National Heart, Lung, and Blood Institute

The NHLBI Clinical Data Science IRB:
A Central IRB for Review of Secondary Research Proposals that Involve NHLBI Datasets for which IRB Approval is Stipulated as a Data Use Limitation

The National Heart, Lung, and Blood Institute (NHLBI), a component of the National Institutes of Health (NIH), is strongly committed to the broad and responsible sharing of data from NHLBI-supported clinical studies *as well as the use of these data for subsequent research* (i.e., secondary analysis using previously collected data). Toward this end, the NHLBI makes available to the research community more than 200 de-identified datasets from clinical trials and observational studies. As well, NHLBI supports the Trans-Omics for Precision Medicine (TOPMed) program, which is providing deep whole-genome sequencing and other omics data (such as metabolic profiles and protein and RNA expression patterns) to pre-existing 'parent' studies having large samples of human subjects with rich phenotypic characterization and clinical, molecular, behavioral, imaging, and/or environmental exposure data.

The extent to which all of these data are made available for sharing depends in part on the terms of the informed consent of the study participants from whom the data were generated. In some cases, a data use limitation (DUL) of "IRB Approval Required" has been stipulated, necessitating that any proposal for secondary analysis of the data must first be approved by the secondary researchers' IRB before NHLBI will grant access to the dataset. While secondary analyses using de-identified datasets are generally not considered human subjects research and therefore not subject to federal human subjects protections regulations, research proposing to utilize NIH data with a DUL requiring IRB approval must still undergo IRB review in accordance with the NIH Genomic Data Sharing Policy. A significant number of NHLBI datasets, including nearly half of the TOPMed datasets, have an associated DUL of "IRB Approval Required."

To enhance and stimulate data sharing and secondary analyses utilizing existing data, NHLBI has developed a cloud-based platform, the BioData Catalyst, that allows investigators to readily find, access, share, store, cross-link, and compute on large scale NHLBI (and other) datasets. Investigators are also be able to access many innovative tools for searching and analyzing datasets. This platform facilitates analyses that are collaborative, cross-study, highly complex, and/or very large. Between the enhanced secondary research capabilities enabled by the BioData Catalyst, the ready availability of clinical trial and observational study datasets, and the continuing generation of TOPMed data, NHLBI anticipates significant increases in requests for access to NHLBI datasets, many of which will require IRB review prior to the secondary analysis.

There is little extant guidance for ethical review of secondary analysis of existing de-identified human datasets. The potential risks associated with secondary analyses are not necessarily the same as the risks associated with primary human subjects research (e.g., direct physical harm to subjects). Ethical review of secondary analyses needs to consider possible risks such as re-identification; breach of privacy; and non-physical harm to the research participants and potentially their families/descendants and communities, including the potential for stigmatization or discriminatory impact. As well, the rapid pace of scientific and technological advances is making possible new research applications that could not have been anticipated even a few years ago and thus could not have been reasonably anticipated in the original informed consent.

To address these challenges, NHLBI established the Clinical Data Science IRB (CDS-IRB) to address ethical issues that may arise in the course of secondary analyses. **The CDS-IRB is intended to provide a useful resource for the research community by offering—at no cost—central review of secondary research proposals utilizing NHLBI datasets for which**

If an institution would like to rely on the NHLBI CDS-IRB for review of proposals for secondary analyses planning to utilize NHLBI datasets for which IRB approval is stipulated as a DUL, please complete the following form.

IRB approval is required. This will ensure consistent, comprehensive review and will also provide an opportunity for the NHLBI and NIH to systematically understand the evolution and range of requests to conduct secondary analyses, recognize emerging trends, and periodically explore with the research community ways to enhance data stewardship.

Authorization Agreement between

and

THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
To Rely on the NHLBI Clinical Data Science IRB

Pursuant to the NIH Genomic Data Sharing Policy, the National Heart. Lung, and Blood Institute (NHLBI) [hereinafter NHLBI], a component of the National Institutes of Health (NIH), and the *Relying Institution* named in section B are entering into this Agreement for NHLBI to conduct Institutional Review Board (IRB) review of the research protocol(s) or activities identified below in section C. This document will be kept on file at NHLBI and the *Relying Institution* and must be provided to applicable regulatory agencies upon request.

A. Name of the institution providing IRB review: NHLBI

Institution #: IORG0009921 (NHLBI IRB for Extramural Research Program)

Federalwide Assurance #: FWA00027544

Name of IRB: NHLBI Clinical Data Science IRB (NHLBI CDS-IRB)

IRB Registration #: IRB00011784

B. Name of institution relying on the NHLBI CDS-IRB:

Federalwide Assurance #:

Note: Any institutional components listed under the *Relying Institution's* FWA must meet certain criteria as defined by NHLBI in order to be included as part of this Agreement. The criteria include:

- the *Relying Institution* maintains legal authority over the institutional components;
- the Component Institution is listed under the same FWA number as the *Relying Institution*;
- the local context considerations are the same as the *Relying Institution*;
- institutional requirements are the same as the *Relying Institution*; and
- the conduct of research at the institutional components is monitored by the *Relying Institution*.

C. Description of Research Activities included under this agreement

This agreement is limited to secondary research submitted to the CDS-IRB Office involving the use of data accessed through the NHLBI BioData Catalyst platform for which IRB approval is stipulated.

D. Division of Responsibilities

1. Responsibilities of the NHLBI (NHLBI IRB for Extramural Research Program)**:**

a. Maintain NHLBI CDS-IRB membership that satisfies applicable federal regulations and provides special expertise as needed to adequately assess all aspects of the reviewed research;

b. Uphold the Institute's commitment and role in ensuring the rights, safety, and welfare of all human subjects in accordance with the Federalwide Assurance (FWA);

c. Communicate and explain to personnel the Institute's commitment and ethical principles under the FWA in the protection of human subjects and provide procedural guidelines to effect their observance; and

d. Notify the *Relying Institution* immediately of any suspension or restriction of the NHLBI CDS-IRB's authorization to review research.

2. Responsibilities of the NHLBI CDS-IRB and the CDS-IRB Office are to:

a. Maintain an active OHRP-approved IRB registration during the duration of this Agreement and maintain compliance with HHS, other applicable regulations, and policies;

b. Conduct ethical review of secondary research proposals that meet the requirement for IRB approval as stipulated in the data use limitations (DUL) and NIH data sharing policies, or as requested;

c. Conduct initial, amendment, and continuing review of secondary research as well as a review of any other study-specific documents submitted to the NHLBI CDS-IRB;

d. Conduct a review of potential unanticipated problems and/or serious or continuing noncompliance when the *Relying Institution* or other entity reports an incident, experience, or outcome to the NHLBI CDS-IRB;

e. Report any suspension or termination of NHLBI CDS-IRB approval to applicable regulatory or other oversight entities, and the *Relying Institution*;

f. Follow written procedures for reporting its findings and actions to appropriate officials and personnel at the *Relying Institution;*

g. Retain IRB records for a minimum of (3) years after completion of the research;

h. Provide documents related to NHLBI CDS-IRB reviews, such as initial and continuing review approval notifications, and IRB determinations via email to the *Relying Institution's* Principal Investigator and designated individuals; and

i. Provide the NHLBI CDS-IRB Standard Operating Procedures (SOPs), a current IRB member roster, and relevant minutes of NHLBI CDS-IRB meetings to the *Relying Institution* upon request.

3. Responsibilities of the *Relying Institution* are to:

a. Maintain an active OHRP-approved FWA for the duration of this Agreement and promptly notify the NHLBI CDS-IRB in writing of any suspension, restriction, termination, or expiration of the FWA;

b. Ensure compliance with the terms of their OHRP-approved FWA, their local Standard Operating Procedures (SOPs), and with any determinations provided by the NHLBI CDS-IRB;

c. Comply with the requirements and directives as encompassed in the NHLBI CDS-IRB standard operating procedures (SOPs) and with communications from the NHLBI CDS-IRB or NHLBI;

d. Verify the initial and ongoing qualifications of investigators and research staff, including required institutional training;

e. Oversee the conduct of the research and maintain compliance with state, local, or institutional requirements;

f. Ensure that any changes to an NHLBI CDS-IRB-approved protocol will be approved by the NHLBI CDS-IRB prior to implementation, to include a change in the principal investigator;

g. Investigate, manage, and provide notification to the NHLBI CDS-IRB of any research-specific incident, experience, or outcome that seems to rise to the level of an unanticipated problem and/or serious or continuing noncompliance within 30 days of incident awareness;

h. Retain the authority to observe any aspect of the research process and to permit the NHLBI CDS-IRB or a third party the right to observe any aspect of the conduct of the research;

i. Notify the NHLBI CDS-IRB when a research-related deficiency is cited for any reason during the time that the NHLBI CDS-IRB is responsible for the research review;

j. Utilize a Privacy Board for the purpose of reviewing the use and disclosure of protected health information (PHI) when applicable, and to maintain any HIPAA compliance or obligations as deemed by the Privacy Board; and

k. Adhere to their institutional conflict of interest (COI) policies and procedures, which includes providing the NHLBI CDS-IRB with any applicable COI management plan related to the research.

E. Authorization

The Officials signing below agree that the NHLBI will provide IRB review as described under section C of this document for the named *Relying Institution*.

This agreement will become effective upon the date of the last signature below and will remain in effect until such time that either NHLBI or the *Relying Institution* provide 30 days written notice of termination to the other party. If the Agreement is terminated prior to the completion of the research, the *Relying Institution* will need to obtain an alternative IRB review. In the event of any termination of this Agreement, the parties will work together to determine the effect of such termination on any research and associated research activities being conducted under the Agreement at the time of termination.

Name and contact information of Signatory Official for the *Relying Institution*:

Signature

Date

Name

Title

Email

Phone

Please provide contact information for any additional individuals at the *Relying Institution* who should be copied on pertinent correspondence regarding the research.

Name	**Email**

Name and contact information of Signatory Official for the NHLBI:

Signature

Date

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