

The NIH/NCATS GRDR® 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 (ORDR), National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH) has initiated the NIH/NCATS Global Rare Diseases Patient Data Repository® (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 represent valuable scientific resources that should be made available, in a timely manner and on appropriate terms and conditions, to qualified investigators for future analysis and publication. NIH encourages the use of these resources to facilitate rapid scientific progress and get more treatments to more patients quickly.

NIH must safeguard the security and confidentiality of submitted data. Data stored in GRDR® must be stripped of all individual identifiers, to protect the privacy of the individual. However, the unique and intrinsically personal nature of DNA, derivative data of which are included in the 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 must adhere to the terms and conditions of a Data Use Certification (DUC). Failure to do so will imperil further access to data.

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

The GRDR® program review data submission agreement (SA) requests from each Submitter and will accept or reject the submission based on the expectations outlined in the GRDR® policy.

Submitters must use the Repository Data Submission Agreement to participate in the GRDR®.

Access to other de-identified data within GRDR® for analysis purposes will be subject to additional GRDR® Repository Data Use Certification and Procedures.

Definitions

“Data” refers to the information and images (if available) that have been collected, de-identified and recorded from the rare disease patient registries, regardless of the source of funding.

“Submitter” refers to as any person (whether individual or entity) that has submitted data to GRDR® according to the policies laid out in the GRDR® Data Repository Submission Agreement.

“Recipient” refers to any individual or entity requesting access to GRDR® data. A Recipient may be a Principal Investigator and his/her organization or a researcher at a non-profit or for-profit organization or corporation with an approved assurance from the Department of Health and Human Services Office for Human Research Protections.

“Research Project” refers to the research project specifically indicated and described in the Research Use Statement of the DUC.

“Data dictionary” refers to 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

“Data questionnaire” refers to a file that contains list of questions about the patient and his/her disease, diagnosis, medication, procedures, family history etc.

“De-identified data” refers to data with all personal identifiers removed in accordance with 45 CFR 164.514

Acronyms

- ❖ **CDEs**-Common Data Elements
- ❖ **CNS IRB**-NIH Combined Neuroscience IRB
- ❖ **DMCC**-Data Management Coordinating Center
- ❖ **DUC**-Data Use Certification
- ❖ **FOIA**-Freedom of Information Act
- ❖ **FWA**-Federal-Wide Assurance
- ❖ **GRDR®**-Global Rare Diseases Patient Registry Data Repository®
- ❖ **GUID**-Global Unique Identifier
- ❖ **IRB**-Institutional Review Board
- ❖ **NCATS**-National Center for Advancing Translational Sciences
- ❖ **NIH**-National Institutes of Health
- ❖ **ORDR**-Office of Rare Diseases Research
- ❖ **OHRP**-Office of Human Research Protections
- ❖ **SA**-Submission Agreement
- ❖ **UDEs**-Unique Data Elements

Data Submission to the GRDR® Repository*

* For requests outside of the U.S., see appendix A.

1. Submitter must 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 GRDR® program that will approve/reject or request additional information.
3. Approved Submitter is provided access to the GRDR® Program Portal to upload all necessary documentation including registry questionnaire, data dictionary and the registry de-identified data.
4. Submitter provides other supporting documentation (if requested) via the GRDR® Program Portal.
5. Approved Submitter shall request access to the Global Unique Identifier (GUID) client software via the GRDR® website, <https://grdr.ncats.nih.gov/>.
6. The GRDR® program conducts quality control to verify that all identified information has been removed. Submitted data with identified information will be discarded and resubmission will be required.
7. The Data Management Coordinating Center (DMCC) reviews submitter's questionnaire, data dictionary and data.
8. DMCC rejects any data that includes identified information.
9. DMCC will communicate directly with the Submitter regarding data mapping.
10. DMCC maps Submitter's data.
11. Submitter assigns *GUID/Registry ID and uploads data into the GRDR® Program Portal.
12. Submitter are notified when the data are ready and approved for integration into the GRDR® Data Repository.
13. DMCC integrates Submitter's data into the GRDR® Repository.
14. Submitter is notified that the data integrated into the GRDR® Repository and ready for 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. 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, nor are subsequent substantive changes without execution of a new SA, in which the new Research Project is designated. Should the Submitter change institutions and wish to retain submission privileges to the GRDR® Data Repository, a new SA is required in which the new institution acknowledges and agrees to the provisions of the SA.

3. Change of Research Project/Registry Data. Submitter agrees that substantive changes to the registry data, including removal/additional Common Data Elements (CDEs) and/or Unique Data Elements (UDEs) and data, also requires re-evaluation by the GRDR® program that may result in execution of a new SA.

4. Use of NIH Global Unique Identifier Client. The Global Unique Identifier (GUID) is a computer-generated alphanumeric code that is unique to each research participant. The GUID allows the GRDR® program to link together all submitted information on a single participant without identifying that participant, giving researchers access to information even if the data were collected at different locations or through different studies. A separate request to access the GUID application is available and required through the GRDR® portal. Recipient must agree to terms and condition for uses of the GUID application. Submitter may use the software program provided free-of-charge by NIH, subject to the GRDR® GUID Software user agreement to assign GUIDs to each patient (when applicable).

5. 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 submitter's data and/or images lack identifiers. Submitter agrees to notify NIH as soon as possible should the Submitter discover identifying information in submitted data.

6. IRB and FWA Approval. Submitter must document IRB approval. Submitter can use an IRB of their choosing or can apply to use the NIH CNS IRB as the IRB of record. Submitter must be covered under an FWA from the U.S. Office of Human Research Protections (OHRP). Information on obtaining an FWA can be found at <http://www.hhs.gov/ohrp/assurances/assurances/index.html>.

7. 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® 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.

8. 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)).

9. 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 GRDR® program. Submitter further agrees to notify NIH as soon as possible if, upon review of the data, the Submitter discovers data quality concerns. Submitters with previous scientific misconduct will not be permitted to submit or access data.

10. 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) or 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 be done by sending an updated biographical sketch or CV of the publishing author to grdrsupport@mail.nih.gov.

11. 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.

12. Non-Research Access. Submitter acknowledges that data and supporting materials submitted to GRDR® become US 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.

13. Acknowledgments. 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 the NIH/NCATS GRDR® Program. The publication should include the following acknowledgement:

Data used in the preparation of this article reside in the NIH/NCATS GRDR® 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 NIH.

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

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 presentation or 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. 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 NIH or of the Submitters submitting original data to GRDR®.

14. Non-Endorsement; Liability. Submitter agrees not to claim, infer, or imply endorsement by the United States Government, the Department of Health and Human Services, NIH, or ORDR 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).

15. 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 consistent with the data submission, and that the data submitted were collected in accordance with 45 CFR Part 46.

16. Submitter's Permission to Post Information Publicly. Submitter agrees to permit NIH to summarize and release for public use on the NCATS/GRDR® website the supporting materials along with the Submitter's name and organization/institutional affiliation.

17. 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 NIH, 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, 289I-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/public/MS/privacy/PAfiles/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, 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 information requested from the Submitter is voluntary. 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 disease analyses to accelerate the development of therapeutics, drugs and hopefully cures for rare diseases.

The Federal Privacy Act protects the confidentiality of the Submitter's NIH records. 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.

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

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

20. 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, extend the deadline to remedy a breach from 5 days to 30 days before termination. Closed accounts may be reactivated upon submission of an updated submission request and SA.

21. 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.

22. Violation of the 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

- You must not attempt to override technical or management controls to access data for which you have no express authorization.
- You must 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.
- You should ensure that anyone directed to use the system has access to, and is aware of, GRDR® Information 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 GRDR® password policy, which includes the following:
 - Choose passwords of at least eight characters including at least three of the following types of characters: capital letters, lowercase 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 the NIH/NCATS GRDR® 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® 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®, 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.

NIH/NCATS GRDR® Data Repository Submitter Information and Certifications*

* For requests from outside of the U.S., see appendix A.

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: _____

Email Address: _____

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

Institution's GRDR® Point-of-Contact Phone: _____ Email: _____

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 GRDR® 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[®]. 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[®] 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:

Yaffa Rubinstein, Ph.D.

Office of Rare Diseases Research (ORDR)

National Center for Advancing Translational Sciences (NCATS)

National Institutes of Health (NIH)

6701 Democracy Boulevard, Suite 940, MSC 4874

Bethesda, MD 20892

Phone: (301) 402-4338

Fax: (301) 480-9655

Email: yaffa.rubinstein@nih.gov

Appendix A: Ethical Guidelines, FWA, and IRB Approval for Non-U.S. Submitters

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 U.S. Office for Human Research Protections (OHRP). FWA registration is available to non-U.S. institutions. Information on obtaining an FWA can be found at <http://www.hhs.gov/ohrp/assurances/assurances/index.html>.

Non-U.S. submitters must be covered by their country's equivalent human subjects regulations. In lieu of an FWA, non-U.S. submitter must provide documentation identifying their country's and institution's ethical regulations, such as the Declaration of Helsinki, and their assurance to abide by those regulations, along with documentation of approval by the appropriate ethical review committee/board.

Non-U.S. submitter's application will be evaluated by the GRDR® program in a case-by-case manner.

We share the fundamental principles for responsible sharing of genomic and health care related data established by the Global Alliance for Genomics & Health:

- Respect Individuals, Families and Communities
- Advance Research and Scientific Knowledge
- Promote Health, Wellbeing and the Fair Distribution of Benefits
- Foster Trust, Integrity and Reciprocity

<http://genomicsandhealth.org/working-groups/our-work/framework>