NCATS N3C Clinical Tenant Real World Data (RWD) Enclave Pilot
INSTITUTIONAL DATA USE AGREEMENT

This Institutional Data Use Agreement ("Agreement") is between the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health and

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("Accessing Institution") which will become effective on the date of the last signature below.

WHEREAS, the NCATS N3C Clinical Tenant RWD Enclave is a data sharing resource, operated under a contract containing de-identified data derived from a Limited Dataset from individuals who have received longitudinal care from Data Contributors and/or, when available, Synthetic Data product(s) derived from the De-Identified Data.

WHEREAS, the NCATS N3C Clinical Tenant RWD Enclave will enable the rapid collection and analysis of clinical, laboratory and diagnostic data from Data Contributors that have transferred this Data via a Data Transfer Agreement to the NCATS N3C Clinical Tenant RWD Enclave. In the NCATS N3C Clinical Tenant RWD Enclave, disease specific clinical data will be aggregated and harmonized within separate Tenants and updated, as appropriate, on a recurring basis from select Data Contributor sites to support health related analytics and statistics that require a large amount of data.

WHEREAS, the NCATS N3C Clinical Tenant RWD Enclave is built upon a state-of-the-art analytics platform that protects data security, patient privacy, and recognizes investigator contributions, it will facilitate investigators' collaborative efforts on an array of innovative technologies and novel analyses.

WHEREAS, Accessing Institutions whose User(s) wish to access and use the Data for public health purposes and health-related/biomedical research will need to submit a Data Use Request (DUR) for every proposed project. This Institutional Data Use Agreement establishes the permitted uses of the Data by the User(s) as assured by the signatory Accessing Institution.

I. Definitions

1. **Accessing Institution** means the institution, entity, organization, or Citizen/Community Scientist that will be signatory of this agreement and the responsible party for the conduct of its User(s) approved to access Data under this agreement.

2. **Citizen/Community Scientist** refers to any member of the public not affiliated with a research organization who may submit a Data Use Request outlining a proposed Research project utilizing Synthetic Data after execution of a Data Use Agreement with NCATS.

3. **Data** collectively means source Data Sets including clinical data to support comparative studies, provided or received herein:

    a. **De-identified Data** De-identified Data Set: Consists of patient data from the Limited Data Set with the following changes:
        i. Dates of service are algorithmically shifted to protect patient privacy.
        ii. Patient ZIP codes are truncated to the first three digits or removed entirely if the ZIP code represents fewer than 20,000 individuals.
    b. **Synthetic Data Set**: Consists of data that are computationally derived from a Limited Data Set and that resemble patient information statistically but are not actual patient data.

4. **Data Access Committee (DAC), referred to as the NCATS N3C Clinical DAC,** is composed of representatives from the NIH or other Federal Agencies and is responsible for reviewing Data Use Requests (DUR) and verifying that conditions for accessing Data are met.

5. **Data Access Incident** is defined to include any access to or use of NCATS N3C Clinical Tenant RWD Enclave outside the bounds of an NCATS N3C Clinical DAC approved Data Use Request. The term is also inclusive of any violation (intentional or not) of any of the Data Use Terms and Conditions in this agreement, or responsible data use expectations defined within the NCATS N3C Clinical Tenant RWD Enclave's User Code of Conduct found here: https://zenodo.org/search?q=n3c&l=list&p=1&s=10&sort=bestmatch.

6. **Data Contributor** is any Institution that transferred Data to the NCATS N3C Clinical Tenant RWD Enclave under a separate NCATS N3C Clinical Tenant RWD Enclave Data Transfer Agreement

7. **Data Use Agreement (DUA)** refers to this document permits Accessing institution's Users access to the Enclave.

8. **Data Use Request (DUR) is** a request that User(s) must complete and submit to the NCATS N3C Clinical DAC for review prior to accessing the NCATS N3C Clinical Tenant RWD Enclave Data**.** For each individual Research Project, the DUR, outlined in Appendix A, will contain overarching use objectives and designs, scientific goals, any testable hypotheses, and an outline of plans for using the Data.

9. **Data Transfer Agreement (DTA)** is a document that permits the transfer of Data from Contributor to the Enclave.

10. **HIPAA Privacy Rule** refers to the Health Insurance Portability and Accountability Act (HIPAA) of 2000, the Health Information Technology for Economic and Clinical Health Act, and all implementing regulations, as may be amended from time to time.

11. **Human Research Protection Program (HRPP)** is defined as the overarching program at an Accessing Institution charged with the responsible oversight of human subject's research and compliance with federal regulations (e.g., the Federal Policy for the Protection of Human Subjects (45 CFR 46) by Users from that Accessing Institution.

12. **NCATS N3C Clinical Tenant Real World Data (RWD) Enclave a.k.a. "Enclave"** is an NIH-managed cloud-based data repository and investigational platform used to capture, integrate, and make available Data for research analysis purposes within individual Tenants.

13. **Research Project** means the Research described in the approved DUR.

14. **Tenant(s)** refers to a collection of Data aggregated and harmonized for a specific disease type and/or purpose and/or group.

15. **User(s)** are authorized by the NCATS N3C Clinical DAC to access and/or analyze Data as described in their approved DUR.

II. Data Use Terms and Conditions

1. <u>Research Use</u>

- **a.** For each proposed Research Project, User(s) agree(s) to submit a Data Use Request (DUR) to the NCATS N3C Clinical DAC for review and approval to access the Data.
- **b.** Users will not be able to download or remove the Data from the Enclave in any form. Research Results may be downloaded with the approval of NCATS N3C Clinical DAC.
- **c.** User(s) agree(s) to use the Data exclusively for the Research Project proposed in the NCATS N3C Clinical DAC approved DUR. Any other use of the Data is prohibited.

d. For Research Projects that involve Users from more than one Accessing Institution, each Accessing Institution will be required to have a DUA in place prior to their User(s) accessing a DUR.

e. User(s) agree(s) to use the Data in compliance with all applicable federal, state, local, and tribal laws, regulations, and policies. The User(s) agree(s) to adhere to the Accessing Institution's HRPP policies regarding oversight expectations for research with the Data.

f. User(s) agree to use the Data in compliance with all Enclave guidelines (such as the User Code of Conduct) included within the Enclave's guideline repository can be found here: https://zenodo.org/search?q=n3c&l=list&p=1&s=10&sort=bestmatch

g. Accessing Institution confirms that its Users(s) will have completed prior to the approval of a DUR and will maintain training in human subject's research protection for the duration of a DUR.

h. If a User leaves the Accessing Institution, the User must notify the NCATS N3C Clinical DAC. The User's new Accessing Institution must have an active DUA and be affiliated with the current DUR before the User may continue work on the approved Research Project within the Enclave.

2. Confidentiality and Data Security

a. Users of the Enclave shall have their identity authenticated and their research activities shall be regularly audited and tracked for data security.

b. Users agree to not attempt to re-identify or contact any individuals whose data are part of the Dataset or any known living relatives unless required by law to maintain public health and safety.

c. Users agree not to attempt to use the Data to identify or contact any Data Contributors or healthcare providers unless such identification is needed for data preparation and management purposes and only at the request of NCATS or required by law to maintain public health and safety.

d. Data access approval is not transferable.

e. Except as required by law, User(s) shall not disclose, release, sell, rent, lease, loan, or otherwise grant access to the Data to any third party without the prior written permission of the NCATS N3C Clinical DAC. If the Accessing Institution believes it is required by law or legal process to use or disclose the Data, the Accessing Institution will promptly notify the NCATS N3C Clinical DAC to the extent allowed by law, prior to such use or disclosure and will disclose the least possible amount of data necessary to fulfill Accessing Institution's legal obligations.

f. Users agree to not photograph, create screen shots, nor download the Data viewed on the Enclave.

g. Users agree to not combine Data from different Tenants and/or DURs unless permitted by the NCATS N3C DAC.

h. Users' access to the approved DUR will be terminated after 1 year. Users' access to their analyses and findings within the DUR may continue with NCATS N3C Clinical DAC approval of DUR renewal.

i. Accessing Institution and its Users agree to report any unauthorized access use(s) or disclosure(s) of the Data not provided for under this Agreement or other Data Access Incident(s) to NCATS at NCATSDataAccessIncidents@nih.gov no later than 2 business days after discovery. As permitted by law, notifications should include any known information regarding the incident and a general description of the activities or process in

place to define and fully remediate the situation. The occurrence of a Data Access Incident may be grounds for termination or suspension of this agreement and any access to the Data. NCATS may also seek injunctive relief against the Accessing Institution to prevent any disclosure of the Data to anyone other than NCATS.

j. NCATS encourages the development of new analytical tools, models, diagnostics, therapeutics, or other interventions building on basic discoveries enabled through Data obtained from the Enclave. The Accessing Institution and its User(s) are free to pursue patent protection on any inventions or discoveries developed through their approved use of Enclave.

k. Data residing in Enclave is protected by a Certificate of Confidentiality pursuant to section 301(d) of the Public Health Service Act. The Certificate of Confidentiality prohibits disclosure, including in any federal, state, or local criminal, civil, administrative, legislative, or other proceeding, of identifiable, sensitive information collected or used during research unless disclosure is made pursuant to a statutory exception. The Certificate of Confidentiality also protects all copies of Data from the Enclave in perpetuity as explained in the NIH Policy for Issuing Certificates of Confidentiality https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html.

l. Accessing Institution and Users agree to establish appropriate administrative, technical, and physical safeguards to prevent unauthorized use of or access to the Data and comply with any other special requirements, such as completing appropriate required NIH IT training, relating to safeguarding of the Data as may be set forth in the NIH website https://irtsectraining.nih.gov/public.aspx. Note that NCATS may request evidence of completion of the NIH IT training from Users (i.e., a screenshot or copy of the Certificate of Completion provided at the end of the course). Users will not share their Enclave log-in credentials with others at any time.

3. Dissemination of Research Descriptions, Results and Acknowledgements

a. Users' research results generated within the enclave will be subject to NIH's Data Management Sharing Policy https://sharing.nih.gov/data-management-and-sharing-policy/about-data-management-and-sharing-policies.

b. Accessing Institution and User(s) agree(s) to allow the following information in the approved DUR to be made publicly available: non-confidential research statement of the Research Project, Project Title, Users' names and Accessing Institution(s).

c. A DUR's workspace and contents therein will be archived including all research results, 12 months after the completion of a DUR's research project or the termination/expiration of this agreement.

d. Users are required to make the results of their research publicly available, ideally in an open access format and consistent with scientifically accepted publication or dissemination practices.

e. In recognition of the effort that Data Contributor(s) made in collecting and providing the Data, User(s) who publish their results, or otherwise publicly present findings, agree(s) to acknowledge the Enclave as the source of these Data and Data Contributors per guidelines in the Enclave's Document Repository.

f. Users' research supported in whole or in part by NIH funding and conducted within the Enclave will be subject to the requirements of the Data Management and Sharing Plan(s) included as terms and conditions of the applicable award(s) in accordance with the NIH Data Management and Sharing Policy (https://sharing.nih.gov/data-management-and-sharing-policy/about-data-management-and-sharing-policies).

g. In recognition of the Enclave as an NIH-supported research resource, the outputs of any research conducted within the Enclave must be publicly disseminated as outlined in the Enclave's User Code of Conduct: "Publicly disseminate findings or new insights into disease etiology, progression, pathobiology, risk or resilience factors, treatment, or prevention based on research conducted using the Enclave, ideally through open access formats. And, as applicable, enable development of new preventive, diagnostic, therapeutic, or other interventions to benefit public health." In keeping with the NIH's stated commitment to improving the reproducibility and reliability of research findings through effective data sharing, Users are expected to share research results, supporting documentation, code, and other knowledge objects generated in the course of conducting the research and irrespective of publication status. In keeping with the NIH DMS Policy, sharing is expected at the time of publication or at the end of the project period, whichever is sooner. Failure to comply may result in termination of DUR(s), DUA(s), and/or prohibition of access to the Enclave.

4. Liability

a. Data Contributors shall retain ownership of any rights they may have to the Data, and neither NCATS nor Accessing Institution and/or Users obtain any rights to the Data other than as set forth herein.

b. Users creating an Enclave workspace(s) are expected to ensure that external data, files, or software that they import into the Enclave are conducted in accordance with all applicable national, tribal, and state laws and regulations as well as relevant institutional policies, procedures and agreements. NCATS assumes no responsibility and/or liability regarding all imported data, files, or software.

c. NCATS must pre-approve all external data, files, and/or software that will be imported by the User(s) into the Enclave. The User(s) may only import the external data, files, or software after NCATS provides written approval. NCATS has the right to remove all unapproved external data, files, or software from the User's Enclave workspace at any time.

d. The Data and software are made accessible "AS IS" and NCATS and the Data Contributor(s) make no representations or warranties, expressed or implied, regarding the Data and software, including but not limited to the marketability, use or fitness for any particular purpose, or that such Data and software do not infringe upon any third-party property rights. Furthermore, neither NCATS nor the Data Contributors shall be liable for special consequential or incidental damages.

e. The Accessing Institution will not claim, infer, or imply endorsement by the United States Government, the Department of Health and Human Services (HHS), the National Institutes of Health (NIH), or the NCATS of the Research Project, the entity or personnel conducting the research, 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).

5. Term and Termination

a. This DUA may be terminated by mutual written agreement between NCATS and the Accessing Institution. Either NCATS or the Accessing Institution can terminate this DUA without cause by providing 30 days written notice to the other party. Upon termination, all access for Users from the Accessing Institution will be terminated. Failure to comply with

the Enclave's User Code of Conduct by Accessing Institution and/or User(s) may result in a suspension of access to the Data for **ALL** Users until NCATS completes an investigation into the specific Data Access Incident. After this time, NCATS may either reinstate or terminate, in whole or in part, User's access to the Data.

b. This DUA will remain in effect for a period of three (3) years from the DUA Effective Date and will automatically expire at the end of this period unless terminated or renewed. The Accessing Institution may request that the DUA be renewed one (1) year prior to the expiration date. Access to the Enclave workspace(s) for NCATS N3C Clinical DAC approved DUR(s) will be effective for a period of one (1) year starting from the date access is granted. A DUA must be in place for the entire term of a DUR. At any time, Users may indicate that they no longer need access to their Enclave workspace.

c. All legal notices related to this agreement will be sent to the below listed contact information. Amendments to this DUA must be made in writing and approved and signed by the Accessing Institution and NCATS Office of Strategic Alliances (OSA).

d. The following terms and conditions of the DUA, 1b, 1d, 2b, 2c, 2e, 2h, 2i, 3 in its entirety and 4a, 4b, 4d, and 4e will survive expiration or termination of this agreement.

Signatures Begin on Next page

AGREED AND UNDERSTOOD by the parties through their authorized signatures.

Authorized Signatory: On behalf of the Accessing Institution and its User(s), the undersigned individual hereby attests that he/she/they is/are authorized to legally bind the Accessing Institution and its User(s) to the terms of this Agreement and agrees to all the terms specified herein.

Accessing Institution: _____

Signatory Name: _____

Signatory Title: _____

Address: _____

Signature: _____ **Date:** _____

Email of Authorized Signatory: _____

Scientific Point of Contact Name: _____

Scientific Point of Contact Title: _____

Scientific Point of Contact Email: _____

Legal Notice Contact (email): _____

For: **National Center for Advancing Translational Sciences (NCATS)**

Name: **Krishna "Balki" Balakrishan MBA Ph.D.**

Title: **Director, Office of Strategic Alliances (OSA)**

Signature:_____

Date:_____

Email for Legal Notices: **NCATSPartnerships@mail.nih.gov**

Appendix A
Sample of Electronic Data Use Request (DUR) for Accessing Data from the NCATS N3C Clinical Tenant Real World Data Enclave *Not to be completed, reference only

NCATS N3C Clinical Tenant Real World Data Enclave **Registration Information:**

If not yet registered, requesting Users can find registration information at https://ncats.nih.gov/n3c/about. An ORCID ID is required for registration (see https://orcid.org/ for more information). Please note that User Name and User's Accessing Institution will be made publicly available.

Accessing Institution:
User Name: **Email:** **ORCID:**

Data Use Request Information:

Each DUR will be reviewed by the NCATS N3C Clinical Data Access Committee (NCATS N3C Clinical DAC) on a project-specific basis. Requesting Users must submit a DUR for each different proposed Research Project.

Please note that Project Title and the Non-Confidential Research Statement will be made publicly available.

Research Project Title:
Project personnel or collaborators on this DUR[1]
Non-Confidential Research Statement:[2] *(250 word max)*
Proposed Research Project Plan:[3] *(500 word max)*

Data Being Requested[4]	Selected Tenant Data Set(s)	Local Human Research Participant Program (HRPP) Oversight[5]
De-identified Data (Level 2)		Follow local institutional policies
Synthetic Data (Level 1)		Follow local institutional policies

[1] *Name all project personnel and their institutional affiliations. Note that collaborating Users from different Accessing Institutions will need to confirm execution of a DUA between their respective institution and NCATS. If joining a previously submitted DUR, you will need to be approved by the originating User prior to NCATS N3C Clinical DAC review.*

[2] *Provide a high-level description of the proposed Research Project suitable for public posting on an NCATS N3C Clinical Tenant Real World Data Enclave website. The description should include the Data type requested along with the Research questions to be addressed.*

[3] *Provide sufficient information for the NCATS N3C Clinical DAC to understand the research and analyses proposed in the proposed Research Project, including the Research question(s) to be addressed, the required level of access to Data necessary to conduct the work proposed, a general outline for the anticipated analyses, and any software that is expected to be utilized within the* NCATS N3C Clinical Tenant Real World Data Enclave *in the course of the Research Project. As stated in the DUA, any software used within the NCATS N3C Clinical Tenant Real World Data* Enclave *must be approved in writing by NCATS prior to being uploaded.*

[4] *Note that Citizen/Community Scientist(s) may only request access to Synthetic Data (Level 1 Data)*

[5] *Per the DUA, User(s) requesting access to De-identified Data (Level 2 Data) are expected to follow their institution's HRPP policies with regard to oversight of research with this data.*

Other Information:

In addition to the above, prior to submitting a DUR Users requesting access to the NCATS N3C Clinical Tenant Real World Data Enclave will:

1. Confirm that their Accessing Institution(s) has executed an Institutional Data Use Agreement (DUA) with NCATS, Citizen/Community Scientist(s) who wish to request access to the Synthetic Data (Level 1) must execute a DUA directly with NCATS.
2. Attest to their review of the NCATS N3C Clinical Tenant RWD Enclave DUA and an understanding of the Terms and Conditions for use of all Data and any software utilized within the NCATS N3C Clinical Tenant Real World Data Enclave.
3. Attest to the NCATS N3C Clinical Tenant Real World Data Enclave Data User Code of Conduct https://zenodo.org/search?q=n3c&l=list&p=1&s=10&sort=bestmatch and compliance with all expectations therein.
4. Complete the standard NIH IT training at https://irtsectraining.nih.gov/public.aspx, provide the date the training was completed, and retain evidence of completion to provide to NCATS upon request (i.e., a screenshot or copy of the Certificate of Completion provided at the end of the course).
5. When requesting any level of Data), complete human subjects research protection training, provide the date the training was completed, and retain evidence of completion to provide NCATS upon request.

User(s): By clicking submit, requesting User(s) state their agreement with the information contained within the DUR and attest to understanding their responsibilities and obligations for NCATS Data Enclave Data use under the Enclave's Data Use Agreement and the NCATS N3C Clinical Tenant Real World Data Enclave Data User Code of Conduct and any applicable institutional, local, state, federal, or tribal laws, regulations, and policies.