I. INTRODUCTION:

The National Institutes of Health (NIH) has supported data collection from participants in numerous clinical trials and epidemiologic studies as part of approved protocols under the Rare Diseases Clinical Research Network (RDCRN). These data from well-characterized population samples constitute an important scientific resource. It is the view of the NIH that their full value can only be realized if they are made available, under appropriate terms and conditions consistent with the informed consent provided by individual participants, in a timely manner to the Rare Diseases Community and the largest possible number of qualified investigators. Accordingly, the RDCRN has adopted a Data Sharing Policy (Appendix A) establishing the criteria and mechanisms for data sharing among investigators within the Rare Diseases Network (RDN) and with the general scientific community.

The Brittle Bone Disorders Consortium (BBD) created this document as a companion piece to the RDCRN Data Sharing Policy. It establishes policies and procedures that the BBD will follow when sharing data within and outside of the Consortium.

II. SCOPE:

This policy addresses how data generated by the Brittle Bone Disorders Consortium (BBD) is to be used.[1]

III. DEFINITIONS:

Commercial Purpose – Data will be considered as being for a commercial purpose if they are to be used by an investigator who is an employee of a for-profit organization, if they are to be used by an investigator as the basis for a consulting relationship with a for-profit organization. Data will also be considered as being for a commercial purpose if the investigator(s) take any affirmative steps to facilitate commercial use of results derived from data.

Data – In this policy, the term data refers to data generated by the BBD and maintained by the Data Management and Coordinator Center at the University of South Florida.

[1]This document does not provide legal information or advice and BBD Consortium members are urged to consult their own institutional officials and legal counsel for such information or advice. The BBD Consortium expects that any use or dissemination of its data or research shall conform to all applicable laws, including those that apply to Member States of the European Union and applicable national, state or provincial, and local law.This document describes certain requirements that apply to such use within the United States.

Data Use Agreement (DUA) - HIPAA allows a researcher who wishes to use a limited data set to enter into an appropriate "data use agreement" with a covered entity providing the limited data set without an authorization or a waiver of authorization from an IRB or Privacy Board[2]. The agreement must list the permitted use and disclosures of the PHI being used and require that the researcher will:

- Use appropriate safeguards for the information,
- Not use or further disclose the information other than as agreed or as required by law,
- Report any uses/disclosures that were not permitted
- Ensure that anyone who has access to the data also agrees to these restrictions
- Not identify the information or contact the individuals

A researcher using de-identified data, where the information cannot be traced to a particular individual or protected health information disclosed by a covered entity in a limited data set under an appropriate data use contract, is exempt from the disclosure accounting requirements.

The DUA may be part of a Services Agreement (see section D) or a stand-alone agreement.

De-identified Data – De-identified data excludes certain identifying information in accordance with certain regulatory standards set forth in the Privacy Rule so that it no longer contains Protected Health Information (PHI) and is exempt from the requirements applicable to PHI under the Privacy Rule.[3] De-identified health information neither identifies nor provides a reasonable basis to identify an individual. Data shall be considered de-identified only when all 18 PHI items are removed from the data in accordance with 45CFR164.514[4].

External Investigator – An Investigator who is not a BBD Member (defined below) who has expressed an interest in using BBD data and/or BBD research generally for an academic purpose or for a commercial purpose.

Internal investigator – An Investigator who is a BBD Member (defined below).

"Other Use" – Use of data other than for publication purposes, such as for a grant application, presentation, to determine the feasibility of a data mining project or study, or to support an IND or NDA application.

Limited Data Set - A limited data set is an exception to the HIPAA Privacy Rule requirement for authorization from the subject for research use of protected health information. A limited data set lacks 16 of the 18 identifiers itemized by the Privacy Rule. A limited data set may contain dates of birth, admission, discharge and death and it may contain geographical information such as town/city, state, and zip code[3].

---

[2] See 45 CFR Part 164.514 (e) (4) (ii).
[3] See, 45 CFR 164.514(b)((2)(i). See also National Institutes of Health (NIH), "How Can Covered Entities Use and Disclose Protected Health Information for Research and Comply with the Privacy Rule?"
[4] See 45 CFR Part 164.514.

BBD Member/Members – Includes all members of the Brittle Bone Disorders Consortium, such as principal investigators, co-investigators, study coordinators, study neuropsychologists, biostatisticians and program administration.

BBD Leadership – Consortium principal investigator (director), co-principal investigator (co-director), and associate director

IV. POLICIES:

A. Data Use

All data generated by the BBD consortium is available to all BBD members for analysis. These participating individuals and institutions are listed below:

- V. Reid Sutton, M.D., Sandesh Nagamani, M.D., Brendan Lee, M.D., Ph.D., – Baylor College of Medicine
- David Eyre, Ph.D. – University of Washington (Mass Spectrometry Core)
- Eric Orwoll, M.D. – Oregon Health and Science University
- Deborah Krakow, M.D. – University of California at Los Angeles
- Cathleen Raggio, M.D. – Hospital for Special Surgery
- Frank Rauch, M.D. & Jean-Marc Retrouvey, M.D. & Francis Glorieux, M.D.– Shriners Hospital for Children, Montreal
- Emily Germain-Lee, M.D. – Kennedy-Kreiger Institute
- Peter Smith, M.D. & Gerald Harris, Ph.D, PE– Shriners Hospital for Children, Chicago/Marquette University
- Laura Tosi, M.D. – Children's National Medical Center
- Eric Rush, M.D. – University of Nebraska Medical Center
- Jeff Krischer, Ph.D. – University of South Florida (Data Collection & Analysis Core)

The only Protected Health Information (PHI) available to all internal investigators are dates of birth, admission, discharge, and death. All other identifying information such as name, address, phone number, fax number, email address, social security number, medical record number, health plan beneficiary number, and account numbers are only available to investigators at the enrolling site. Certificate/license numbers, vehicle identifiers, device identifiers, web URLs, IP address numbers, biometric identifiers, full face photographic images, and other unique identifying numbers or codes are not collected as part of BBD research.

External investigators will specify whether de-identified data or a limited data set is requested. If a limited data set is requested, only data from subjects that have consented to share a limited data set will be shared. To ensure that the confidentiality and privacy of study participants are protected, all external investigators seeking access to data from BBD studies must execute and submit an appropriate standard data use agreement form prior to obtaining BBD data.

B. General Data Released to the Scientific Community

Data will be shared with the scientific community as is required for all NIH-funded studies and will follow NIH Data Sharing Policy and Implementation Guidance[5] and the RDCRN Data Sharing Policy (see Appendix A). The general release of data will not include customized data reports or analysis but will include a data dictionary.

C. Specific Data Requests

External commercial and non-commercial investigators interested in using data generated by the BBD prior to its general release to the scientific community or who would like customized data reports and/or analysis have several options as described below.

- Collaboration with a BBD member on analysis and publication (or other use) - External investigators (commercial or non-commercial/academic)
- Independent analysis
- Services Agreement

D. Data Request Process

Individuals and institutions participating in the BBD consortium, as well as, non-participating persons should submit a concept sheet for executive committee review. This concept sheet should be submitted to the BBD project manager. Please see Appendix B.

This concept sheet will be reviewed by the BBD executive committee for feasibility and scientific merit within 1 month of submission of all materials. The executive committee is comprised of all BBD PIs listed above. If the concept sheet is submitted by a member or the executive committee, then they must recuse themselves from the evaluation.

Approval will be determined by taking a majority vote. If a proposal is rejected, then written documentation must be issued within 4 weeks of the decision. Rationale must be provided along with the determination. An appeal can be made and the concept sheet can be resubmitted to the executive committee. This resubmission must occur within 2 months of the rejection documentation being received.

Once a concept has been approved, the BBD project manager will forward this request to the Data Management and Coordinating Center (DMCC). The DMCC will then insure that this request is processed in a timely manner.

Once data requests have been completed the DMCC will send the data reports to the executive committee for review. This information will be transmitted via email unless requested otherwise. It is the executive committee's responsibility to approve this information before it is sent out to the requestor(s) listed on the approved concept sheet.

---

[5] See NIH Data Sharing and Implementation Guidance.

E. Services Agreements and Contracts

A service agreement needs to be executed for any data mining project involving external investigators. This template incorporates the following elements: statement of work, fee schedule, invoicing instructions, nondisclosure and trade secrets terms, ownership and use of work product arrangements, publication and presentation rights and other standard legal terms. Services Agreements will also set forth a project cost and budget and will contain a data use agreement. If it is anticipated that data will be requested more than once or will require complex analyses, a BBD infrastructure fee will be assessed for support provided.

Service agreements will be executed by a designated representative of the executive committee or by the consortium PI.

F. BBD Site Responsibilities

BBD sites agree to submit data in a timely manner so that it is available for analysis. Sites are routinely audited by the Data Management and Coordinating Center. Sites also may be audited by federal funding agency or other governmental agencies with oversight over federally funded research or clinical trials. In addition, industry trials may also require the sites to accept additional monitoring or auditing. If additional audits or other requests for access to data and records result from sharing data (e.g. with a company that submits it to the FDA as part of a drug filing), BBD sites will comply with the audits and make source documents and other records available as necessary.

G. Intellectual property

Each site owns the data collected at their own site. The Brittle Bone Disorders Consortium owns the complete set of data collected at all sites (collective ownership). Data will be entered into dBGap, therefore, the NIH will also own the data set. At the completion of the study, the Osteogenesis Imperfecta Foundation will have ownership of the data set.

H. Conflict of Interest, Data Release & Publication Agreement

Please see appendix C.

APPENDIX A:

Rare Diseases Clinical Research Network
Data Sharing Policy
Version 22 Feb 2011

The National Institutes of Health (NIH) has supported data collection from participants in numerous clinical trials and epidemiologic studies as part of approved protocols under the Rare Diseases Clinical Research Network (RDCRN). These data from well-characterized population samples constitute an important scientific resource. It is the view of the NIH that their full value can only be realized if they are made available, under appropriate terms and conditions consistent with the informed consent provided by individual participants, in a timely manner to the Rare Diseases Community and the largest possible number of qualified investigators. Accordingly, this document establishes the policy of the RDCRN for when data from these studies will be available for sharing with the scientific community for the purposes of scientific research. This policy does not include tissues or specimens collected in RDCRN studies.

This policy relates to the transfer of data into an ORDR-governed repository. A separate policy will be developed with respect to access to the repository by qualified scientists.

Informed consents for RDCRN studies should include consent for sharing the study data without personal identifiers with the scientific community for research purposes. Data sets without an informed consent permitting use by non-study researchers will placed in the RDCRN repository only if the institutional review board (IRB) has approved a waiver of informed consent.

Data in the RDCRN data management center under this policy will not include personal identifiers such as name, address, social security number, or medical record numbers. The identifiers will be held by the original investigators who collected the information. Although the data will be coded, the data center will have IRB-approved written policies and operating procedures that prohibit the release of the link to investigators/recipients under any circumstances. In addition, the recipient of the data must enter into an agreement prohibiting, under any circumstances, seeking or receiving any links or keys that could lead to personal identification of subjects.

Any publications arising from use of data should include reference(s) to relevant publications from the original investigators, if appropriate, and should in all cases acknowledge the RDCRN repository as the source of the data AND the depositing investigators of the utilized data.

Timing of Release of Data to Repository

a. *Clinical Trials* – Data sets will be made available to the scientific community after publication(s) of planned analyses (as set forth in the protocol) of the clinical trial

results OR no later than 3 years after the final visit of the last participant to a clinical trial site, whichever comes first.

b. *Observational/Longitudinal/Natural History/Epidemiology Studies* –Available data will be released to the repository and available to the scientific community every 5 years (after initial accrual date) OR publication of planned analyses, whichever comes first.

c. *Ancillary Studies* – In those cases in which the timeline for an ancillary study differs from that of its parent study, the date of the release of data to the repository and availability to the scientific community will relate to the timeline of the ancillary study.

Rare Diseases Clinical Research Network Consortia Data Sharing Policy

Each consortium is expected to maintain a data sharing policy. This policy shall be reviewed by the ORDR, Data Management and Coordinating Center, and the consortium's funding institution.

APPENDIX B:

Brittle Bone Disorders Consortium

Concept Sheet for Data Request

My submission of this concept sheet indicates my willingness to discuss with and enter into a research agreement with the Brittle Bone Disorders Consortium, according to standard procedures for data analysis, data confidentiality, authorship and intellectual property sharing.

Submission Type: □ Initial Submission □ Revised Submission or Resubmission

Date Submitted: _____

Principal Investigator

Name	
Institution	
Address	
Email	
Phone	
Fax	

Co-Investigator(s)

Name	
Institution	
Address	
Email	
Phone	
Fax	

Name	
Institution	
Address	
Email	
Phone	

Fax	

Proposed Study

Title:

Hypothesis:

Primary Objectives:

Secondary Objectives:

Brief Justification:

I. Background and choice of trial:

II. Preliminary Data:

Requested Data:

Statistical Endpoints:

I. Clinical Endpoints to be used in analyses:

II. Primary comparisons:

IV. Data Analysis performed by:

Budget Considerations:

I. Estimated expenses:

II. Funding Source:

Expected Project Milestones/Timeline for Publication:

Disclosure of Conflict of Interest:

Please attach a copy of your CV when submitting this concept form.

Signatures

I verify that all information provided on this form is accurate to the best of my knowledge.

Signature: _____ Date: _____
Signature: _____ Date: _____
Signature: _____ Date: _____

For BBD Use Only: This request has been: □ approved □ respectfully declined.

Signature: _____ Date: _____

APPENDIX C:

Brittle Bone Disorders Consortium

Conflict of Interest, Data Release & Publication Agreement

Name:
Institution/Affiliation:
Associates who will have access to data:

I certify that upon receipt of the Brittle Bone Disorders Consortium (BBDC) data that I will abide by all stipulations listed below:

- The data belongs to the BBDC and continues to be BBDC property, even after release to an investigator. As such, release to a 3rd party is prohibited without written permission from the BBDC.
- The BBDC must be acknowledged in all publications as providing support for the data collection and as owners of the data.
- The Brittle Bone Disorders Consortium must be listed as an author on the manuscript since the group members will have contributed significantly to the publication through study design, data collection and analysis. Publications resulting from BBD will acknowledge all the PIs that contributed to the dataset as "Members of the BBD". This will include an asterisk to list all PI names on the first page or include the PI names in the acknowledgements section. PIs to be included: Brendan Lee, V. Reid Sutton, Sandesh CS Nagamani, Frank Rauch, David Eyre, Francis Glorieux, Gerald Harris, Tracy Hart, Deborah Krakow, Jeffrey Krischer, Eric Orwoll, Cathleen Raggio, Emily Germain-Lee, Peter Smith, Laura Tosi, Eric Rush.
- When a member of the BBDC participates in the analysis and interpretation of the data or writing or editing of a manuscript for publication, that individual will receive authorship on the manuscript in accordance with the contribution.
- Data included in the publication will be restricted to the hypothesis proposed in the application to the BBDC.
- A good faith effort will be made to have the data published within the timeframe stipulated in the application submitted to the BBDC. It is understood that after a period of 12 months, the BBDC may release the same data to another individual for a similar or related hypothesis.

Name

Date