NIH/NCATS GRDRSM Program

Global Rare Diseases Patient Registry Data Repository (GRDR)

Data Submission Agreement

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GRDR Repository Data Submission Agreement

Overview

Introduction

The Office of Rare Diseases Research, National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH) has initiated the NIH/NCATS GRDR℠ Program. As part of the GRDR℠ program NCATS has developed a central data repository to aggregate and store de-identified patient data initially collected by rare disease patient organizations.

The data stored in this repository – the Global Rare Disease Patient Data Repository (GRDR) – represent valuable scientific resources that should be made available, in a timely manner and on appropriate terms and conditions, to the largest possible number of qualified investigators in order to maximize their research value. NIH has responsibility to the public in general, and to the scientific community in particular, to encourage the use of these resources to achieve rapid scientific progress.

NIH also has responsibility to take steps to promote the security and confidentiality of the information in GRDR. Accordingly, data stored in GRDR have been stripped of all individual identifiers, and the system conforms to FISMA requirements to protect the Data. However, the unique and intrinsically personal nature of DNA, derivative data of which are included in GRDR repository, combined with the recent increase in the accessibility of conducting genotype and other sequence analyses (in terms of technological capacity and cost), has altered the framework through which "identify-ability" can be defined.

Therefore, to further promote the confidentiality and privacy of patients, any Recipient who is granted controlled access (see below) to GRDR Data is expected to adhere to the terms and conditions of a Data Use Certification (DUC). Failure to do so could result in denial of further access to data.

In addition, those rare disease organizations which have submitted data to GRDR have made a substantial long-term contribution to GRDR repository. Accordingly, NCATS seeks to encourage appropriate data use and collaborative relationships by outside investigators with GRDR and the submitters and to ensure that the contribution of the submitters and NCATS is appropriately acknowledged.

The GRDR Review Committee (GRC) approves submission of data and, when applicable and feasible, images to the GRDR Repository. The GRC will review the Repository Data Submission Request from each Submitter and will decide whether to permit the submission based on the expectations outlined in the GRDR policy. In the event that submissions raise concerns related to privacy and confidentiality, risks to populations or groups, or other concerns, the GRC will consult with other experts as appropriate.

Submitters may only use this Repository Data Submission Agreement to submit Data to GRDR. All submission requests are subject to approval by the GRC. Completing this Repository Data Submission Agreement is a necessary step to submit Data to GRDR.

Access to other Data within GRDR for analysis purposes will be subject to the GRDR Repository Data Use Certification and procedures.

Definition and Abbreviation

- **GRDR-**Global Rare Diseases Patient Registry Data Repository
- **GRC-**GRDR Review Committee
- **Deidentified data-**data that all personal identifiers were removed
- **Data (in capital D)-** Deidentified data
- **SA-**Submission Agreement
- **Data questionnaire-**A file that contains list of questions about the patients and his disease, diagnosis, medication, procedures, family history etc.
- **Data dictionary-** A file (based on the Data questionnaire) that contains question text, variable names, variable labels, all possible values for each variable, the meaning of those values, source table from database (if applicable), and type of question.
- **DMCC-Data** Manegment Coordinating Committee
- **CHOP-**Childrens Hospital Of Philadelphia
- **CDEs-**Common Data Elements
- **UDEs-**Unique Data Elelemnts
- **GUID-**Global Uniqe Udentifier
- **IRB-**Institutinal Review Board
- **CNS IRB-** NIH Combined NeuroScience IRB
- **FWA-**Federal Wide Assurence
- **NCATS-**National Center for Advances Translational Research
- **ORDR-**Office of Rare Diseases Resrach

Steps to Request to Submit Data and/or Images to GRDR℠ Repository

1. Submitter request, complete and sign on the *Submitter Information and Certifications and submission agreement (SA)* (this form) and submit it to the GRDR support group at: grdrsupport@mail.nih.gov
2. The application form will be reviewed by the support group for completion and the GRC will review to approve/reject or request additional information.
3. Submitter is notified of approval/rejection of their application.
4. Approved Submitter is provided access to the GRDR Program Portal to upload all necessary documentations including registry questionnaire, data dictionary and the registry de-identified data (Data).
5. Submitter provides questionnaire, data dictionary, Data and other supporting documentation (if requested) via the GRDR Program Portal.
6. Approved Submitter request access to the Global Unique Identifier (GUID) client software via the GRDR website https://grdr.ncats.nih.gov/
7. GRC conducts quality control to verify that all identified information has been removed. It is the responsibility of the submitters to remove all identified information. Submitted data with identified information will be discarded and resubmission will be required.
8. The DMCC-CHOP reviews Submitter's questionnaire, data dictionary and Submitter's Data.
9. DMCC-CHOP rejects any data that includes identified information.
10. The DMCC-CHOP will communicate directly with the submitter regarding Data mapping.
11. DMCC-CHOP completes mapping Submitter's Data.
12. Submitter assigns *GUID/ Registry ID and uploads Data into the GRDR Program Portal
13. Submitter are notified when the Data is ready and approved for integration into the GRDR Data Repository.
14. DMCC-CHOP integrates Submitter's Data into the GRDR repository.
15. Submitter is notified that the Data is integrated into the GRDR repository and it is ready for potential access requests.

Data Submission Agreement for NIH/NCATS GRDR℠ Program-the Global Rare Disease Patient Registry Data Repository (GRDR)

I request approval to submit Data and/or images to the NIH/NCATS GRDR℠ Program's Global Rare Diseases Patient Registry Data Repository (GRDR) for the purpose of sharing Data for research. I agree to the following terms:

1. Research Project/Registry Goals. These Data will be submitted solely in connection with the Registry Goals, specifically indicated and described in the Submitter Information and Certifications section.

Data submitted to GRDR may be made available by NIH for either collaborative research (e.g., to accelerate research on ongoing studies) or general research purposes to the research community (e.g., meta-analyses and other secondary uses of the data).

This Data Submission Agreement (SA) for the GRDR Data Repository applies only to the source registry as identified, and covers only the Research Project and Registry Goals as contemplated, in the Submitter Information and Certifications section.

Submitter must submit a completed SA (this document) for each source registry for which submission is requested.

2. Non-Transferability of Agreement. This SA is not transferable. Submitter agrees that substantive changes Submitter makes to the Research Project requires execution of a new SA, in which the new Research Project is designated. If the Submitter changes institutions and wishes to retain submission privileges to GRDR Data Repository, a new SA in which the new institution acknowledges and agrees to the provisions of the SA is necessary.

3. Change of Registry Data. Submitter agrees that substantive changes to the registry data including removal/additional Common Data Elements (CDEs) and/or Unique Data Elements (UDE) and data requires re-evaluation by the GRC that may result in execution of a new SA.

3. Use of NIH Global Unique Identifier Client. Submitter has used the software program provided free-of-charge by NIH, subject to the GRDR Global Unique Identifier (GUID) Software user agreement, to assign GUIDs to each patient (when applicable). Submitter has re-sorted the data according to GUID.

4. Non-Identification of Subjects. Submitter agrees the data and/or images have been 'de-identified' according to the following criterion: the identities of subjects cannot be readily ascertained or otherwise associated with the Data by the repository staff or secondary Data users (45 C.F.R. 46.102(f)). Submitter further agrees not to disclose the identities of research participants to GRDR in the future and to verify that Data and/or images lack identifiers after submission. Submitter agrees to notify NIH as soon as possible if the Submitter discovers identifying information in submitted data.

5. IRB and FWA approval. Submitter must also have documentation of IRB approval. Submitter can use an IRB of their choosing or can apply to use the NIH CNS IRB as the IRB of record. In addition, submitter must be covered under a Federal-Wide Assurance from the USA Office of Human Research Protections (OHRP). Information on obtaining an FWA can be found at http://www.hhs.gov/ohrp/assurances/assurances/index.html.

6. Data Disclaimers. Submitter agrees that NIH does not and cannot warrant the results that may be obtained by using any data or data analysis tools provided by the GRDR[SM] Program. NIH disclaims all warranties as to the accuracy of the data in GRDR Data Repository or the performance or fitness of the data or data analysis tools for any particular purpose.

7. Supporting Materials. Submitter agrees to provide GRDR Program with supporting information and documentation (Supporting Materials) to enable efficient use of the submitted Data by investigators unfamiliar with the Data (e.g., registry protocol(s) or other supporting documentation, as appropriate, and questionnaire(s)).

8. Data Accuracy. Submitter certifies to the best of his/her knowledge and belief that the Data submitted to GRDR are accurate. Submitter also agrees to perform the specified quality control activities (data curation) within a timeframe that will be specified by the GRC. Submitter further agrees to notify NIH as soon as possible if, upon review of the Data, the Submitter discovers Data quality concerns. Submitter with previous scientific misconduct will be rejected from submitting or accessing Data.

9. Notification to NIH of Publication. Prompt publication or other public disclosure of the results of the Research Project is encouraged. Submitter agrees to notify NCATS via email at grdrsupport@mail.nih.gov as to when and where a publication (or other public disclosure) of a report from the Research Project will appear. Notification of such publications can occur by sending an email to grdrsupport@mail.nih.gov with the title, authors, place of publication, and publication date. Notification of such publications can also occur by sending to the grdrsupport@mail.nih.gov an updated biographical sketch or CV of the publishing author.

10. Data Access for Research. Submitter agrees that Data and Supporting Materials submitted to GRDR may be accessed and used broadly by qualified (agreed to Terms and Conditions) researchers for research and other activities as authorized by and consistent with law and applicable NIH policies and procedures.

11. Non-Research Access. Submitter acknowledges that data and Supporting Materials submitted to GRDR[SM] become U.S. Government records that are subject to the Freedom of Information Act (FOIA). NIH is required to release Government records in response to (FOIA) requests unless they are exempt from release under one of the FOIA exemptions. Submitter further acknowledges that data and Submitting Materials may be used or released consistent with applicable law.

12. Acknowledgments.

1. In any and all publications based upon use of dataset(s) submitted to GRDR including cases where patients were recruited to studies as a result of access to the GRDR data, Submitter agrees to cite NIH/NCATS GRDR[SM] Program. The publication should include the following acknowledgement:

> *Data used in the preparation of this article reside in the NIH/NCATS GRDR[SM] Program's Global Rare Diseases Patient Registry Data Repository (GRDR). This manuscript reflects the views of the authors and does not reflect the opinions or views of the NIH.*

Data used directly from the source of the submitter (source registry) is subjected to the source registry policy and doesn't require the acknowledgment of the GRDR Program.

2. Submitter agrees to acknowledge the contribution of the GRDR Program and the contributing registry(ies) in any and all oral and written presentations, disclosures, and publications resulting from any

use of data, or analyses of data using GRDR Data. The manuscript should include the following acknowledgement:

Data used in the preparation of this article reside in and were analyzed using the NIH/NCATS GRDR℠ Program's Global Rare Diseases Patient Registry Data Repository (GRDR). Data used for this research was contributed by xx registry. The GRDR is a collaborative biomedical resource created by the National Center for Advancing Translational Sciences at the National Institutes of Health to provide a national resource to support and accelerate research in rare diseases. This manuscript reflects the views of the authors and does not reflect the opinions or views of the NIH or of the submitters submitting original Data to GRDR.

13. Non-Endorsement; Liability. Submitter agrees not to claim, infer, or imply endorsement by the United States Government, the Department of Health & Human Services, the National Institutes of Health, or the Office of Rare Diseases Research at the National Center for Advancing Translational Sciences (NCATS) of the Research Project, the submitter institution, or personnel conducting the Research Project or any resulting commercial product(s). The United States Government assumes no liability except to the extent provided under the Federal Tort Claims Act (28 U.S.C. § 2671-2680).

14. Submitter's Compliance with Institutional Requirements. Submitter acknowledges that these Data were collected in manner consistent with all applicable laws and regulations, as well as institutional policies. Submitter further acknowledges that the Data were collected pursuant to an informed consent that is not inconsistent with the Data submission, and that the Data submitted were collected in accordance with 45 CFR Part 46.

15. Submitter's Permission to Post Information Publicly. Submitter agrees to permit NIH to summarize and release for public use on the NCATS/GRDR Web site the Supporting Materials along with the Submitter's name and organization/institutional affiliation.

16. Privacy Act Notification. The Submitter agrees that information collected from the Submitter, as part of the SA and submission certification, may be made public in part or in whole for tracking and reporting purposes. This Privacy Act Notification is provided pursuant to Public Law 93-579, Privacy Act of 1974, 5 U.S.C. Section 552a. Authority for the collection of the information requested below from the Submitter comes from the authorities regarding the establishment of the National Institutes of Health, its general authority to conduct and fund research and to provide training assistance, and its general authority to maintain records in connection with these and its other functions (42 U.S.C. 203, 241, 289l-1 and 44 U.S.C. 3101), and Section 301 and 493 of the Public Health Service Act. These records will be maintained in accordance with the Privacy Act System of Record Notice 09-25-0200 (http://oma.od.nih.gov/ms/privacy/pa-files/0200.htm) covering "Clinical, Basic and Population-based Research Studies of the National Institutes of Health (NIH), HHS/NIH/OD." The primary uses of this information are to document, track, and monitor and evaluate the submission of data from clinical, basic, and population-based research activities and to notify Submitters in the event a potential error in the dataset is identified or in the event of updates or other changes to the database.

The Federal Privacy Act protects the confidentiality of the Submitter's NIH records. NIH will use the Data in the GRDR repository for the purposes of integrating de-identified patient data in order to stimulate biomedical research studies and cross diseases analyses to accelerate the development of therapeutics, drugs and hopefully cures for rare diseases. In addition, the Act allows the release of some information in the Submitter's records without the Submitter's permission; for example, if it is required by members of Congress or other authorized individuals. The information requested is voluntary, but necessary for submitting Data to GRDR.

17. Security. Submitter acknowledges the expectations set forth by the attached GRDR Information "Security Best Practices" for the use and security of data.

18. Amendments. Amendments to this SA must be made in writing and signed by authorized representatives of both parties.

19. Termination. Submitter agrees that either party may terminate this SA without cause by providing 30 days written notice to the other party. NCATS may terminate this agreement with 5 days written notice if the NCATS determines, in its sole discretion, that the Submitter has committed a material breach of this SA. NCATS may, in its sole discretion, provide Submitter with 30 days notice to remedy a breach before termination. Closed accounts may be reactivated upon submission of an updated Submission Request and SA.

20. One-Year Term and Access Period. Researchers who are granted permission to submit data to GRDR receive an account that is valid for a period of one year. This SA will automatically terminate at the end of one year. An account may be renewed upon recertification of a new SA. Accounts that remain inactive for 12 consecutive months may be closed at the discretion of NIH.

21. Violation of NIH/NCATS GRDR℠ Program Policy.

Submitters agree to immediately report violations of GRDR Policy to the GRDR support group at: grdrsupport@mail.nih.gov

GRDR Information Security Best Practices

The purpose of these Security Best Practices, which are subject to applicable law, is to provide minimum security standards and best practices for individuals who use GRDR to submit, access, and analyze Data. Keeping GRDR information secure through these best practices is important. Subject to applicable law, Submitters agree to immediately report breaches of data privacy and/or security to the GRDR support group grdrsupport@mail.nih.gov.

Best Practices

We suggest that you:

- Do not attempt to override technical or management controls to access data for which you have no express authorization.
- Do not use your trusted position and access rights to exploit system controls or access Data for any reason other than in the performance of the approved proposed research.
- Ensure that anyone directed to use the system has access to, and is aware of, GRDRInformation Security Best Practices and all existing policies and procedures relevant to the use of GRDR, including but not limited to, the GRDR℠ Program policy, and 45 CFR Part 46.
- Follow the GRDRpassword policy which includes:
    - Choose passwords of at least seven characters including at least three of the following types of characters: capital letters, lower case letters, numeric characters and other special characters.
    - Change your passwords every six months.
    - Protect your GRDR℠ password from access by other individuals—for example, store it electronically in a secure location.

- Notify NIH/NCATS GRDR[SM] Program at grdrsupport@mail.nih.gov of security incidents, or any incidents of suspected fraud, waste or misuse of GRDR or when access to GRDR[SM] is no longer required.

Security Standards

- Protect the data, providing access solely to authorized researchers permitted access to such data by your institution.
- Neither store nor transmit links between personally identifiable information and GUIDs.
- When you download GRDR data, download the Data to a secured computer or server with strong password protection.
- For the computers hosting data contributed to GRDR[SM], ensure that they have the latest security patches and are running virus protection software.
- Make sure the data are not exposed to the Internet or posted to a website that may be discovered by Internet search engines such as Google or MSN.
- If you leave your office, close out of data files or lock your computer. Consider the installation of a timed screen saver with password protection.
- Avoid storing data on a laptop or other portable medium. If storing data on such a device, encrypt the data. Most operating systems have the ability to natively run an encrypted file system or encrypt portions of the file system. (Windows = EFS or Pointsec and Mac OSX = File Vault).
- When finished using the data, destroy the data or otherwise dispose of it properly.

OMB No 0925 XXXX

Exp. Date XX/XX/20XX

Burden Disclosure: Public reporting burden for this collection information is estimated to average 10 minutes response, including the time reviewing instructions, searching existing data source, gathering and marinating the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to , a collection of information unless it display a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN:PRA#0925-XXXX. Do not return the completed form to this address.

NIH/NCATS GRDR℠ Data Repository Submitter Information and Certifications

1. Submitter Information: *Authorized Institutional Business Official (all fields are required)*

Date: _____Type of Application: _____ New _____ Renewal

First Name_____ Last Name_____

Degree: _____ Academic Position (or Title): _____

Institution: _____Department: _____

Street Address: _____

City: _____State/Province: _____

Zip/Postal Code: _____Country: _____

Telephone: _____FAX: _____

E-mail Address: _____

Institution's GRDR℠ Point of Contact Name (if different from the Submitter): _____

Institution's GRDR℠ Point of Contact Phone: _____E-mail: _____

Registry goals (title and brief description): _____

_____

_____

_____

If data are from biospecimens that have restrictions on sharing, please state those restrictions here:

_____

2. Certificate of Confidentiality: (applied / obtained / does not have, please circle one). Although it is not required, it is strongly encouraged by NIH. For more information go to http://grants.nih.gov/grants/policy/coc/contacts.htm#ncats

3. Attachments:
Upload electronic copies of the questionnaires, data dictionary and Data via the GRDRSM SharePoint. Other supporting documentation, should be sent to grdrsupport@mail.nih.gov

4. Signatures
By signing and dating this SA as part of submitting Data to GRDR℠, our Institutional/registry officials and I certify that we will abide by the SA and the NIH principles, policies and procedures for the use of the GRDR Repository. We further acknowledge that we have shared this document and the NIH policies and procedures with any research staff who will

participate in the use of GRDR[SM]. My Institutional/registry business official(s) also acknowledges that they have shared this document and the relevant NIH policies and procedures with appropriate institutional organizations.

Signature: _____Date: _____

*FWA#:_____IRB_____

For GRDR[SM] administrator only:

Access Approved_____ Access Denied: _____

Inquiries and Request Contact

Inquiries and Requests to Submit Data to NIH/NCATS GRDR℠ Program should be sent to the GRDR℠ Program Director

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