

The NIH/NCATS GRDR[®] Program

Global Rare Diseases (Patient Registry) Data Repository[®] (GRDR[®])

Data Access Request

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GRDR® Data Repository Access Request & Data Use Certification

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 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, to protect the privacy of the individual. However, the unique and intrinsically personal nature of DNA derivative data of which are included in GRDR®, 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 “identifiability” 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 will imperil further access to data.

In addition, those rare disease organizations that have submitted data to GRDR® have made a substantial long-term contribution to GRDR®. 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.

Data Access Options

GRDR program provides two levels of access to the GRDR® data: [open data access](#) and [controlled data access](#). Requests may not be submitted simultaneously for open access and controlled access.

Open data access:

Open access allows broad release of non-sensitive data, including general information, trends, and charts of aggregated data or any information that is available to the public without restrictions and can be browsed online. Open data access does not require prior permission, authorization or review by a committee. However, persons seeking open access will be required to register on the GRDR® Repository site and provide the minimal information requested.

Based on the summary data available through open access, a person may determine if submitting an application to request access to more detailed information (controlled access) would be beneficial.

Controlled data access:

Controlled data access allows download of GRDR® data, including individual de-identified data within a disease and across diseases. Any request for controlled access will require completing the Data Use Certification (DUC) form and agreeing to the following terms and conditions.

Definitions

For purposes of this DUC:

“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.

“De-identified data” refers to data with all personal identifiers were 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
- **ERC**-Ethical Review Committee
- **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
- **OHRP**-Office of Human Research Protections
- **ORDR**-Office of Rare Diseases Research
- **SA**-Submission Agreement
- **UDEs**-Unique Data Elements

GRDR® Repository Request for Open Access

Although open data access does not require prior permission, authorization or GRDR® review, persons seeking open access are required to register on the GRDR® program portal and provide the minimal information as requested in the form below.

*Date: _____ *Type of Application: _____ New _____ Renewal

*First Name: _____ *Last Name: _____

*Degree: _____ *Academic Position (or Title): _____

*Institution: _____ *Disease Interest: _____

*Street Address: _____

*City: _____ *State/Province: _____

*ZIP/Postal Code: _____ *Country: _____

*Telephone: _____ Fax: _____

*Email Address: _____

Steps to Request Controlled Access to the GRDR® Data Repository*

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

1. Read the GRDR® Data Use Certification (DUC) (this document).
2. Complete Recipient Information and Certifications pages, including your Institution's IRB approval and Federal-Wide Assurance (FWA) number. Information on obtaining an FWA can be found at <http://www.hhs.gov/ohrp/assurances/assurances/index.html>.
3. Complete a Research Use Statement—a brief description and objectives of your Research Project in the text box provided. Provide a statement as to whether you have/will apply for, obtain, or do not have a Certificate of Confidentiality for the Research Project. List all the collaborating investigators at your organization. By submitting collaborators' individual names on the form, you and your Institutional Official affirm that each such individual has read and agreed to the Terms and Conditions within the DUC.

You (Recipient), as well as each Principal Investigator, designated Institutional Official and collaborator at different organizations, must complete a separate access request for the data and DUC. Coordinated requests by collaborating organizations should all use the same title in their request and each should reference the others in the Research Use Statement.

4. Complete and sign the Recipient Information and Certifications page, and obtain your Institutional Official's signature and date.
5. Requests for Controlled access will be reviewed by the GRDR® program. They will strive to complete the review within 14 business days of receipt.
6. The GRDR® program will notify the GRDR® Administrator if the access request has been approved, and an account will then be activated. The Recipient will receive an automated notification of their account update with any modified user name, passwords, or instructions for accessing the GRDR® data.

**Data Use Certification
for the
NIH/NCATS GRDR® Program
Global Rare Diseases Patient Registry Data Repository®**

Terms and Conditions

I acknowledge that the following Terms and Conditions apply to any and each access to and use of data from the Global Rare Diseases Patient Registry Data Repository® (GRDR®) and by my signature below, I, as Recipient, agree to abide by the following Terms and Conditions. As the Recipient, requesting access to data is at my sole risk and at no expense to the source registry contributing the data to GRDR® and/or to the NIH.

1. Research Project. This Data Use Certification (DUC) covers only the proposed Research Project in this application and does not cover multiple projects. Data will be used by the Recipient solely in connection with the Research Project. Recipient agrees that data will not be used in any research that is not disclosed to and approved by the GRDR® program as part of the Research Project. Recipient will complete and submit a new DUC for each research project for which data are requested.

2. Non-transferability of DUC. This DUC is not transferable. Recipient may neither transfer this DUC for use in any other research project nor transfer this DUC to any other person or persons seeking to participate in the approved Research Project. Recipient agrees that any substantive change Recipient makes to the Research Project requires execution of a new DUC, in which the new research project is designated. If the Recipient appoints another Principal Investigator to complete the Research Project, a new DUC in which the new Principal Investigator is designated is necessary. If the Recipient changes institutions and wishes to retain access to the GRDR® data, a new DUC in which the new institution acknowledges and agrees to the provisions of the DUC is necessary.

3. Non-Identification of Research Participants. Recipient agrees that it will not use data, either alone or in conjunction with any other information, in any effort whatsoever to establish the individual identities of any of the research participants from whom data were obtained. Recipient agrees to notify NCATS immediately if, upon access to or use of the GRDR® data, the Recipient discovers identifying information in those data.

4. GUID and Access to Submitted Data. 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 and over time. A separate request to access the GUID application is required and is available through the GRDR® portal. Recipient must agree to terms and condition for uses of the GUID application.

If a Recipient requests access to data on individuals for whom the Recipient has previously submitted data to GRDR®, the Recipient may have the capability of re-identifying the newly obtained GRDR® data. Consequently, these research activities may be considered “human subjects research” within the scope of 45 C.F.R. 46.

5. IRB and FWA Approval. Recipient must consult with the appropriate IRB representative whether an IRB approval is required for this research project. Recipient must have documentation of IRB approval or documentation of exemption from the IRB of the recipient institution for the planned research. In addition, recipient must be covered under a Federal-Wide Assurance 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>.

6. Data Disclaimers. Recipient agrees that NCATS does not and cannot warrant the results that may be obtained by using any data included in the GRDR® Repository. Recipient further agrees that NCATS disclaims all warranties as to the accuracy of data in GRDR® as well as the relevance of the data for any particular purpose.

7. Notification to NCATS of Publication. Recipient agrees to notify NCATS promptly via email at grdrsupport@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 to NCATS at grdrsupport@nih.gov an updated biographical sketch or CV of the publishing author.

8. Data Restriction and No Distribution of Data. Except as described in this paragraph, NCATS prohibits Recipients who receive GRDR® data from further disclosing, sharing and distributing the data to a third party or otherwise using the data for any purposes other than what was stated in the approved DUC.

Accordingly, Recipient agrees to retain control over data, and further agrees not to transfer data, with or without charge, to any other entity or any individual. Recipient agrees not to sell the data in any form to any entity or individual or to distribute the data to anyone other than his/her research staff who will also agree to the terms within this DUC.

9. Publication and Acknowledgments Policy. Recipient agrees to acknowledge the contribution of the NCATS and the Submitter(s) provision of the data in any and all oral and written presentations, disclosures, and publications resulting from any and all analyses of data using the GRDR® tools, whether or not Recipient is collaborating with Submitter(s). The manuscript should include the following acknowledgement or other similar language:

Data and/or research tools used in the preparation of this manuscript were obtained and analyzed from the controlled access datasets available through the NIH/NCATS GRDR® program (Global Rare Disease Patient Registry Data Repository®) and contributed by xxx registry/organization. GRDR® is a collaborative resource created by the Office of Rare Diseases, National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health to provide a global resource to support and accelerate research in rare diseases in pursuit of developing drugs and therapeutics. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or of the individuals and entities submitting original data to GRDR®.

If the Research Project involves collaboration with Submitters or NIH staff (as indicated in the DUC), then Recipient will acknowledge Submitters or NIH staff as co-authors, if appropriate, on any publication.

In addition, Recipient agrees to include a reference to GRDR® datasets and to cite the NIH/NCATS GRDR® program, the data contributing registry/organization, and the federal funding sources in abstracts (when applicable) as space allows.

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

11. Recipient's Compliance with Institutional Requirements. Recipient acknowledges that data access, if provided, is for research that is approved by the affiliated Institution, which must be operating under an Office

of Human Research Protections (OHRP)-approved Assurance. Furthermore, Recipient agrees to comply with all applicable rules for the protection of human subjects, which may include Department of Health and Human Services regulations at 45 C.F.R. Part 46, and other federal and state laws for the use of these data. Recipient agrees to report promptly to NCATS any proposed change in the Research Project and any unanticipated problems involving risks to subjects or others. This DUC is made in addition to, and does not supersede, any of Recipient's institutional policies or any local, State, and/or Federal laws and regulations that provide additional protections for human subjects.

12. Recipient's Permission to Post Information Publicly. Recipient agrees to permit NCATS to summarize on the GRDR® website the Recipient's research use of the GRDR® data along with the Recipient's name and organizational/institutional affiliation.

13. Privacy Act Notification. In order to access the GRDR® Repository, the Recipient agrees to provide the information requested below.

The Recipient agrees that information collected from the Recipient, as part of the Data Access Request, 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 Recipient 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 09-25-0156

(<http://oma.od.nih.gov/public/MS/privacy/PAfiles/0156.htm>) covering "Records of Participants in Programs and Respondents in Surveys Used to Evaluate Programs of the Public Health Service, HHS/PHS/NIH/OD." The primary uses of this information are to document, track, and monitor and evaluate the use of the GRDR® datasets, as well as to notify interested recipients of updates, corrections or other changes to the database. The information requested from the Recipient is voluntary. NIH and any individuals that are provided access to the datasets will have access to the data collected from the Recipient for the purposes described above.

The Federal Privacy Act protects the confidentiality of the Recipient's NIH records. The Act allows the release of some information in the Recipient's records without his/her permission; for example, if it is required by members of Congress or other authorized individuals.

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

15. Annual Update. When requested, Recipient will provide to grdrsupport@nih.gov a summary of research accomplishments from using GRDR® data in an updated biographical sketch or CV.

16. Amendments. Amendments to this DUC must be made in writing and signed by authorized representatives of the Recipient and NCATS.

17. Termination. Recipient agrees that either party may terminate this DUC without cause by providing 30 days written notice to the other party. Additionally, NCATS may terminate this DUC with 5 days written notice if the NCATS determines, in its sole discretion, that the Recipient has committed a material breach of this DUC; however, NCATS may, prior to the expiration of those 5 days, extend the deadline to 30 days on response to Recipient intent to remedy such breach. Closed accounts may be reactivated upon submission of an updated GRDR® Repository Access Request and DUC.

18. One-Year Term and Access Period. Recipients who are granted permission to access data from the GRDR® Repository receive an account that is valid for a period of one year that can be renewed year by year; however, the Terms and Conditions are perpetual. This DUC will automatically terminate at the end of one year. An account may be renewed upon recertification of a new DUC. Accounts that remain inactive for 12 consecutive months may be closed at the discretion of NCATS.

19. Accurate Representations. Recipient expressly certifies that the contents of any statements made or reflected in this document are truthful and accurate.

20. Violation of GRDR® Policy. Recipient agrees to immediately report violations of GRDR® policy to the GRDR® program director or to NCATS office at grdrsupport@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, Recipients agree to immediately report breaches of data confidentiality to the GRDR® program.

Best Practices

- You must not attempt to override technical or management controls to access data for which you have not been expressly authorized.
- 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.
- Ensure that anyone directed to use the system has access to, and is aware of the GRDR® Information Security Best Practices and all existing policies and procedures relevant to the use of GRDR® data, including but not limited to the GRDR® program policy at <https://grdr.ncats.nih.gov> and 45 C.F.R. 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 GRDR® staff, as permitted by law, at grdrsupport@nih.gov of security incidents, or any incidents of suspected fraud, waste or misuse of the GRDR® data or when access to the GRDR® Repository is no longer required.

Security Standards

- Protect the data, providing access solely to authorized researchers permitted access to such data by your institution or to others as required by law.
- When you download GRDR® data, download the data to a secured computer or server with strong password protection.
- For the computers hosting GRDR® data, 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, as permitted by law.

**NIH/NCATS GRDR® Data Repository Request for Controlled Access
Recipient Information and Certifications***

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

*Date: _____ *Type of Application: _____ New _____ Renewal

*First Name: _____ *Last Name: _____

*Degree: _____ *Academic Position (or Title): _____

*Institution: _____ *Disease Interest: _____

*Street Address: _____

*City: _____ *State/Province: _____

*ZIP/Postal Code: _____ *Country: _____

*Telephone: _____ *Fax: _____

*Email Address: _____

Research Project (Title): _____

By signing and dating this DUC as part of requesting access to data in GRDR®, my Institutional Officials and I certify that we will abide by the DUC and the NIH principles, policies and procedures for the use of GRDR® data.

I further acknowledge that I have shared this document and the NIH policies and procedures with any research staff who will participate in the use of GRDR® data.

My Institutional Business Official(s) also acknowledges that they have shared this document and the relevant NIH policies and procedures with appropriate institutional organizations.

Authorized Institutional Business Official

*Name: _____ *Title: 1 _____

*Signature: _____ *Date: _____

*IRB#: _____ *FWA#: _____

1 Signatory should specify whether he/she is (1) Principal Investigator, (2) Institutional Official, or (3) Research Collaborator.

Project Director/Principal Investigator Contact Information (if different from above):

*First Name: _____ *Last Name: _____

*Degree: _____ *Academic Position (or Title): _____

*Institution: _____ *Department: _____

*Street Address: _____

*City: _____ *State/Province: _____

*ZIP/Postal Code: _____ *Country: _____

*Telephone: _____ *Fax: _____

*Email Address: _____

Institutional Official(s):

*First Name: _____ *Last Name: _____

*Degree: _____ *Academic Position (or Title): _____

*Institution: _____ *Department: _____

*Street Address: _____

*City: _____ *State/Province: _____

*ZIP/Postal Code: _____ *Country: _____

*Telephone: _____ *Fax: _____

*Email Address: _____

Other Project Information

- 1. Are human subjects involved? ____ Yes ____ No
If yes to human subjects:
Is the project exempt from federal regulations? ____ Yes ____ No
If yes, check appropriate exemption number: ____ 1 ____ 2 ____ 3 ____ 4 ____ 5
If no, is the IRB review pending? ____ Yes ____ No
IRB approval date: _____

- 2. Research Use Statement/Project Summary: (see section 5 of the terms and conditions)

***Please insert your project summary here.
The box will expand as needed.***

Optional for Collaborators

Senior/Key Profile (Collaborating Investigator):

- *First Name: _____ *Last Name: _____
- *Degree: _____ *Academic Position (or Title): _____
- *Institution: _____ *Department: _____
- *Street Address: _____
- *City: _____ *State/Province: _____
- *ZIP/Postal Code: _____ *Country: _____
- *Telephone: _____ *Fax: _____
- *Email Address: _____
- *Project Role: _____ *Other Project Role Category: _____

Senior/Key Person Profile (Collaborating Investigator):

*First Name: _____ *Last Name: _____

*Degree: _____ *Academic Position (or Title): _____

*Institution: _____ *Department: _____

*Street Address: _____

*City: _____ *State/Province: _____

*ZIP/Postal Code: _____ *Country: _____

*Telephone: _____ *Fax: _____

*Email Address _____

*Project Role: _____ *Other Project Role Category: _____

Use additional sheets for additional profiles as needed.

For GRDR® Administrator only:

Access Approved _____

Access Denied: _____

Inquiries and Request Contact

Inquiries and requests to submit data to the 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 B: Ethical Guidelines, FWA and IRB Approval for Non-U.S. Recipients

Recipient must consult with the appropriate IRB/ethical review committee (ERC) representative about whether IRB/ERC approval is required for this research project. Recipient must have documentation of IRB/ERC approval or documentation of exemption from the IRB/ERC review of the recipient institution for the planned research. In addition, recipient must be covered under an FWA 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. recipients must be covered by their country's equivalent human subjects regulations. In lieu of an FWA, a recipient can 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.

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>