:

Organization or 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 files requested: TRACK-TBI Pilot ☐ TRACK-TBI U01 Currently Enrolling Study ☐

TED Metadataset ☐ TED Metadataset Imaging ☐

Purpose of Data Request (check all that apply)		**TED Core (check all that apply)**	
☐	Exploratory	☐	Clinical Core
☐	Data analysis for manuscript	☐	Biospecimens Core
☐	Preliminary data for grant proposal	☐	Neuroimaging Core
☐	Inputs for simulation model	☐	Biostatistics/CER Core
☐	Development of statistical methods	☐	Outcomes Core
☐	Other (describe)		

Please attach a 2-page description of your analysis plan including:

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?

For exploratory requests, complete item 1 now and submit items 2 through 4 within 60-days of accessing the dataset(s).

Research Collaboration Request Tracking Log			
☐	Received by Executive Committee Member	By:	Date:
☐	Reviewed by Executive Committee		Date:
☐	Decision communicated to Requestor	By:	Date:
Decision:	☐ Accept ☐ Decline	☐Return for revision	

Appendix 2: Data Use Agreement/Human Materials Transfer Agreement

TED METADATASET
DATA USE AGREEMENT AND HUMAN MATERIAL TRANSFER AGREEMENT

This Data Use Agreement and Human Material Transfer Agreement ("DUA/HMTA") is between The Regents of the University of California, on behalf of its San Francisco campus ("UCSF") and [INSERT NAME OF INSTITUTION and PI] ("Data User") and is effective as of the "Effective Date."

UCSF and Data User are hereinafter also referred to individually as "Party" and collectively as "Parties."

Preamble:

1. The Parties wish to collaborate and share data with the ultimate goal of furthering progress in research on traumatic brain injury related to the specific aims of the TBI Endpoints Development Study (TED) initiative and any adjunct research activities generated by the TED initiative; and

2. Under this Agreement's terms and conditions, Data User will be provided access to original and/or derivative clinical data file(s) ("Clinical Data"), and/or human materials (hereafter "Biospecimens"), and/or neuroimaging studies ("Imaging Studies"), provided that TED Executive Committee ("Executive Committee") has approved the transfer of Biospecimens, Imaging Studies, and/or Data.

3. The Parties acknowledge the Clinical Data, Biospecimens, and/or Imaging Studies have come in through related Data Contribution and Use Agreements ("DCUAs") from collaborators in the field of traumatic brain injury ("Data Contributors") with the undertaking to provide UCSF as the administrative custodian ("Custodian"), information that is integrated and stored as part of the TBI Endpoints Initiative's "TED Metadataset," on a data integration platform or repository, as relevant ("Repository or "Repositories"); and

4. The TED Executive Committee ("Executive Committee") controls decisions surrounding the storage and use of such data in the Repository; and

5. The Parties acknowledge that any publications or presentations generated from investigation and analysis of the TED Metadataset are governed by policies set forth in the TED Publication and Authorship Guideline incorporated herein by reference, subject to future amendment by TED Executive Committee as needed, along with recognition and disclosure of the source grant(s) for the utilized dataset(s).

6. Data User will also have the opportunity to explore the TED Metadataset pursuant to the TED Research Collaboration Policy, incorporated here by reference, subject to future amendment by the TED Executive Committee as needed.

7. Notification shall be in writing either electronic or by mail:

UCSF Principal Investigator facilitating this Agreement for Custodian:
Geoffrey T. Manley, MD, PhD
Study Title: TED
Address: University of California, San Francisco
Department of Neurological Surgery
Brain and Spinal Injury Center
1001 Potrero Avenue, Bldg. 1, Room 101
San Francisco, California, USA
Contact: Email: manleyg@ucsf.edu Tel: 415-206-8300 Fax: 415-206-3948

Administrative Contact for Custodian:
The Regents of the University of California, on behalf its San Francisco Campus
Address: UCSF - Office of Innovation, Technology, & Alliances

3333 California St., S-11
San Francisco, CA 94143-1209
Contact: industrycontracts@ucsf.edu

Data User Agreements and Obligations

8. Except as otherwise specified herein, the Data User may make all uses and disclosures of the sample of the de-identified Clinical Data, Biospecimens, and/or Imaging Studies to conduct the Research Project as described in Data User's Research Proposal (Exhibit A) and this section. For the purposes of the Agreement, derivative data file(s) are any and all data file(s) created using the original data in any way. This Agreement addresses the terms and conditions pursuant to which the Data User is permitted to obtain, use, reuse, and disclose the Clinical Data, Biospecimens, and/or Imaging Studies, or derivatives of any. Data Contributor retains all applicable rights to the Clinical Data, Biospecimens, and/or Imaging Studies referred to in this Agreement, and the Data User does not obtain any intellectual property rights related to, or any other right, title, or interest in any of the Clinical Data, Biospecimens, and/or Imaging Studies or derivatives other than those which are expressly granted in this Agreement. Data User understands and acknowledges that the Clinical Data, Biospecimens, and/or Imaging Studies may be protected by copyright and other intellectual property rights, and that duplication, except as reasonably necessary to carry out the Research Proposal, or sale of all or part of the Clinical Data, Biospecimens, and/or Imaging Studies is not permitted.

a) The following original Clincal Data are being made available pursuant to this Agreement for research purposes:

Name of Study Providing the Biospecimens, Imaging Studies, and/or De-Identified Data
[insert list]

b) The following Biospecimens are being made available pursuant to this Agreement for research purposes:

Name of Study Providing the Biospecimens, Imaging Studies, and/or De-Identified Data
[insert list]

c) The following original Imaging Study Files are being made available pursuant to this Agreement for research purposes:

Name of Study Providing the Biospecimens, Imaging Studies, and/or De-Identified Data
[insert list]

9. The TED Metadataset access and/or access to Clinical Data, Biospecimens, and/or Imaging Studies is provided to Data User for the purpose of ongoing collaboration in TBI research and will be used only as described in Research Proposal.

10. Data User will provide to UCSF a Research Completion Report on a form to be provided by UCSF PI, upon completion of the agreed project. The Research Completion Report shall include a recitation of the findings of the project, and a copy of all derivative data that Data User develops in the course of the project. The Report will contain a completed form (the "Minimal Dataset Form") that describes the "minimal dataset" – that is, the dataset used to reach the conclusions reached in the report and any manuscript produced, with related metadata and methods, and any additional data required to replicate the reported study findings in their entirety. Core descriptive data, methods, and study results should be included within the report, regardless of data deposition.

11. The facts and statements made by Data User in the Research Proposal are complete and accurate;

12. The requested Clinical Data, Biospecimens, and/or Imaging Studies are the minimum necessary to achieve the purposes set forth in the Research Proposal;

13. Data User has obtained Institutional Review Board approval to use the Clinical Data, Biospecimens, and/or Imaging Studies;

14. Data User has sufficient resources to and intends to complete the research project as set forth in User's Research Proposal; and

15. Data User agrees to use the Clinical Data, Biospecimens, and/or Imaging Studies strictly in accordance with applicable local and federal laws, including but not limited to the following related to confidentiality, privacy, and security regulation:

i. The Privacy Act of 1974, as most currently amended
ii. California's Confidentiality of Medical Information Act (CMIA)
iii. "HIPAA": the Health Insurance Portability and Accountability Act of 1996, Public Law 104-191. The data provided to UCSF is de-identified in accordance with the de-identification standards set forth under the Health Insurance Portability and Accountability Act (HIPAA) and all implementing regulations, including, but not limited to 45 CFR § 164.514(a)-(c) and § 164.502(d) as well as applicable human subjects regulations and guidance, 45 C.F.R. Part 46, 21 C.F.R. Parts 50 and 56.

16. Data User will receive access to de-identified data and will not attempt to establish the identity of, or attempt to contact any of the individuals, whose data are contained in the TED Metadataset.

17. Data User and members of their research team that are under the direct supervision of the Data User shall be entitled to use Clinical Data, Biospecimens, and/or Imaging Studies from the TED Metadataset, and agree to do so in a secure manner using appropriate administrative, physical storage and technical safeguards to prevent use or disclosure of such in ways other than are permitted under this Agreement. **All personnel certify that they have completed a Collaborative Institutional Training Initiative (CITI Program) module, with specific certification in Human Subjects Protection Training.**

18. Except as otherwise required by law, any transfer to or from third parties of Clinical Data, Biospecimens, and/or Imaging Studies is prohibited without authorization from the TED Executive Committee with the exception that User may transfer to, and permit the use of such by the subcontractors or collaborators listed in Research Proposal to aid in the performance of the Research Project under a data use and human materials transfer agreement with terms that are no less strict than the terms of this Agreement. It is incumbent on the Data User to seek out and engage in separate agreements with non-UCSF third parties such as other repositories or collaborators providing Clinical Data, Biospecimens, and/or Imaging Studies. These separate agreements shall not contain terms that conflict with the rights and obligations under this Agreement of UCSF, the TED Executive Committee, or the Data User or Data Contributor, and shall have no less stringent obligations than are imposed under this Agreement. Under these separate agreements, the terms of this agreement shall be incorporated through reference, including but not limited to those contained in the TED Research Collaboration Policy and the TED Publication and Authorship Guideline.

19. If Data User moves to another institution or company, Data User will notify the UCSF Principal Investigator in writing within 30 days regarding disposition of the TED Metadataset as well as the Clinical Data, Biospecimens, and/or Imaging Studies in possession or control by Data User.

20. Data User and Other Users entitled to use the Data from the TED Metadataset agree to notify the UCSF Principal Investigator within 2 days of becoming aware of any use or disclosure of the Data in violation of this Agreement.

21. The TED Metadataset as a whole, and any of its constituent data, are experimental in nature and are provided without any warranties, express or implied, including any warranty of merchantability, accuracy, or fitness for a particular purpose. UCSF makes no representation and provides no warranty that the use of the Data Contributors' Data or the TED Metadataset will not infringe any patent or other proprietary rights.

22. To the extent allowable under applicable laws, Data User agrees to indemnify, defend and hold harmless UCSF and its trustees, officers, staff, representatives and agents against all damages, expenses (including without limitation legal expenses), claims, demands, suits or other actions arising from Data User's negligence or intentional misconduct in its acceptance, storage, use and disposal of the Data Contributors' Data and TED Metadataset, as well as all other information provided to Data User under this Agreement or arising in connection with this Agreement.

23. This Agreement is not assignable by Data User.

24. Neither party will use the name of the other party or its employees in any advertisement, press release, or other publicity without prior written approval of the other party.

25. The term of this Agreement shall commence on the Effective Date (indicated above) and shall continue for a period of two (2) years, unless terminated sooner as set forth in this Agreement. This Agreement may be renewed for additional one (1) year terms by written amendment signed by authorized officials of both parties.

26. Upon termination or expiration of this Agreement, the Data User agrees to promptly provide UCSF with a summary of the results of the research conducted using the TED Metadataset in accordance with the Research Proposal ("Research Summary"), as well as all materials and data provided by Data Contributors and UCSF under this Agreement, without limitation. The Data User further agrees to promptly provide UCSF with a Research Summary prior to the execution of a written amendment to extend the term of this Agreement.

27. The Data User may terminate this Agreement at any time by notifying the UCSF Principal Investigator in writing, and promptly returning all Data provided to Data User under this Agreement.

28. UCSF or the TED Executive Committee may terminate this Agreement at any time by denying the Data User's access to additional data and other study materials. UCSF may terminate with or without cause, for any reason, and shall indicate so in writing to Data User. In the event that UCSF terminates this Agreement, Data User shall at UCSF's option, return or destroy (and confirm in writing such destruction), the Clinical Data, Biospecimens, and/or Imaging Studies and all copies, including all documents created by Data User where portions of the TED Metadataset, Biospecimens, and/or Imaging Studies are reproduced. Use of the Clinical Data, Biospecimens, and/or Imaging Studies for a new purpose or project will require a new application to and subsequent approval by Executive Committee.

29. This Agreement may be executed in one or more counterparts. Delivery of an executed counterpart of this Agreement by facsimile or a .pdf data file or other scanned executed counterpart by email shall be equally as effective as delivery of a manually executed counterpart of this Agreement.

Signatures

If Data User and Data User principal investigator acknowledge and agree to the above terms and conditions for transfer of the TED Metadataset Clinical Data, Biospecimens, and/or Imaging Studies, please so indicate by returning one copy of this Agreement signed and dated by Data User principal investigator and by a duly authorized representative of Data User. Upon receipt of signed Agreement by UCSF Principal Investigator and UCSF authorized representative, and confirmation that CITI Human Subjects Protection Training certification has been completed, the Data described in Paragraphs 8 (a)-(c) will be provided to Data User for the purposes set forth in Research Proposal. **All members of Data User's Research Team who will access or analyze data must individually sign this Agreement.**

READ AND ACKNOWLEDGED

PRINCIPAL INVESTIGATOR

Signature: _____

Printed Name: _____

Title: _____

Date: _____

ADDITIONAL DATA USER

Signature: _____

Printed Name: _____

Title: _____

Date: _____

SIGNATURE OF DATA USER INSTITUTION

Signature: _____

Printed Name: _____

Title: _____

Date: _____

AUTHORIZED SIGNATURE FOR UCSF

Signature: _____

Printed Name: _____

Title: _____

Date: _____

READ AND ACKNOWLEDGED BY UCSF PRINCIPAL INVESTIGATOR

Signature: _____

Printed Name: _____

Title: _____

Date: _____

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). 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). 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.

<u>Acknowledgements</u>

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		
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	University of Pennsylvania
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	University of Pennsylvania
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

READ AND ACKNOWLEDGED

PRINCIPAL INVESTIGATOR

Signature: _____

Printed Name: _____

Date: _____