Overview

The National Human Genome Research Institute (NHGRI) Ethical, Legal and Social Implications (ELSI) Research Program frequently receives requests for examples of funded grant applications. Several investigators and their organizations agreed to let excerpts of their ELSI grant applications be posted online.

Acknowledgement

We are grateful to the investigators and their institutions for allowing us to provide this important resource to the community. To maintain confidentiality, we have redacted some information from these documents (e.g., budgets, social security numbers, home addresses, introduction to revised application), where applicable. We do not include other SF 424 (R&R) forms or requisite information found in the full grant application (e.g., budgets, biographical sketches, letters of recommendation or letters of support). NIH grant formats or rules may have changed since these applications were prepared; therefore, applicants should always follow the application format instructions included in the funding announcement.

PI: **Brothers, Kyle Bertram**	Title: Addressing Ethical Challenges in Networked Biorepositories	
Received: 12/09/2015	FOA: PA14-276	Council: 05/2016
Competition ID: FORMS-C	FOA Title: ETHICAL, LEGAL, AND SOCIAL IMPLICATIONS (ELSI) OF GENOMIC RESEARCH REGULAR RESEARCH PROGRAM (R01)	
1 R01 HG008988-01A1	Dual: CA	Accession Number: 3888658
IPF: 4679701	Organization: UNIVERSITY OF LOUISVILLE	
Former Number:	Department: Pediatrics	
IRG/SRG: ZRG1 SEIR-R (01)Q	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 257,157 Year 2: 273,067 Year 3: 278,441 Year 4: 293,215	Animals: N Humans: Y Clinical Trial: N Current HS Code: Evaluative Info HESC: N	New Investigator: Y Early Stage Investigator: Y
Senior/Key Personnel:	*Organization:*	*Role Category:*
Kyle Brothers	University of Louisville	PD/PI
Aaron Goldenberg	Case Western Reserve University	MPI
Richard Sharp	Mayo Clinic	Co-Investigator
Jean Cadigan	The University of North Carolina at Chapel Hill	Co-Investigator
Mark Rothstein	University of Louisville	Co-Investigator
Heather Harrell	University of Louisville	Co-Investigator
Suzanne Rivera	Case Western Research University	Co-Investigator

OMB Number: 4040-0001
Expiration Date: 06/30/2016

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	**State Application Identifier**

1. TYPE OF SUBMISSION*

❍ Pre-application ❍ Application ● Changed/Corrected Application

4.a. Federal Identifier
HG008988

b. Agency Routing Number

2. DATE SUBMITTED

Application Identifier
OGMB160709

c. Previous Grants.gov Tracking Number
GRANT12052272

5. APPLICANT INFORMATION

Organizational DUNS*: 0575888570000

Legal Name*: University of Louisville Research Foundation, Inc.
Department: Office of Sponsored Programs
Division: Grants Administration
Street1*: 300 East Market Street, Suite 300
Street2:
City*: Louisville
County: Jefferson
State*: KY: Kentucky
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 40202-1959

Person to be contacted on matters involving this application
Prefix: Mr. First Name*: David Middle Name: L Last Name*: White Suffix:
Position/Title:
Street1*: 300 East Market Street, Suite 300
Street2:
City*: Louisville
County: Jefferson
State*: KY: Kentucky
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 40202-1959
Phone Number*: 502-852-3788 Fax Number: 502-852-2594 Email: grntmgmt@louisville.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1611029626A1

7. TYPE OF APPLICANT* M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

❍ New ● Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Addressing Ethical Challenges in Networked Biorepositories

12. PROPOSED PROJECT
Start Date* 07/01/2016
Ending Date* 06/30/2020

13. CONGRESSIONAL DISTRICTS OF APPLICANT
KY-003

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Dr. First Name*: Kyle Middle Name: Bertram Last Name*: Brothers Suffix:

Position/Title: Assistant Professor
Organization Name*: University of Louisville
Department: Pediatrics
Division: KCPCRU
Street1*: 231 East Chestnut Street, N-97
Street2:
City*: Louisville
County: Jefferson
State*: KY: Kentucky
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 40202-1821
Phone Number*: 502-588-0797 Fax Number: 502-629-5285 Email*: kyle.brothers@louisville.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$1,759,037.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$1,759,037.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Mr. First Name*: Barbara Middle Name: Last Name*: Sells Suffix:

Position/Title*: Associate Director
Organization Name*: University of Louisville
Department: Office of Sponsored Programs
Division: Grants Administration
Street1*: 300 East Market Street, Suite 300
Street2:
City*: Louisville
County: Jefferson
State*: KY: Kentucky
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 40202-1959
Phone Number*: 502-852-3788 Fax Number: 502-852-2594 Email*: bfsell01@louisville.edu

Signature of Authorized Representative*
Barbara Sells

Date Signed*
12/09/2015

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:1249-Cover Letter.pdf

424 R&R and PHS-398 Specific Table Of Contents

OMB Number: 4040-0010
Expiration Date: 06/30/2016

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	University of Louisville Research Foundation, Inc.
Duns Number:	0575888570000
Street1*:	231 East Chestnut Street, N-97
Street2:	
City*:	Louisville
County:	Jefferson
State*:	KY: Kentucky
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	40202-1821
Project/Performance Site Congressional District*:	KY-003

Project/Performance Site Location 1

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	Case Western Research University
DUNS Number:	0777584070000
Street1*:	10900 Euclid Avenue
Street2:	
City*:	Cleveland
County:	Cuyahoga
State*:	OH: Ohio
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	44106-4979
Project/Performance Site Congressional District*:	OH-011

Project/Performance Site Location 2

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	Mayo Clinic
DUNS Number:	0064717000000
Street1*:	200 First Street
Street2:	
City*:	Rochester
County:	Olmsted
State*:	MN: Minnesota
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	55905-0001
Project/Performance Site Congressional District*:	MN-001

Funding Opportunity Number: PA-14-276. Received Date: 2015-12-09T15:54:16.000-05:00

Project/Performance Site Location 3

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The University of North Carolina at Chapel Hill
DUNS Number:	6081952770000
Street1*:	333 South Columbia Street
Street2:	343-A MacNider Hall
City*:	Chapel Hill
County:	Orange
State*:	NC: North Carolina
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	27599-1340
Project/Performance Site Congressional District*:	NC-004

	File Name
Additional Location(s)	

OMB Number: 4040-0001
Expiration Date: 06/30/2016

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. 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 _ 6

If NO, is the IRB review Pending? ● **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number 00002211

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	1245-Project Summary Abstract.pdf
8. Project Narrative*	1246-Project Narrative.pdf
9. Bibliography & References Cited	1247-Bibliography and References Cited.pdf
10.Facilities & Other Resources	1248-Facilities and Other Resources.pdf
11.Equipment	

Funding Opportunity Number: PA-14-276. Received Date: 2015-12-09T15:54:16.000-05:00

PROJECT SUMMARY/ABSTRACT

Individual institutions across the country have worked to support research in a wide variety of areas, including precision medicine research, by developing large biorepositories comprised of biospecimens and health data collected from local patients and controls. However, these local cohorts rarely provide the diversity and size needed to identify and study subsets of patients who share biological mechanisms for their disease, and are thus more likely to respond to the same targeted therapies. To address this need, researchers have begun to promote the networking of multiple repositories within or across multiple institutions. This *networked biorepository* approach makes it possible for researchers to access larger, more diverse sets of data and biospecimens in a way that leverages the research relationships that local institutions have built with their own communities of donors. In order for this approach to be successful, networked biorepositories need to address important ethical, legal, and social challenges. Networked biorepositories are comprised of diverse sets of specimens and data from different institutions, each with their own governance structures and donor needs. For these reasons, they encounter complex issues related to consent and donor permission, privacy and data security, and data access. These novel challenges have not previously been examined in detail, and best practices for addressing these issues through governance and oversight processes are lacking. This study will address these important needs through a rigorous, mixed-methods study of the perspectives and experiences of stakeholders currently engaged in designing, operating, and governing networked biorepositories. It will also aim to develop approaches to consent and donor permission, privacy and data security, data access, governance, and oversight that are most appropriate and effective for a variety of networked biorepository configurations.

PROJECT NARRATIVE

Networked biorepositories make it possible for investigators in a wide variety of research domains to access large, diverse collections of biospecimens and health data across multiple institutions. At the same time, they also raise complex issues related to consent and donor permission, privacy and data security, and data access. Developing a detailed account of these challenges and identifying appropriate solutions, including effective governance and oversight processes, will enable new and developing networked biorepositories to support important health research while at the same time meeting the needs of donors and protecting the interests of contributing institutions.

FACILITIES AND OTHER RESOURCES

Resources for New, Early Stage Investigators (ESIs)

Kyle B. Brothers, MD, PhD (corresponding multiple PD/PI)

The University of Louisville School of Medicine, including the Department of Pediatrics, has made a substantial institutional investment to support the success of Dr. Brothers and his research program. Dr. Brothers is currently in his third year of an institutionally-supported five year development package. The resources provided through this contract include salary support for EFFORT FTE for career development in research, as well as $100,000 in research development funds and $5000 annually for continuing medical education and research-related travel. His career development is also supported by a dedicated five member mentorship committee that meets annually to provide feedback and advice on career goals and planning. As described below, the Department of Pediatrics, through the Kosair Charities Pediatric Clinical Research Unit, provides administrative, budget, and regulatory support for Dr. Brothers' research program. It also provides access to a faculty statistician to support the development of research projects and funding proposals.

Aaron Goldenberg, PhD, MPH (multiple PD/PI)

The Case Western Reserve University School of Medicine, including the Department of Bioethics, has made a substantial institutional investment to support the success of Dr. Goldenberg and his research program. Dr. Goldenberg is in his seventh year as an Assistant Professor in the Department and is supported by at least EFFORT FTE from departmental funds to support his research, service, and educational work. He also has access to $1500/year for research related travel or other research expenses. Additionally, the department currently supports approximately EFFORT of a full-time research assistant and 1-2 student researchers that help support Dr. Goldenberg's research. His career development is also supported by a dedicated mentorship team, including senior faculty from the Bioethics, Genetics and Genome Sciences, and Epidemiology/Biostatistics.

Rationale for Multiple Site Environment

The proposed project involves the collection of qualitative data mixed methods, including a retrospective aim (Aim 1) and a prospective aim (Aim 2) that will proceed simultaneously. In light of this, we have adopted the strategy of pooling the resources of two research team (Dr. Brothers' team at the University of Louisville and Dr. Goldenberg's team at Case Western Reserve University). This approach allows our project to get started more rapidly (because it does not require a large number of new hires) and to take advantage of complimentary resources at the two primary sites. Our plan for this study involves a range of specific strategies intended to maximize coordination between the two primary sites, including twice monthly conference calls, internet-based video calls, and cloud services like Dropbox to share documents and data. All of these services are available to our teams through our home institutions. This approach seems especially apt given the focus of this project – networked biorepositories – which also seek scientific advantages by pooling resources across sites.

University of Louisville School of Medicine

The School of Medicine opened as the Louisville Medical Institute in 1837, making it one of the oldest medical schools in North America. It is located in downtown Louisville, Kentucky at the heart of a large health sciences center comprised of research and educational facilities, as well as a variety of affiliated hospitals and other healthcare institutions. Its nearly eight hundred full-time faculty members are divided among 22 academic departments.

Institute for Bioethics, Health Policy, and Law

The institute is a free standing research and education institute within the School of Medicine. This institute is associated with the Louis D. Brandeis School of Law, the College of Arts and Sciences, the Department of Philosophy, and the School of Public Health & Information Sciences. It brings together experts in bioethics and health policy, with a particular focus on research ethics. Mark A. Rothstein, JD (co-investigator for this project) directs the Institute. Dr. Brothers and Heather Harrell, MD, JD (co-investigator) are active members of the Institute, with dedicated time and office space for their collaborative work in the institute. The Institute provides faculty offices as well as a combined library/lecture hall space. Faculty offices are equipped with computers and internet access to all essential online resources, including the subscription legal databases WESTLAW

and LEXIS. The library is equipped for teleconference applications, and provides an extensive collection of current and archived publications related to bioethics, genetics and genomics, health policy, and health law.

Kosair Charities Clinical Research Unit (KCPCRU)
Dr. Brothers' primary academic appointment is in the Department of Pediatrics, where he is a faculty member in the KCPCRU. The Unit is a state-of-the art clinical facility dedicated to the conduct of inpatient and outpatient pediatric clinical pharmacology studies. It occupies approximately 5,100 ft^2 on the second floor of Kosair Children's Hospital, as well as a separate suite of offices where Dr. Brothers' research team is housed. Importantly for this project, the KCPCRU provides a three-person administrative and budget team, as well as a three-person regulatory team. These team members will provide support for the current project, including management of budget and finance issues, coordination among research sites, and communication with the University of Louisville Human Subjects Protection Program. Private offices are provided for both Dr. Brothers and the primary research analyst who will work on this project, including computers with qualitative research analysis software (Atlas.ti) and dual computer monitors, which facilitate qualitative coding. The facility provides ample storage space, including a secured research record storage area, as well as a conference room/library.

Library Resources
The University of Louisville libraries, including the Ekstrom (Main) Library, Kornhauser (Health Sciences Center) Library, and Brandeis (Law School) Library are also available for the use of the investigators. The library system provides a wide range of digital book and journal resources, as well as interlibrary loan and digital delivery of scanned paper journal articles at no cost to faculty.

Case Western Reserve University School of Medicine
The School of Medicine was organized in 1843 and has occupied its current site in University Circle on Cleveland's east side since 1924. The School was one of only two schools mentioned in the Flexner Report, written by Louisville, Kentucky native Abraham Flexner, as providing models for American medical education. Nine hundred full-time faculty are currently divided among the 22 clinical and basic science departments; in addition, there are over 709 interdisciplinary centers and programs.

Department of Bioethics
The Department of Bioethics has provided advanced training in bioethics for students and professionals since 1995. The Department occupies over 7,000 ft^2 of office/library/conference room space. Offices are available for project staff, including temporary workspace for members of the research team from other locations to use when working on site. All CWRU faculty and staff have access to the latest software at no charge, including Microsoft Office and Adobe Acrobat. Department faculty are nationally- and internationally-renowned, with backgrounds in medicine, nursing, philosophy, law, religious studies, anthropology, sociology and public health. Both Dr. Goldenberg and Sue Rivera, Ph.D., M.S.W., (co-investigator on this project) are assistant professors in the Department of Bioethics.

Center for Genetic Research and Law (CGREAL)
The CWRU component of this project will be conducted within the context of the CWRU Center for Genetic Research and Law (CGREAL). Its mission is to conduct transdisciplinary studies of ethical and societal issues in human genetic research and introduce new genetic technologies into patient care and public health. This context augments the core resources available to our proposed project, and places it in a multi-disciplinary portfolio of ongoing research on related themes. Dr. Goldenberg serves as the Assistant Director for Research in the CGREAL.

Mayo Clinic
Mayo Clinic Biomedical Ethics Program
The Biomedical Ethics Program provides institutional and national leadership on ethical issues raised by translational research and integration of new medical technologies into patient care. The core activities of the program include (1) bioethics research; (2) institutional service and bioethics consultation; (3) education; and (4) bioethics programming and outreach. The Program serves as an academic home for full-time bioethics researchers and clinicians engaged in bioethics research. Currently approximately 20 research and clinical

faculty are affiliated with the Program. The Program includes a program manager, 3 bachelor's & master's level research analysts/study coordinators, and 2 administrative assistants.

An integral component is the *Center for Individualized Medicine (CIM) Bioethics Program***.** The goal of the CIM Bioethics Program is to develop ethically robust strategies for integrating genomic technologies into medicine, with a focus on the best interests of the patient. Its areas of focus include (1) consultation and education on ethical and social issues related to individualized medicine; (2) empirical research on patients' needs in relation to genomic technologies, including potential motivations for pursuing genomic testing, concerns about the use of genetic findings, and potential barriers to pursuing clinically appropriate forms of individualized medicine; (3) engaging with members of the community, including the Mayo Clinic Biobank Community Advisory Board (CAB); and participation in national and regional policy initiatives to promote the responsible use of new forms of individualized medicine.

University of North Carolina

Department of Social Medicine

The Department of Social Medicine is an academic unit that incorporates the long-standing interest of the University of North Carolina and the School of Medicine in community medicine and health care delivery systems. The mission of the Department is to inform clinical care on: (1) the social conditions and characteristics of patients, the social causes of illness and the social barriers to effective care; and (2) the social responsibilities of the medical profession. Members of the faculty apply their various disciplines to problems of the poor, elderly, chronically ill, and other categories of people with special health and medical care needs; questions of allocation, distribution, organization and financing of health resources; and health and medical care problems in North Carolina. The Department carries out its mission through a variety of educational, research, and service activities in several venues and almost always in interdisciplinary collaboration throughout the UNC-CH campus. Though not an exclusive list, the following areas are those in which the Department has active research and ongoing interests: cultural anthropology and medical anthropology, epidemiology, health economics, history of medicine and public health, literature and medicine, medical care organization, medical ethics, medical sociology, medicine and the law, preventive medicine, public policy in health and medical care. The Department of Social Medicine, unlike other departments in the University, serves as an interdisciplinary department, and employs faculty and researchers from across the campus and beyond to accomplish its mission. This means that the administrative staff in the department is exceptional in terms of their ability to comprehend and coordinate activities across the wide array of constituencies served by the department. Social Medicine is a bridge between medicine and public health, and between medicine and the arts and humanities disciplines, and those who work here have strong skills in translation and organization. Dr. Cadigan has an office in the Department of Social Medicine, and has ready access to members of the Center for Genomics and Society and other members of the Department of Social Medicine, as well as experienced administrative staff. She has a telephone and Skype for telecommunication with off-site investigators. The intellectual environment is rich and includes other extramurally funded investigators doing complementary work in the ELSI field.

Center for Genomics and Society

The Center for Genomics and Society at UNC-Chapel Hill (CGS) was funded as a Center for Excellence in Ethical, Legal and Social (ELSI) Research in 2007. CGS is housed within the Department of Social Medicine, but its investigators are members of many different departments and disciplines. The CGS has a current roster of 21 investigators and 7 trainees, who represent multiple disciplines, including human genetics, medical anthropology, behavioral science, ethics and law.

BUDGET JUSTIFICATION – UNIVERSITY OF LOUISVILLE (PRIMARY SITE)

SENIOR / KEY PERSONNEL

Kyle B. Brothers, MD, PhD (Corresponding Multiple PD/PI)
Dr. Brothers will have (with Dr. Goldenberg) joint responsibility for all aspects of the study, including: coordinating a systematic search for established and developing networked biorepositories; conducting and analyzing semi-structured interviews with stakeholders in these biorepositories; performing a longitudinal observation of the governance, oversight, and problem-solving processes utilized by networked biorepositories; analyzing findings from observations; developing generalization recommendations for addressing consent, privacy and data security, data access, governance, and oversight within different networked biorepository configurations; leading focus groups to refine these recommendations; and disseminating findings through publications and professional meetings. **Dr. Brothers' effort will be** EFFORT **calendar months** EFFORT **effort) in years 1-4.**

Mark A. Rothstein, JD (Co-Investigator)
Professor Rothstein will contribute to this study in three key ways. First, he will assist with the analysis of data related to privacy and data security throughout the course of the study. Second, he will contribute to the analysis of semi-structured interviews and embedded ethnographic observations, especially with respect to legal issues that are identified in this data. Third, he will contribute his health policy expertise to the development of generalizable recommendations in the fourth year of this study. **Professor Rothstein's effort will be** EFFORT **calendar months** EFFORT **effort) in years 1-4.**

Heather L. Harrell, MD, JD (Co-Investigator)
Dr. Harrell will contribute to the analysis of semi-structured interviews and embedded ethnographic observations during the first three years of this study, and in particular will lead the analysis of primary documents that will supplement our analysis of established, developing, and failed networked biorepositories in Specific Aim 1. In the fourth year of the study, she will contribute to the development of generalizable recommendations for networked biorepositories. **Dr. Harrell's effort will be** EFFORT **calendar months** EFFORT **effort) in years 1-4.**

OTHER PERSONNEL

Carla Rich, MA (Research Analyst)
Ms. Rich will assist with the design, planning, and conduct of semi-structured interviews in Specific Aim 1, and will coordinate the qualitative analysis of this data as well as data collected through embedded ethnographic observations. She will also assist with the preparation of findings for publications and professional meetings. **Ms. Rich's effort will be** EFFORT **calendar months** EFFORT **effort) in years 1-4.**

TBD (Project Manager)
The project manager will serve as the coordinator for research activities across the three sites contributing to this project. He or she will schedule and plan regular project-wide conference calls, coordinate progress reports and regulatory continuing review, and will plan the focus groups and expert symposium planned for Specific Aim 3. For the University of Louisville site, he or she will coordinate scheduling and travel arrangements for semi-structured interviews and embedded ethnographic observation activities and will manage study-related data including primary documents and audio recordings from semi-structured interviews and observations. **The effort for this project manager will be 3.6 calendar months (30% effort) in years 1-4.**

EQUIPMENT
N/A

TRAVEL

During Years 1, 2, and 3 of the study, key University of Louisville personnel will travel to various sites to

conduct semi-structured interviews with biorepository stakeholders and conduct embedded ethnographic observation at in-person meetings of networked biorepository case studies. We will also hold an annual project-wide in-person collaboration meeting to review project progress and collaborate on data analysis and deliverables. During Year 4 of the study, we will conduct focus groups, hold a national expert symposium, and present project findings at professional meetings. Consequently, we request $5,000 annually for travel.

OTHER DIRECT COSTS

Case Study Administrative Stipends/Honoraria
The networked biorepository case studies participating in our embedded ethnographic observations for Specific Aim 2 will each receive a $1000 stipend for each year of the study. This stipend is intended to defray the administrative costs associated with coordinating our participation in conference calls, in-person meetings, and other activities, as well as the coordination of focus groups with case study stakeholders for Specific Aim 3. The members of our Advisory Committee representing this networks will also receive an annual honorarium of $1000 for service on this committee. Dr. Gail Henderson, who will serve on our Advisory Panel as an expert on the ethics of biorepository research and the use of empirical methods to study these issues, and Dr. Eric Juengst, who will serve on our Advisory Panel as an expert on the application of normative analysis to policy and practice, will each receive an annual honorarium of $1000 for their service.

Transcription
Audio recordings of in-depth interviews (Specific Aim 1) and focus groups (Specific Aim 2) will be professionally transcribed. We anticipate that we will perform 34 one-hour interviews each year in years 1, 2, and 3 (~100 interviews total). In years 3 and 4, we will perform up to 10 two hour focus groups (with transcription of these focus groups taking place in year 4). At $120 per transcribed hour (based on previous work), total transcription costs are estimated at $4080 per year for years 1, 2, and 3; and $2500 for year 4.

Expert Symposium
As a part of Specific Aim 3, we will invite stakeholders from our case study networks and national experts on ethical, legal, and regulatory issues in biorepository research to participate in a symposium focused on refining our generalizable recommendations for networked biorepositories. The budget requested for this event in Year 4 includes travel and accommodations for symposium participants and meeting facilities.

Budget Justification – Case Western Reserve University

Personnel

Aaron Goldenberg, PhD, MPH (PI, EFFORT calendar months' effort and salary support requested for all years). Dr. Goldenberg is an Associate Professor of Bioethics in the Department of Bioethics and Associate Director of the Center for Genetic Research Ethics and Law at Case Western Reserve University. Dr. Goldenberg holds a doctorate in Bioethics and a Master's Degree in Public Health. He has expertise in ethical issues in clinical and public health genomics and policy, newborn screening, uses of stored biological specimens, and pediatric ethics, and is experienced in both quantitative and qualitative research methods. Dr. Goldenberg will lead the data collection related to Aim 1 and Co-lead aim 3. He will work with Kyle Brothers on the translation of study results into recommendations for Biorepository policy and practice. Dr. Goldenberg will also assist in the development of interview and discussion group guides and other study instruments, as well as the development and implementation of study recruitment and consent materials. He will assist in the analysis of project data and dissemination of findings.

Suzanne Rivera, PhD, MSW (Co-Investigator, EFFORT calendar months' effort and salary support requested for all years). Dr. Rivera is the Vice President for Research and Assistant Professor of Bioethics at Case Western Reserve University. She provides expertise in regulations regarding human subject protections, regulatory oversight for research, scientific integrity, and policies regarding data sharing across academic institutions. Dr. Rivera will assist in the scientific direction of the project, the development of the study instruments, and analysis of data. She will focus on the regulatory and governance components of this study and will aid in the interpretation of study data and the dissemination of findings.

Roselle Ponsaran MA (Project Manager EFFORT calendar months' effort and salary support requested for all years). Ms. Ponsaran will be responsible for coordinating the activities of the research team for Aims 1 and 3. This will include managing and coordinating in-depth interviews and site discussion groups, tracking subject accrual for the study, scheduling meetings for the research team and conference calls with national consultants with regard to Aims 1 and 3. She will also prepare IRB materials and ensure their timely submission to the IRB, and assist in the preparation of study reports and manuscripts. Ms. Ponsaran will also assist in conducting audio-taped interviews and discussion groups for the study.

Laura Morello, MSW (Research Assistant EFFORT calendar months' effort and salary support requested for all years). Ms. Morello will be responsible for assisting in the coordination and implementation of the activities related to Aims 1 and 3. She will be responsible for conducting interviews with Key informants from each site, and will assist in coordinating and conducting the discussion groups in Aim 3. Ms. Morello will also assist in the creation of study instruments and data analysis and assist in the preparation of study reports and manuscripts.

TRAVEL
Travel costs are budgeted for the PI and a Research Assistant to travel to each of the primary biorepository sites for data collection. Additionally, travel costs are budgeted for the PI to disseminate study findings at national scientific meetings. Total Costs requested ($5000 per year for years 1-4)

Fringe benefits are calculated at 27.5% in Year 1, 28% in Year 2, 28.5% in Year 3, and 29% in Year 4. Salaries are increased 2% per year for personnel whose salaries are not at or above the NIH salary cap.

Indirect costs are calculated at 58.5%, the currently negotiated rate between DHHS and Case Western Reserve University.

BUDGET JUSTIFICATION – UNIVERSITY OF NORTH CAROLINA

SENIOR / KEY PERSONNEL

Jean Cadigan, PhD (Co-Investigator; Principal Investigator, UNC subcontract)
Dr. Cadigan is an assistant professor in the Department of Social Medicine. Dr. Cadigan is a medical anthropologist. She has worked on several projects related to the ethical, legal, and social implications of biobanking and data sharing, and has specific experience in participant observation. Specifically, with Gail Henderson, she was funded by a recent National Human Genome Research Institute R01 to examine how organizational diversity and ethical issues within biobanks have emerged and changed over time, and how these have shaped biobanks' work and policies. As part of this study, she also conducted an inventory and survey of biobanks in the US. For the proposed project, Dr. Cadigan will help create a systematic inventory of networked biorepositories in the United States and to develop and implement the key informant interviews with personnel and other stakeholders associated with these repositories (Specific Aim 1). She will also serve as the lead on methodological considerations in participant observations of biobank networks, and will help with the analysis of these data (Specific Aim 2). She will also work with the principal investigators to translate study findings into models for governance and practice (Specific Aim 3). Lastly, she will provide expertise on the implications of these data for policy and practice within biorepositories and help to disseminate study findings. Dr. Cadigan will have an increased effort in years 2 and 3 in order to allow additional effort to work on methodological considerations in participant observations (Specific Aim 2). **Dr. Cadigan's effort will be** EFFORT **calendar months** EFFORT **effort) in years 1 and 4, and 2.4 calendar months** EFFORT **effort) in years 2 and 3.**

Fringe Benefits: Salaries are increased by 3% each year for cost-of-living increases. Fringe benefits are calculated at the UNC standard rate of 22.741%, plus hospitalization at the standard UNC rate of $5,471/year, based on FTE. Hospitalization costs are increased by 3% each year for inflation.

TRAVEL

In years 1, 2 and 3, we request $2500 for Dr. Cadigan to travel to Louisville and Cleveland, respectively, for two investigator meetings each year [$600 airfare, $450 hotel, $200 car rental, meals and incidentals x 2]. In year 4 we request $2500 for Dr. Cadigan to travel to one investigator meeting (Louisville or Cleveland) and one symposium (Bethesda) [$600 airfare, $450 hotel, $200 car rental, meals and incidentals x 2].

BUDGET JUSTIFICATION – MAYO CLINIC

SENIOR / KEY PERSONNEL

Richard Sharp, PhD (Co-Investigator; Principal Investigator, Mayo Clinic subcontract)
Dr. Sharp will participate in the development of semi-structured interview guides and embedded ethnographic activities with participating biorepositories. He will participate in data analysis and communication of research findings in published reports and at national conferences. Dr. Sharp will also assist Drs. Brothers and Goldenberg in developing recommendations for managing ethical, legal and social issues in biobank oversight and governance, with a particular focus on normative analysis. Dr. Sharp will participate in weekly research meetings via videoconference and travel to Louisville or Cleveland for twice yearly in-person research meetings. In year 4, Dr. Sharp will assist with planning and leading a national symposium at which best practices for biorepository oversight will be developed. **Dr. Sharp's effort will be** EFFORT **calendar months** EFFORT **effort) in years 1-4.**

TRAVEL

In years 1, 2, and 3 we request $5000 for travel by Dr. Sharp. This includes $2500 to travel to Louisville and Cleveland, respectively, for two investigator meetings each year [$600 airfare, $450 hotel, $200 car rental, meals and incidentals x 2]. It includes an additional $2500 for travel to conduct embedded observations with networked biorepository case studies. In year 4, we request $2500 for travel to Louisville for an investigator meeting as well as to the national expert symposium.

OTHER DIRECT COSTS

Case Study Administrative Stipend
We request $1000 annually to reimburse the Mayo Clinic Biobank for administrative costs associated with arranging in-depth interviews with biobank stakeholders (Specific Aim 1); including our investigators in biobank governance, oversight, and problem-solving activities (Specific Aim 2); and arranging stakeholder focus groups to engage with our recommendations (Specific Aim 3).

Total Direct Costs less Consortium F&A

NIH policy (NOT-OD-05-004) allows applicants to exclude consortium/contractual F&A costs when determining if an application falls at or beneath any applicable direct cost limit. When a direct cost limit is specified in an FOA, the following table can be used to determine if your application falls within that limit.

Category	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Total Direct Costs less Consortium F&A	257,157	273,067	278,441	293,215	0	**1,101,880**

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

1. Project Director / Principal Investigator (PD/PI)

Prefix:	Dr.
First Name*:	Kyle
Middle Name:	Bertram
Last Name*:	Brothers
Suffix:	

2. Human Subjects

Clinical Trial?	● No	○ Yes
Agency-Defined Phase III Clinical Trial?*	○ No	○ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

● Yes ○ No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested? ○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

Budget Period*	Anticipated Amount ($)*	Source(s)*

Funding Opportunity Number: PA-14-276. Received Date: 2015-12-09T15:54:16.000-05:00

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5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?* ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): Specific stem cell line cannot be referenced at this time. One from the registry will be used.

6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ○ Yes ○ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ○ Yes ○ No

7. Change of Investigator / Change of Institution Questions

❑ Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

First Name*:

Middle Name:

Last Name*:

Suffix:

❑ Change of Grantee Institution

Name of former institution*:

PHS 398 Research Plan

Please attach applicable sections of the research plan, below.

OMB Number: 0925-0001

1. Introduction to Application (for RESUBMISSION or REVISION only)	1250-Introduction to Application.pdf
2. Specific Aims	1251-Specific Aims.pdf
3. Research Strategy*	1252-Research Plan.pdf
4. Progress Report Publication List	
Human Subjects Sections	
5. Protection of Human Subjects	1253-Protection of Human Subjects.pdf
6. Inclusion of Women and Minorities	1254-Inclusion of Women and Minorities.pdf
7. Inclusion of Children	1255-Inclusion of Children.pdf
Other Research Plan Sections	
8. Vertebrate Animals	
9. Select Agent Research	
10. Multiple PD/PI Leadership Plan	1256-Multiple PD PI Leadership Plan.pdf
11. Consortium/Contractual Arrangements	1257-Consortium Contractual Arrangements.pdf
12. Letters of Support	1258-Letters of Support.pdf
13. Resource Sharing Plan(s)	
Appendix (if applicable)	
14. Appendix	

A. Specific Aims

Research in precision medicine aims to identify subsets of patients who share the same biological mechanisms for their disease, and are thus more likely to respond to the same targeted therapies. To achieve this level of personalized health care, researchers need large collections of biospecimens and associated data. While there are a number of large cohorts at individual institutions across the country, individual repositories rarely provide the diversity and size needed to support further development of precision medicine. To address this need, researchers are beginning to promote the networking of multiple biorepositories within or across institutions. This *networked biorepository* approach permits researchers to access larger, more diverse sets of data and biospecimens through one common interface, while leveraging and preserving the relationships local institutions have built with their communities of donors. This approach is expected to conserve resources and time and facilitate more representative data within studies, benefits that are especially important in the study of rare diseases or rare genetic variation that contributes to common diseases.

The ethical and regulatory challenges faced by networked biorepositories are not the same as those faced by conventional biorepositories. Each institution that contributes to a networked biorepository has its own governance structures and donor needs. For this reason, the networking of cohorts adds a level of complexity to ethical and regulatory considerations, while at the same time introducing a number of novel challenges. There are many unknowns regarding how to combine research cohorts; how to address consent, privacy, data security, and data access; and which governance and oversight structures are best suited for addressing these challenges. We propose to fill this gap by conducting a rigorous, mixed-methods study of the perspectives and experiences of stakeholders actively engaged in designing, operating, and governing networked biorepositories. Our overall aim will be to characterize the ethical and regulatory challenges created by existing and proposed models for networked biorepositories, and identify policy and practice solutions available for addressing these challenges. The project will achieve the following specific aims:

Specific Aim 1: Examine the ethical and regulatory challenges that have been raised within current networked biorepositories and identify the solutions that have been utilized to address these challenges (Retrospective Aim).

- Aim 1a. We will conduct a systematic search for established and developing networks that link data and/or samples from multiple repositories. We will utilize online search tools and existing literature to identify networked biobanks in the US, and contact key informants to collect information about their configuration.

- Aim 1b. We will assess the ethical and regulatory challenges raised within networked biorepositories by interviewing key personnel associated with established and developing networks to explore perspectives and experiences addressing challenges related to *consent, privacy and data security, and data access.*

Specific Aim 2: Conduct a longitudinal observation of the governance, oversight, and problem-solving processes utilized by networked biorepositories (Prospective Aim). To assess how networked biorepositories discuss and address new ethical and regulatory challenges that emerge over time, we will conduct participant observations with at least five representative networked biorepositories to examine how stakeholders adapt *governance, oversight, and problem-solving processes* to context. Over the first two years of the project, we will observe these processes in real time by participating in conference calls, in-person meetings, and other contexts in which stakeholders are working together.

Specific Aim 3: Identify approaches to consent, privacy and data security, data access, governance, and oversight that are most appropriate and effective for networked biorepositories (Translational Aim). Building on Aims 1 and 2, our investigator team will develop a set of generalizable recommendations or best practices for addressing ethical and regulatory challenges in networked biorepositories. We will refine these thorough focus groups with stakeholders affiliated with five networked biorepositories and assess how these recommendations might be applied to future challenges. This process will be followed by external review at a symposium with other national experts.

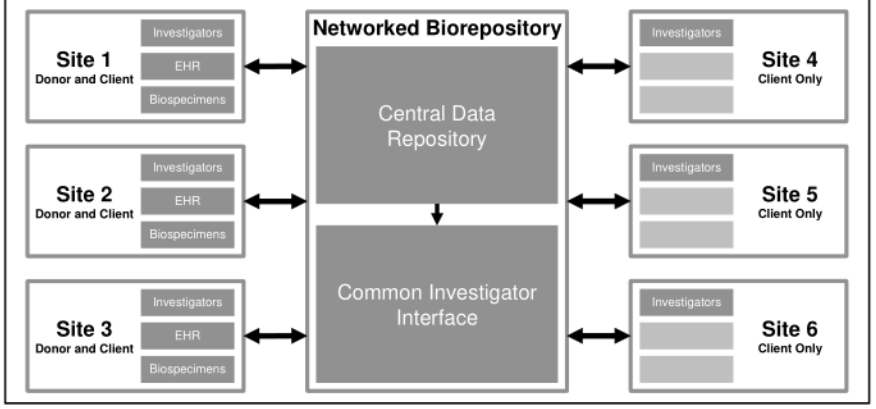
Impact Statement: These aims address high-priority areas for NHGRI, including issues related to consent, privacy and data security, data sharing, and governance structures for genomic repositories. In addition, this project will help address a knowledge gap central to the development of President Barack Obama's proposed Precision Medicine Initiative. A key element of this initiative will be a national cohort that will include biospecimens and medical data from 1 million Americans. This cohort will leverage existing cohorts from across the country to form a "consortium of cohorts," and will later be augmented with new participants.

A. SIGNIFICANCE

Research in precision medicine will increasingly depend on the combination of cohorts from multiple institutions. Research in precision medicine aims to identify subsets of patients who not only share the same disease, but also the same biological mechanisms for their disease, and are thus more likely to respond to the same targeted treatments.[1] Because this approach involves stratifying research cohorts into multiple small subpopulations, it requires especially large sample sizes. Individual healthcare institutions are rarely capable of recruiting the number of participants required, so pooling samples and data across sites is critically important.

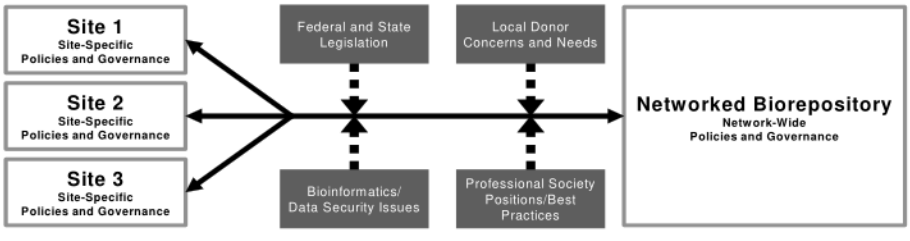
A number of approaches can be used to facilitate sharing of biospecimens, genotyping data, and health-related data among multiple institutions. We define a *networked biorepository* as a research collection that provides investigators with centralized access to biospecimens, genotyping data, and/or health-related data that have been collected at multiple institutions. These networks can be formed through a variety of methods, but generally are created when institutions combine research cohorts through a shared set of policies and procedures. The Electronic Medical Records and Genomics (eMERGE) Network, for example, facilitates sharing through standardized study procedures, standing IRB protocols, and common data-use agreements.[2] Conversely, the Virtual Repository of Dried Blood Spots (VRDBS) utilizes information technologies to allow investigators to access and search multiple cohorts as if they are a single "virtual" biorepository.[3] In addition to variation in the way networked biorepositories are configured, they also vary with respect to size and scale. A networked biorepository may be built to link cohorts from a small number of local institutions, or to create a large international collection of biospecimens and data from many sites. Access to these samples may be restricted to those investigators or institutions who contribute samples (*donor sites*), or they may be accessible to other investigators and institutions (*client sites*) (**Figure 1**). In this project, we will examine the distinctive ethical and regulatory challenges that arise in the design and operation of networked biorepositories across , including networks reflecting a wide range of configurations and scales.

Figure 1: Example design for a networked biorepository. In this model, some data (typically deidentified) are stored in a central database; biospecimens and identifying phenotype data remain at the donor sites. Sites that do not contribute EHR or biosample data may still contribute to the virtual biorepository by performing genotyping and redepositing data into the central repository.



Networked biorepositories raise important ethical, legal, and social challenges that extend beyond those raised by conventional biobanks. Previous research, including substantial work by investigators on our project team, has addressed important issues related to individual biorepositories, including those regarding obtaining informed consent for data collection,[4-6] assuring adequate protections for privacy and other donor interests,[7,8] addressing the potential for returning research results,[9,10] and managing access by client investigators to research data.[11,12] As shown in **Figure 2**, however, the relationship between donor sites and a centralized networked biorepository introduces additional organizational, regulatory, and ethical complexity around these well-recognized challenges. Since donor and client sites are responsible to their own institutional priorities, governance structures, and donor perspectives, networked biorepositories must account for these differences in their deliberations on research ethics challenges, and operationalize these insights through network policies and procedures. In other words, networked biorepositories must develop ethical means for combining sites that have adopted different morally permissible schemes for storing and using biospecimens and data. In order to understand how these unique challenges can and should be addressed, innovative new research is needed to examine the ethical and regulatory challenges raised by networked biorepositories.

Figure 2: Conceptual model for ethical and regulatory issues in networked biorepositories. Novel challenges are introduced by inconsistences among site-specific policies and governance, which must be addressed in network-wide policies and governance (white boxes). A number of additional factors (solid boxes) influence the relationships that are formed among sites, and between sites and the network as a whole.



Novel challenges related to the informed consent process. The difficulty of obtaining informed and considered consent to biorepository research has been a focus of ethical analysis in this domain, given the open-ended nature of data-sharing and client research studies.[13] How can networked biorepositories communicate with participants about future research in a way that maximizes self-determination? How can they harmonize incongruent policies and practices related to informed consent and donor authorization across multiple institutions? These challenges have been identified within networked biorepositories, such as the eMERGE Network,[14] but previous empirical and conceptual work on biorepository consent has not accounted for these special challenges.[4,15,16] New, focused research on consent and authorization in this context is needed.

Novel challenges related to participant control of specimens and data. In many biorepositories, donors are given the ability to restrict the scope of their consent, such as limiting the sharing of data or the types of diseases that can be studied.[17] In some cases, donors are even offered the opportunity to control their samples through an online interface.[18] Offering these types of choices is thought to provide a number of goods, including a sense of control by donors. However, these benefits must be balanced with scientific aims, since the tracking of preferences within and across biorepositories can create significant challenges.[19] When institutions have selected different, morally permissible approaches for offering participants control of their samples, the work to create a network must involve ethical deliberation on the best way to respect previously elicited preferences while harmonizing practices across sites. Focused research on how networked biorepositories can and do engage in such normative work, and careful analysis of the ethical implications if donor preferences are not respected, is clearly needed.

Novel challenges related to investigator access to specimens and data. The use of banked data and samples by "client" investigators raises at least two important ethical issues: (1) Who should be granted access to data? (2) What kind of data should they be able to receive? Some biorepositories provide access to samples and data by approving individual studies. This model allows biorepositories to effectively steward stored biospecimens, since they are a depletable resource, and protect participant's privacy by titrating data access on a "need-to-know" basis. At the same time, however, this benefit in participant privacy is attained with a scientific cost in the form of restricted data access for investigators. Alternatively, biorepositories may certify investigators for open access to data on the basis of their overall research aims and expertise. This model reduces the need for ongoing review, but can still be onerous for investigators.[20] These important ethical questions concerning the protection of participant privacy through de-identification and data reduction, the benefits to research made possible by less restrictive access controls, and the value of retaining identifiers to allow for ongoing connections to participants' health data are a central concern of biorepositories,[21] and is a central concern in the ongoing work to develop a networked biorepository as a part of the President's Precision Medicine Initiative (PMI).[22] Such efforts will benefit from new research to examine how practices like informed consent, de-identification, and data use agreements can address these issues in the context of networked biorepositories, as well as their practical and ethical trade-offs.

Novel challenges related to returning research results to participants. Significant previous research has explored whether it is acceptable, or in some cases compulsory, for biorepositories and client investigators to provide participants with research results that could have a significant impact on their health or that of their family members.[23-25] Returning results across a network of biorepositories requires careful attention to local donor concerns and relationships, as well as the responsibilities of these involved in these networks, including client investigators, donor investigators, and central data managers. Efforts to return results generated at client sites potentially creates responsibilities for donor sites, including the provision of genetic counseling and help with navigating appropriate follow-up services. It also requires institutions across the network to assure that both local and centralized processes are consistent with donor values, public values, and standards for human subjects protections. For example, one of our partner repositories, SAGE Bionetworks, is currently struggling with identifying the responsibilities of central data managers to respond to a perceived desire among donors to receive results, given that network participants are not recruited locally, and may have little or no contact with the repository itself (see Letter of Support). Research is needed to reconsider normative analyses on return of research results in the context of networked biorepositories, as well as to develop best practices for governance and oversight of network efforts to return results to participants.

Novel challenges related to IRB governance and oversight. Since networked repositories involve multiple institutions, they raise important issues related to the way Institutional Review Boards (IRBs) undertake review and oversight. Since local IRBs are an important locus for incorporating community priorities into research governance

and oversight, they tend to arrive at different conclusions about the way consent, donor control, and data access should be handled. To some extent, networked biorepositories may be able to accommodate differences in local processes necessitated by differing IRB perspectives. But conflicting IRB requirements may also pose barriers to the development of networked biorepositories. A number of solutions have been proposed for this challenge, including the federated IRB and central IRB models.[26] The suitability of these models for networked biorepositories, including relevant barriers, requires further study, as evidenced by the focus given to this topic in the recent PMI report[22] and changes to the Common Rule proposed in the recent Notice of Proposed Rulemaking (NPRM), which would make such an approach compulsory for multi-site research efforts like networked biorepositories.[27]

In addition to these challenges, the recent NPRM also proposes a major shift on requirements for consent for the storage and research use of biospecimens. The current proposal would require a broad consent for de-identified sample collection in most situations. While it remains unclear what form the final rule will take, the implications for networked biorepositories could be significant. For example, these changes could require networks to more closely track the sharing of de-identified samples, since such samples could previously be shared freely across networks.

Novel challenges related to participant and community engagement. In addition to oversight by IRBs, many biorepositories have adopted governance and oversight structures that include community advisory boards (CABs) and external ethics advisory boards (EABs). These bodies have proven useful for incorporating the concerns and interests of local stakeholders into the design and operation of institutional biorepositories.[28] The networked biorepository approach, however, requires that stakeholders consider both local and network-wide concerns of stakeholders. An important task for networked biorepositories, then, is to develop appropriate methods for incorporating input from donors and other stakeholders into the governance and oversight of the network, a challenge raised by existing networked biorepositories, including the eMERGE network (see Letter of Support).

Networked biorepositories will play an increasingly important role in research on precision medicine, genomics, and other health-related domains. In his 2015 State of the Union address, President Obama introduced a proposal to invest $215 million into a multifaceted research initiative focused on precision medicine.[29] The President's Personalized Medicine Initiative (PMI) would include, among other projects, a $130 million effort to build a national research cohort that would include biospecimens and medical data from one million Americans. NIH director Francis Collins has indicated that this national cohort will leverage existing cohorts from across the country to form a large "consortium of cohorts."[30,31] This is just one proposed networked biorepository that demonstrates the increasing role this model will play in healthcare research going forward.

This project will examine the ethical and regulatory issues raised by networked biorepositories in general; it is not focused exclusively on the PMI or the proposed national cohort. Still, we believe the findings generated by this study could provide important insights for those working to build the proposed national cohort. In fact, many of the issues discussed above were highlighted as important challenges in a recent report by the PMI Working Group.[22] For this reason, we plan to engage with the PMI planning process in two ways. First, we will make our findings available to PMI planning committees on a pre-publication basis, and contribute relevant insights to planning discussions as needed. Second, we will invite those involved in building the national cohort to the expert symposium described in Specific Aim 3 (see below). At this symposium, we will elicit expert perspectives on our analysis. This will allow those involved with the PMI to hear our findings in a concise format, hear the latest thinking on these issues from other experts, and contribute their own insights to our capstone work as a part of this project.

Table 1: Recent and upcoming regulatory changes that will impact biorepository research.

Regulatory Change	Year	Impact on Biorepository Research
NIH Genomic Data Sharing Policy	2014 (Effective 2015)[32]	Requires explicit consent for sharing genomic data with national databases, even if deidentified.
Newborn Screening Saves Lives Reauthorization Act of 2014	2014[33]	Requires that research on newborn dried blood spots be considered research on human subjects, even if deidentified.
Upcoming Revisions to the Common Rule	2016 (anticipated)[33]	Although not yet final, a revision to the Common Rule was mandated under the Newborn Screening Saves Lives Reauthorization Act of 2014. This revision may reflect changes previously proposed in a Notice of Proposed Rulemaking published by DHHS in 2015. [27,34]

The proposed study will examine the implications of recent and upcoming federal policy changes for emerging models of biorepository research. Networked biorepositories currently in development face a rapidly changing regulatory milieu. Two significant regulatory changes have recently been introduced that will impact biorepository research going forward. An additional regulatory change discussed above – a revision to the Common Rule – is anticipated in the next two years (**Table 1**). By examining how networked biorepositories manage ethical challenges in this changing regulatory milieu (Aim 2), and by engaging in normative work to

analyze these challenges (Aim 3), our project will provide an important opportunity to examine research ethics issues in biorepository research in this emerging context.

Overall, this project is significant because it will (1) assess the novel ethical and regulatory challenges raised by networked biorepositories, (2) identify successful solutions to these issues, including effective governance and oversight processes, and (3) translate these empirical findings into recommendations that will enable new and developing networked biorepositories to support important health research while meeting the needs of donors and protecting the interests of contributing institutions.

B. Innovation

The proposed study is both methodologically and conceptually innovative. It uses a unique approach that integrates qualitative research, stakeholder observation and engagement, and the development of empirically-based recommendations that address key ethical and regulatory challenges for networked collections.

B.1. Methodological Innovation

While the research methodologies we will utilize in each aim are not unique, we believe the particular combination of empirical methods (Aims 1 and 2) we will utilize to develop generalizable recommendations (Aim 3) is novel. In particular, we will collect the **retrospective** experiences of a large cross-section of networked biorepositories through in-depth interviews, while at the same time collecting **prospective**, real-time data through embedded observation of five selected case studies. We will also utilize focus groups with stakeholders to evaluate generalizable solutions to shared ethical and regulatory challenges and address future challenges. The triangulation of these three types of data will support the generation of policy and practice recommendations that are adaptable to a variety of network configurations and can be used to develop successful networks in the future.

Another innovative element of our empirical data collection is our inclusion of networked biorepositories at all stages of development. While we will develop a more comprehensive accounting of networked biorepositories in Aim 1a, we have already identified networks that are currently in development. These include the Mayo Clinic system-wide biobank and a virtual biobank based on the NCI Surveillance, Epidemiology, and End Results (SEER) Program. We have also identified an effort undertaken by healthcare institutions in Cleveland to build a networked biorepository that was ultimately abandoned. Through interviews and observation of stakeholders across such a variety of developmental stages, we will be able to capture a broader set of perspectives and identify ethical and regulatory challenges that arise in different stages of development.

Review of our recommendations by biorepository stakeholders and external experts will support translation to a wide variety of new and emerging networked biorepositories. When developing generalizable recommendations (Aim 3), we will utilize both internal focus groups with stakeholders from our case studies as well as a national symposium that also includes an external set of experts. These external experts will assist with the translation of network-specific approaches to a more generalized set of best practices for the development of new networked biorepositories.

B.2. Conceptual Innovation.

No previous studies of the ethical, legal, and societal implications of biorepositories have specifically addressed the unique challenges raised by networked biorepositories. Although individual biorepository networks have published about their experiences,[2,35] our proposal to systematically study networked biorepositories as a category is unprecedented. Previous bioethical thinking around biobanking has typically been limited to individual repositories; our study is meant to expand on that work, exploring the normative challenges that are raised by networks. For example, individual banks may see themselves as the moral agents, responsible for the stewardship of the samples in their repository. However, networked biorepositories can involve multiple layers of governance that share responsibility for the appropriate use of specimens and data, while at the same time developing conflicting views on how best to protect donors and address ethical questions. We have identified a number of novel challenges through our engagement with partners at our case study networks, and anticipate that we will discover additional “unexpected” ethical issues.[36] Our aim is to develop a set of generalizable recommendations for networked biorepositories that offers robust strategies for addressing the governance and oversight challenges of networks that bring together diverse sets of specimens and data.

C. Approach

C.1. General Overview of Research Design and Methods.

This proposed study utilizes a multi-method approach to assess the ethical and regulatory challenges raised by networked biorepositories. The proposed project uses primarily qualitative strategies to provide insight into the experience and perceptions of a diverse set of specimen and data repositories. **Aim 1** will develop an inventory of existing networks and their organizational characteristics, and then utilize semi-structured interviews to assess the **retrospective** experiences of stakeholders of networked biorepositories. **Aim 2** will utilize participant observation methods to **prospectively** observe the kinds of ethical and regulatory issues that arise during the development and implementation of a data and/or specimen network, and to assess how those issues are addressed in "real-time" within representative networked biorepositories. **Aim 3** will utilize the data from Aims 1 and 2 to develop a set of **recommendations for policy and practice**, including suggested models for governance, that will be discussed and refined through focus groups with our representative networked biorepositories and then with a larger audience of stakeholders through a national expert symposium.

C.2. Specific Aim 1: Examine the ethical and regulatory challenges that have been raised within current networked biorepositories and identify the solutions that have been utilized to address these challenges.

Specific Aim 1a: We will conduct a systematic search for networks that link data and/or samples from multiple repositories.

Preliminary data and relevant team experience. Drs. Goldenberg and Cadigan were co-investigators on a study, funded in part by NHGRI, that examined how organizational diversity and ethical issues within biobanks have emerged and changed over time, and how these factors have shaped banks' work and policies (Gail Henderson, PI). For this study, we conducted an inventory and survey of 465 biobanks in the US as well as an in-depth qualitative case study analysis of six banks. Results from this study revealed that 16% of biobanks surveyed identified that they were part of a larger "network of biobanks." Open-ended survey responses indicated that a biobank network was interpreted broadly to include "registries, cooperative groups, multi-site studies, and consortia."[37] These networked banks included "NIH sponsored, state-sponsored and population based, intra- and inter-institutional, and national and international" repositories.[37] In-depth case studies identified a number of governance issues that are important to networked biobanks, including concerns regarding data management and the fate of samples and data if the larger central or organizing bank were to close or lose funding.[36] This specific aim will build on these preliminary data: (1) we have already identified a subset of existing networked biorepositories through this previous study; (2) we will adapt this systematic search methodology to comprehensively identify additional networked biorepositories, including smaller-scale and informal networks.

Systematic search methodology. Starting with the list of networked biobanks we identified in our previous study from 2011, we will conduct online searches to verify whether each of these networks remains in operation. We will then search for additional networks using a search strategy similar to the one we employed in 2011. This approach used electronic searches of PubMed, NIH RePORTER, Google, and member websites of the American Association of Medical Colleges (AAMC) and NIH-sponsored Clinical and Translational Science Award (CTSA) institutions. As we discovered in our 2011 search, there is no agreed-upon definition of biobanks or networked biobanks. Consequently, we developed nested Boolean search strings for use in PubMed and RePORTER, and keyword searches for Google and the AAMC and CTSA sites, which we will adapt for this study. This approach was successful at identifying networked biorepositories in various forms, including small networks and those that operate informally. For each network we identify, we will record a contact person whom we will email or call by telephone to verify the existence of the network and its organizational details. We will then ask whether he or she is a suitable stakeholder to be recruited for an interview in Aim 1b. If not, we will request the contact information for at least one person who may be more suitable. This approach proved successful in our 2011 study.[37]

Specific Aim 1b: We will conduct in-depth interviews with key personnel associated with established and developing networks and review primary documents including informed consent documents and data-use agreements. These methods will allow us to explore stakeholders' perspectives and experiences addressing challenges related to consent, privacy and data security, and data access.

Preliminary data and relevant team experience. Drs. Goldenberg and Rivera are currently completing an NHGRI-funded R01 (Rivera, PI) examining the range and variation of policies and practices among CTSA institutions for human subjects protection in biobanking, with an emphasis on informed consent and biospecimen/data sharing. This study included a survey of IRB Administrative Directors from 60 institutions affiliated with CTSAs about their policies and practices related to secondary use and sharing of biospecimens. These data documented divergent practices regarding data sharing across CTSA institutions, indicating an important area of concern for harmonization within networked biorepositories. Many of these policies attributed importance to the identifiability of samples and whether the original researchers who collected the specimens were involved in the ongoing research with those data.[11] Additionally, this project included an in-depth analysis of CTSA institution policies regarding biospecimens and data sharing. Forty-one percent of current publicly available policies contained information regarding sample or data sharing with researchers outside their own institution. Further, only 13% had any policies regarding the contribution of samples or data into public databases or repositories, such as dbGaP. This study will utilize a similar methodology to review informed consent documents, data-use agreements, and other policies relevant to networking biorepositories. Drs. Brothers, Goldenberg, and Cadigan all have experience with semi-structured interview methodology and document analysis, and have previously utilized this approach to study ethical and regulatory issues relevant to biorepositories.[8,38-40]

Sampling approach for semi-structured interviews. For each network identified in Aim 1a, we will invite the person identified by our initial contact to participate in an interview. This interview will involve a structured component focused on the configuration of the networked biorepository (i.e. the number and types of sites contributing to the network, where data and biospecimens are stored, and the organizational structure of the network) as well as a semi-structured component. We will utilize both snowball sampling and publically-available information about the network to identify other stakeholders with knowledge about important ethical and regulatory challenges encountered by the network. Stakeholders of interest could include scientific or administrative leaders for the biorepositories, operations managers, informaticists, internal and external ethics advisors, institutional review board (IRB) members, community advisory board members, donor study principal investigators (PIs) or coordinators, and client study investigators. Drs. Cadigan and Goldenberg used a similar approach in their recent case studies of biobanks, described above.[8] In a subsample of networks, we will take a "deep dive" in an attempt to identify stakeholders in positions with less power or who may have dissenting opinions about the issues addressed in our interviews. This approach will help address bias potentially introduced by the snowball sampling approach. Overall, we will interview as many as 5 stakeholders involved with each network, or up to 100 interviews total (divided among years 1, 2 and 3 of the study). The perspectives of biorepository donors are of great interest, but we are not proposing to speak directly with biorepository donors within the context of this proposed study. We will, however, interview stakeholders who are tasked with representing donor priorities in the operations of networked biorepositories, such as members of Community Advisory Boards. Given the importance of donor perspectives, we hope to dedicate an entire future project to studying this dimension of ethical issues in networked biorepositories.

Table 2: Domains to be addressed in semi-structured interviews

Domain	Sample Prompts
Consent	- "What challenges related to consent have you encountered?" - "How has the content of consent documents been harmonized across the network, if at all?"
Donor Control of Data	- "What deliberations have network members undertaken to consider the role for donors in controlling how their samples are used?" - "Have the sites participating in this network taken different approaches to giving donors control over their samples and data? If so, how have you dealt with this challenge?"
Return of Research Results	- "How aligned are perspectives on return of results across the network?" - "What processes, if any, do you use for returning research results uncovered by client investigators?"
Data Access by Client Investigators	- "What deliberations, if any, have members of the network undertaken on weighing client investigator access and benefits for research against donor/participant privacy?" - "How does this networked biorepository vet client investigators or client studies?"
Privacy and Data Security	- "What measures have been most effective for protecting the privacy or identity of donors?" - "What trade-offs between privacy and researchability have you encountered?"
Oversight	- "How does this network balance the interests of local and network-wide oversight bodies?" - "How are local external bodies, including those representing the community, involved in network-wide oversight?"
Governance	- "How does your network make important decisions? Which local and network-wide stakeholders are involved?" - "Which stakeholders would you like to see more involved?"

Semi-structured interview methodology. Stakeholders invited to participate will be scheduled for a 60-minute interview with a study co-investigator experienced with semi-structured interviewing techniques. Interviews will take place either by video conference or "on the sidelines" of site visits or consortium in-person meetings. The interviewer will use a discussion guide to direct a conversation covering a range of domains (**Table 2**). Within each of our interview domains we will design prompt questions to discriminate between practical or programmatic issues and ethical or normative challenges they may face. For example, when asking about data management, we will

explore distinctions between the logistic barriers to sharing and the ethical responsibility repositories may feel they have as stewards of their samples. The interviewer will start the conversation by posing one or more open-ended questions and will then encourage the stakeholders to explain and elaborate using non-directive prompts. All interviews will be audio recorded for accuracy. We do not plan to offer an incentive for stakeholders participating in interviews.

Qualitative analysis of semi-structured interviews. Audio recordings will be transcribed by a professional transcription service. Once 10 interviews have been transcribed, research personnel will begin to read and code transcriptions using a Framework Analysis methodology. This technique is well suited to studies utilizing previously identified themes.[41] They will start with a set of themes identified in previous research and add common topics in participant responses. These topics will then be divided into several subtopics, based on re-occurring themes within the larger topics. The creation of sub-topics will allow for a more in-depth analysis and more complex understanding and interpretation of each particular theme.[42,43] Each of the themes and sub-themes will be given a code, and all codes will be compiled in a codebook. Researchers will meet to discuss the codebook and provide clear definitions for each code. Once the codebook has been developed, two coders, one at each of the primary sites, will code the same ten interviews independently using ATLAS.ti software. Once these interviews have been coded, the study team will meet to compare results and calculate inter-coder reliability.

If necessary, codes will then be revised and interviews recoded to ensure greater coding reliability.[44] Once a reliability score of 90% or greater has been established between the two coders, the remaining interviews will be divided among the research team and will undergo a thorough coding analysis. In order to lend greater coherence to important themes across the course of the study, we will combine qualitative data across all three aims of the study into a single ATLAS.ti hermeneutic unit, and will utilize a shared set of codes across all data types.

Qualitative analysis of primary documents. In order to characterize the approaches utilized by each network to address ethical and regulatory issues in greater detail, we will collect consent documents, data use agreements, IRB protocols, and other primary documents from as many identified networks as possible. We will then examine and compare these documents utilizing qualitative coding methodology. Specifically, we will load documents into ATLAS.ti software and code passages of text using a set of themes shared across all three Specific Aims.

C.3. Specific Aim 2: We will conduct a longitudinal observation of the governance, oversight, and problem-solving processes utilized by networked biorepositories.

Preliminary data and relevant team experience. Dr. Brothers has been a co-investigator with the eMERGE Network since 2008, and Dr. Goldenberg has been a member of the Ethics and Legal Workgroup for the Newborn Screening Translational Research Network (NBSTRN) since 2012. Through this work in “embedded” ethics, they have identified a range of ethical and regulatory challenges that have arisen for participants in these consortia. This experience is reflected in publications on a range of issues raised by biorepositories, including analyses addressing informed consent,[4,45] return of results,[46,47] and data-sharing.[48] Dr. Goldenberg has also been trained in participant observational methods. Dr. Cadigan has significant experience using participant observation in research. She is currently completing a participant observation study of scientific meetings focused on selecting gene variants to screen in a pilot adult preventive genomic screening program. Participant observation is highly effective at elucidating how clinicians and researchers from different disciplines identify and discuss ethical considerations of the criteria used for selecting gene variants, and how decisions regarding which variants to screen are made.[49]

Overview. This aim will utilize *participant observation methodology* to assess three key questions about networked biorepositories: (1) What types of ethical and regulatory challenges arise for networked biorepositories in their everyday work to develop and sustain a networked research cohort? (2) How do networked biorepositories with a variety of organizational configurations identify and discuss ethical and regulatory challenges, and how do they generate, evaluate, and settle on specific solutions? (3) Which solutions for ethical and regulatory challenges tend to be used in different types of networked biorepositories, and what factors can account for these patterns? We will utilize virtual and in-person observations with our five partner repositories to assess these questions.

Participant observation methodology will allow us to observe both the social processes of networked biorepositories (how stakeholders go about deliberating on and addressing ethical and regulatory challenges) and the outcomes of those social processes (the solutions that are utilized by these networks). Participant observation

methods are a widely used set of qualitative and ethnographic approaches. In this study, they will allow our research team to observe networked biorepository stakeholders (including representatives of donor perspectives, such as Community Advisory Boards) in everyday settings – e.g., on conference calls, at in-person meetings, etc. – with a focus on understanding how context (including, among many other factors, the organizational and scientific configuration of the networks) influences the way stakeholders solve ethical and regulatory challenges.[50] In order to understand the meanings behind stakeholders' actions, such as why they select one solution over another, our investigators will be able to stimulate conversations about underlying assumptions or preferences.

Addressing concerns related to our participant observation. Because we will be observing repository stakeholders, they will become participants in our research. Working with the leadership of these groups and with our own IRB, therefore, we will identify the most appropriate methods to obtain authorization for our observation and consistently maintain transparency about our research and its aims. Due to the potential for frequent changes in the stakeholders participating in these activities, it may not be practicable to obtain explicit informed consent from every person who participates in conference calls, in-person meetings, or other activities. Nevertheless, we will continually work with repository leadership to remain transparent, remind participants about our ongoing project, and describe assurances about confidentiality, including that participants will not be individually identifiable in any products of our work. Our research team will also work to limit its influence on the development of solutions to ethical or regulatory challenges, since our aim is to observe how each network develops its own approach to addressing these issues. Some influence is inevitable, and is a well-recognized limitation of ethnographic methods. In order to account for this influence, however, we will engage in a reflexive process (described below) with the aim of assessing how our presence and participation affect the discussions and processes of each networked biorepository. Dr. Cadigan has successfully addressed all of these concerns in her study of the deliberations of the gene variant selection committee for the adult preventive genomic screening program, described above.

Table 3: Overview of networked biorepositories case studies that will be observed in Specific Aim 2 of this proposed project.

Network	Stage of Development	Configuration
Electronic Medical Records and Genomics (eMERGE) Network	Mature	**Donor sites** (eMERGE sites) pull biosamples, genotype data, and medical record data for each client study, and submit to coordinating site. Standing data use agreements (DUAs) facilitate sharing. This network also includes the Sequence, Phenotype, and Pharmacogenomics Integration Exchange (SPHINX), a **central repository** where pharmacogenomics-specific genotypes and phenotypes are stored centrally.
Kentucky Cancer Registry	Mature	**Donor sites** (local hospitals and pathology labs) store tissue samples and report cancer surveillance data to state cancer surveillance programs. The Kentucky Cancer Registry operates as a **central repository**, linking client investigators to available tissue samples across the state. The national SEER program is working to connect state surveillance programs into a **national central repository**, an effort that we will have an opportunity to study as it moves forward.
Newborn Screening Translational Research Network (NBSTRN)	New	**Donor sites** (state newborn screening programs) store biosamples locally and submit deidentified phenotype data to the **central repository** called the Virtual Repository of Dried Blood Spots (VRDBS), which is operated by the American College of Medical Genetics and Genomics (ACMG).
Sage Bionetworks-Synapse	New	**Donor Sites** (multiple academic, non-profit, and industry biodata contributors) utilize a cloud-based, networked environment for sharing and tracking data, results, methods and tools with collaborators from multiple sites. Synapse users are responsible for the processing of data and information, however Sage Bionetworks acts as a steward of the data, tools, and analysis available through their platform
Mayo Clinic Biobank	In Development	**Donor sites** (Mayo campuses) store biosamples. Current work is underway to build a system-wide, cloud-based **central repository** containing genotype and phenotype data.

Selection of case studies. We have provisionally selected five networked biorepository case studies that reflect a diversity of potential networked biorepository configurations and approaches. As shown in **Table 3**, these virtual biorepositories vary with respect to the network infrastructures used to combine the component cohorts, the types of institutions involved, and the types of biosamples and medical data collected and shared. They also differ with respect to their current stage of development. The eMERGE Network has been in operation for over eight years; its stakeholders have developed extensive experience with important ethical questions related to networked biorepositories. On the other hand, the networked biorepository proposed by the three medical campuses of the Mayo Clinic system is currently in development. Based on our systematic search of biorepositories and interviews with stakeholders in Aim 1, we may replace one or more of these case studies or add additional case studies, as allowed by budget and time constraints. We have listed five provisional case studies here to demonstrate: (1) the diversity of network characteristics that we plan to examine; (2) the feasibility of obtaining permission to observe and participate in the operations of networked biorepositories.

Access to governance, oversight, and problem-solving processes. The leaders of each of these networks have committed to opening their operations to observation and participation by our investigators, as demonstrated by the attached letters of support. These networks utilize a variety of governance, oversight, and problem-solving processes, and all sites have committed to including us in all relevant meetings (i.e., none have placed restrictions on our observation and participation) (**Table 4**).

Table 4: Contexts where we plan to conduct participant observation of governance, oversight, and problem-solving processes.

Network	In-Person Collaborator Meetings	Advisory Board Meetings	Conference Calls	Community Advisory Boards	Ethics Advisory Boards	IRB Meetings
eMERGE Network	✓	✓	✓	✓	✓	NA
Kentucky Cancer Registry	✓	NA	✓	NA	NA	NA
NBSTRN	✓	✓	✓	NA	✓	NA
Sage Bionetworks-Synapse	✓	✓	✓	NA	✓	NA
Mayo Clinic Biobank	✓	✓	✓	✓	✓	✓

Participant observation approach. One investigator and one research coordinator will serve as the primary contacts for each case study repository. The primary contacts will coordinate with the administrative staff of each repository to track the times and locations of meetings, phone calls, or other sessions of interest. Whenever possible, the primary contacts will participate in each session of interest in order to maximize familiarity and acceptance by stakeholders.[51] When the primary contacts are unable to attend, another member of the investigator team will act as a substitute. During each session, the investigator will observe the conversation and other social processes, and participate by asking stakeholders to clarify or elaborate on their perspective or respond to alternative proposals. The investigator will record fieldnotes in a secure digital collaboration space immediately following each observed session.[52] Many of these observations will take place through virtual communication and engagement via conference calls and video conferencing technologies. However, we will plan on a number of site visits with each of the repositories to attend in-person meetings or retreats when possible. We plan on visiting each bank two times each year for in-person meetings. Dr. Cadigan will utilize her extensive experience with participant observations to help coordinate the training and oversight for each observation team.

Reflexive processing and qualitative analysis of field notes. During investigator phone calls every two weeks, each investigator will report on their observations during the previous interval. These reports will serve two purposes: (1) to provide investigators an opportunity to engage in self-reflection and receive feedback on their participation in the observed sessions;[53] (2) to provide an opportunity for investigators to identify significant insights on governance, oversight, and problem-solving processes. Based on these reports, other members of the investigator team will ask clarifying questions, provide feedback, and contribute to the interpretation of observed processes. Significant points of this discussion will then be used to amend fieldnotes, which will be coded and analyzed as described in Aim 1.

C.4. Specific Aim 3: We will utilize normative and policy analysis methods to develop a set of generalizable recommendations for addressing ethical and regulatory challenges in networked biorepositories. We will then refine these recommendations through focus groups with stakeholders affiliated with our case study networked biorepositories, and through external review at a symposium with other national experts.

Preliminary data and relevant team experience. Dr. Brothers recently led a project within the eMERGE Network focused on developing workable and ethically appropriate consent procedures for the inclusion of children in biorepositories. Like the work described in this Aim, this project utilized available literature and empirical observations from existing biorepositories to develop guidance for biorepository processes, including a qualitative, thematic analysis of assent documents, parental permission documents, and other consent-related resources from nine biorepositories.[4] Dr. Goldenberg has also been involved in projects in which empirical data were translated into normative recommendations for policy and practice, including a study of public perceptions on the storage and use of newborn screening bloodspots for research. The project culminated with a national expert symposium to review findings and refine a set of policy recommendations for bloodspot research.[54] Prof. Rothstein and Dr. Harrell are involved in an ongoing project to develop policy recommendations to facilitate international data-sharing.

Identify key challenges. To ensure that our recommendations are targeted toward ethical and regulatory challenges encountered by networked biorepositories, we will begin our work on this Aim by reviewing qualitative coding findings from our semi-structured interviews, primary document analysis (Aim 1), and ethnographic observations of our case studies (Aim 2). We will extract codes identifying commonly encountered ethical and regulatory challenges, and organize them by domain (e.g., consent; privacy and data security; data access). We will then select key challenges that could benefit from recommendations specific to the context of networked biorepositories. This effort will focus on key challenges that are distinctive to networked biorepositories or pose special considerations in the context of networked biorepositories, and for which the potential solutions are not identical to those already proposed by available recommendations directed toward conventional biorepositories.

Identify available solutions and prepare preliminary recommendations. After identifying key challenges, we will analyze their normative and policy dimensions, using our empirical data as our analytic basis. As appropriate, we will utilize the expertise of our "normative core" comprised of a number of our Co-investigators and Advisory Board members, all of whom have extensive experience translation of empirical findings to normative recommendations for policy and practice (*see description of normative core below*). We will also utilize available conceptual and legal literature. We will identify potential solutions, paying particular attention to each solution's: (1) compatibility with relevant ethical and legal standards, (2) costs and practical trade-offs; and (3) utility for networked biorepositories with different configurations. We will use our bi-monthly team conference calls to review the solutions available for addressing each key challenge, deliberate on the normative and policy underpinnings of each, and develop a set of preliminary recommendations. We will close this phase of Aim 3 by developing a preliminary report for each domain describing the key challenges, summarizing our recommendations, and providing an analysis of the normative concerns and empirical data supporting these recommendations. Each report will be developed by the investigator team as a whole, with one investigator taking the lead.

Conduct focus groups. Focus groups provide an ideal approach to further refine our recommendations with the stakeholders most likely to use and benefit from them.[55] In order to ensure that our recommendations will meet the needs of biorepository stakeholders and be translated effectively into practice, we will conduct focus groups with stakeholders involved with our five case study repositories. We will conduct as many as 10 focus group sessions, with each session dedicated to one report. We will utilize purposive sampling methods to ensure that the participants in each focus group have practical experience in the domain addressed by the report to be considered. We will carefully constitute each group so that participants can express their perspectives freely, paying particular attention to power imbalances among stakeholders within networks. Prior to each focus group session, we will provide participants with the preliminary text of the assigned report, and then begin the session with a brief presentation by an investigator explaining the key challenges and reviewing the rationale for the recommendations provided. One of the investigators will then utilize a discussion guide to moderate conversation among stakeholders. Among other aims, the investigator will encourage participants to provide a "reality check" on the suitability of the recommendations for the types of challenges they encounter in their own network. Seven members of our study team (Goldenberg, Brothers, Sharp, and Cadigan; and "other personnel" Rich, Ponsaran, and Morello) are experienced with moderating focus groups.

Analysis of focus group data and revision of recommendations. Focus group sessions will be audio recorded and professionally transcribed. Transcriptions will undergo qualitative coding using Atlas.ti software, as described above. The investigator team will review the coding, with particular attention to those solutions perceived by focus group participants to be inadequate for meeting a key challenge or especially difficult to implement. The preliminary recommendations will then be revised based on these findings.

Expert symposium. In order to receive feedback on our near-final recommendations, we will host a symposium focused on our key ethical and regulatory challenges in networked biorepositories. We will invite national and international experts as well as key stakeholders from our case studies to attend. To the extent possible, we will invite other stakeholders who may be interested in our recommendations, including those involved with developing networked cohorts, including those working on the PMI national cohort. We will hold this symposium at a time and place that increases broad attendance, such as immediately before or after a relevant national meeting. The symposium will follow a workshop format. We will present each set of recommendations, followed by time for large and small group discussions on their adequacy for addressing the identified key challenges and their real-world utility for networked biorepositories with different configurations. We will have dedicated time during the symposium to consider future directions in networked biorepositories and proposed visions for addressing new ethical and regulatory challenges anticipated to emerge with these future directions.

Final recommendations. Immediately following the completion of the expert symposium, our investigator team will meet in person to consider the feedback received on our recommendations in each domain, and develop a plan for finalizing each set of recommendations. Once the recommendations are complete, we will disseminate them to the community, as described below.

D. Research Team

Dr. Kyle Brothers and Dr. Aaron Goldenberg will serve as Co-Principal Investigators for this project. We have selected a two PI format for this study because (1) Drs. Brothers and Goldenberg have complementary skills in the

areas of normative analysis and empirical research methods. (2) They each have significant experience working with different types of biorepositories. Dr. Brothers has extensive experience working with institutional/clinical repositories (BioVU at Vanderbilt University) as well as work with the eMERGE Network. Dr. Goldenberg has worked closely with a number of Public Health-related biorepositories, including extensive experience studying the storage and use of newborn screening bloodspots and empirical work on the collections and storage of blood samples from underserved communities. (3) Their personal connections with networked biorepositories will facilitate study of a broader range of networks. (4) The proposed project is ambitious and complex, and will benefit from collaborative leadership. Similarly, having two lead sites will allow us to pool the resources of two research teams, an important strategy given the ambitious scope of this project. Drs. Brothers and Goldenberg will share overall oversight and decision making regarding the implementation of all project Aims, and will take primary leadership roles for the Aims most related their expertise (**Table 5**).

Table 5: Leadership Plan

Project Component	Lead	Special contributions from co-investigators
Specific Aim 1a: Network inventory	Dr. Goldenberg	Dr. Cadigan will contribute her experience from the earlier project that involved an inventory of biorepositories
Specific Aim 1b: Stakeholder interviews	Dr. Goldenberg	All co-investigators will participate in conducting interviews. Both lead sites will contribute to analysis.
Specific Aim 1b: Primary document analysis	Dr. Brothers	Dr. Harrell will take primary responsibility for analysis of primary documents
Specific Aim 2: Participant observations	Dr. Brothers	Dr. Cadigan will serve as lead on methodological considerations in participant observation. All co-investigators will participate in fieldwork. Both lead sites will contribute to analysis.
Specific Aim 3: Policy development	Dr. Brothers	The normative core (see below) will contribute to analyses relevant to their domains of expertise (philosophy, law, and regulation).
Specific Aim 3: Focus groups	Dr. Goldenberg	The Case team will organize focus groups, which will be moderated by Drs. Goldenberg, Brothers, Cadigan, or Sharp.
Specific Aim 3: National expert symposium	Drs. Brothers and Goldenberg	The full team of co-investigators will contribute to planning and presenting findings at the expert symposium.

Five co-investigators will assist with this project, with each bringing unique expertise to its design and implementation. Importantly, each of these co-investigators has collaborated and/or published with either Dr. Goldenberg, Dr. Brothers, or both on issues related to this proposed study.

- **Dr. Richard Sharp** has extensive experience studying the ethical and social implications of biobank research. He will help develop and implement the in-depth interviews and participant observations (Aims 1 and 2), and will serve as lead on normative considerations in developing generalizable solutions (Aim 3).
- **Dr. Jean Cadigan** is a medical anthropologist who has worked on several projects related to the ethical, legal, and social implications of biobanking and data sharing. Dr. Cadigan will lend her experience to the inventory of networked biorepositories (Aim 1a) and will play a key role in developing and implementing participant observation (Aim 2).
- **Dr. Suzanne Rivera** is a national expert on the protection of human subjects and regulatory issues related to biomedicine. She will assist in the development of all study Aims, with particular attention to questions regarding the regulatory and IRB implications of networked biorepositories (Aim 3).
- **Mark Rothstein, JD** is an internationally-recognized expert on health policy. He will assist with the analysis of data related to privacy, data security, and other legal issues, as well as with the development of policy recommendations (Aim 3).
- **Heather Harrell, MD, JD** will assist with the analysis of primary documents (Aim 1b), as well as the collection and analysis of data through interviews and participant observations (Aims 1b and 2).

All co-investigators will also assist Drs. Brothers and Goldenberg with analyzing study data and developing recommendations for managing ethical and regulatory challenges in networked biorepository oversight and governance. The team will participate in bi-monthly research meetings via videoconference as well as bi-annual in-person research meetings in either Cleveland or Louisville.

E. Advisory Committee

The team will also work closely with an Advisory Committee comprised of representatives from our case study partners and other national experts in the areas of ELSI and genomic research (**Table 6**). The Committee will provide ongoing guidance to the overall project and assist in interpreting research findings, disseminating study results, and developing our models and recommendations for networked biorepository policy and practice. Advisory committee members who are permitted to an honorarium will receive $1,000/year for their contributions.

Table 6: Membership of the Advisory Committee

Name	Affiliation	Role on Advisory Committee
Gail Henderson, PhD	Professor, Department of Social Medicine University of North Carolina, School of Medicine	National expert on ELSI research and biobanking
Eric T. Juengst, PhD	Professor, Department of Social Medicine University of North Carolina, School of Medicine	National expert on the application of philosophical and normative considerations to research ethics issues
Jonathan Haines, PhD	Director, Institute for Computational Biology Chair, Department of Epidemiology & Biostatistics Case Western Reserve University	National expert on biorepository and genomic research
Janet E. Olson, PhD	Mayo Clinic Biobank Project Director Assistant Professor of Epidemiology, Mayo Clinic	Representative for Mayo Biobank
Rex L. Chisholm, PhD	Adam and Richard T. Lind Professor of Medical Genetics Vice Dean for Scientific Affairs and Graduate Studies Feinberg School of MedicineAssociate Vice President for Research, Northwestern University	Representative for eMERGE Network
Michael S. Watson, MS, PhD,	Executive Director, Newborn Screening Translational Research Network	Rep. for Virtual Repository of Dried Blood Spots
Thomas Tucker, PhD	Associate Professor, University of Kentucky College of Public Health Director, Kentucky Cancer Registry	Representative for Kentucky Cancer Registry
Megan Dorr, MS, LGC	Director of Governance, Sage Bionetworks	Representative for Sage Bionetworks

F. Normative Core

Throughout each stage of this project, we will utilize a "normative core" made up of the PI's, co-investigators, and advisory board members, each of whom have experience in both normative analysis and the translation of empirical findings into normative recommendations for policy and practice. This group will include Dr. Sharp and Advisory Committee member Dr. Eric Juengst (Philosophy), and Prof. Rothstein and Dr. Rivera (Legal/Regulatory). The core meet several times each year and will work to assure integration of normative questions into the development of our interview guides and participant observation methods. Additionally, they will contribute to ethical analyses and development of the normative aspects of our recommendations.

G. Timeline for the Proposed Research

Table 7: Proposed timeline

Project Milestone	Year 1		Year 2		Year 3		Year 4	
	Q1 - Q2	Q3 - Q4	Q5 - Q6	Q7 - Q8	Q9 - Q10	Q11 - Q12	Q13 - Q14	Q15 - Q16
Specific Aim 1								
Systematic search for established and developing networks	X	X	X	X				
In-depth interviews with network stakeholders		X	X	X	X			
Transcription and qualitative analysis of interview data				X	X	X		
Collection and analysis of primary documents			X	X	X	X		
Specific Aim 2								
Final selection of case study repository networks	X							
Observation and participation in governance, oversight, and problem-solving processes		X	X	X	X	X	X	
Team review of case study observations (every 2 weeks)		X	X	X	X	X	X	
Specific Aim 3								
Identify key challenges and available solutions				X	X			
Prepare preliminary recommendations					X	X		
Refine recommendations through stakeholder focus groups						X	X	
Expert symposium on recommendations and vision for the future							X	
Finalize and disseminate recommendations							X	X

H. Proposed Products and Dissemination Plan:

We propose a multi-tiered approach to disseminating our research findings among biorepository stakeholders, including researchers, repository officials, state and federal health agencies, and representatives of sample and data donors such as community advisory committees. **First, we plan to disseminate our findings and inform stakeholders through traditional academic venues.** Once primary data collection and analysis is completed, we will: 1) present our findings at meetings of professional societies, such as the American Society for Human Genetics, the American Society of Bioethics and Humanities, Public Responsibility in Medicine and Research, the American Society for Molecular Pathology, and the American Public Health Laboratory Association; 2) publish our findings in peer-reviewed journals related to genetics, pathology, data storage and management, computational biology, human subjects protections, and bioethics. In addition to these more traditional approaches, it is crucial to reach out to the biorepository networks themselves. **Second, we plan to disseminate our policy recommendations, models for addressing ethical and regulatory challenges, and any best practices we are able to identify directly to biorepository networks.** We will offer to review these materials with networks though phone conferences or webinars when possible. We will also work to establish partnerships with a number of organizations and federal agencies in order to reach a wider audience with interest in this area (e.g., the National Cancer Institute, the National Human Genome Research Institute, and the International Society for Biological and Environmental Repositories). These methods will allow us to disseminate our findings and recommendations to the stakeholders who will be using them, as well as to those who helped generate them.

PROTECTION OF HUMAN SUBJECTS

Description of proposed involvement of human subjects

Human subjects are involved in the proposed project. The goal of this study is to identify and address the ethical and regulatory challenges of sharing samples and data across multiple cohorts through a centralized networked biorepository. This requires interaction with human subjects in the context of in-depth interviews, participant observation, and focus groups with key repository personnel.

Research material obtained from human subjects

Data will be collected through interviews, focus groups, and participant observation. Only basic demographic information will be stored, including gender, ethnicity, age, education, and occupation. All participants will be provided with an explanation of the intended study. Verbal or written informed consent will be obtained from all individuals who are interviewed or participate in focus groups. Consent will include the agreement that collected information will be published as group observations without individual identification.

No permanent record of interview or focus group participant identifiers will be kept. All field notes and paper copies of the transcripts will be kept in a locked cabinet in the PI's office; only research team members will have access to both the paper and computer files. The files on the computer will be password protected as well. Once transcription and coding of the interviews, participant observations, and focus group data are complete, the original tapes will be destroyed. Participants will be asked to sign a consent form prior to participating, and a copy of the form will be given to them for their own records; the originals will be stored in a locked cabinet.

Plans for recruitment of subjects and consent procedures

For interviews and focus groups, potential participants will be identified through their role as professionals or other stakeholders working in the area of biorepository research. We will approach potential participants either because they are identified in public materials as a representative of a networked biorepository, or because they were identified by a colleague as an important stakeholder in such a repository.

All participants in interview and focus groups will have the opportunity to review a consent document, discuss study procedures, and have their questions answered prior to participation. All participants will be explicitly informed that they have the option to withdraw from the study at any time, have the tape recorder turned off at any time, and choose not to answer any questions. Participants will be asked to join this study for its potential scientific and public health merit. No individual benefit will accrue to the participants. The benefits of this research are largely professional and societal. The potential benefit will be to improve how biorepository networks identify and address ethical and regulatory challenges.

For the participant observations, repository stakeholders will become participants whenever they participate on conference calls or in-person meetings where we are conducting observation. Working with the leadership of these groups and with our own IRB, therefore, we will identify the most appropriate methods to obtain participant authorization for our observation in each case study. Due to the potential for these observations to involve a large number of stakeholders, including some whose participation will be transient, it may not be practicable to obtain explicit informed consent from every person who participates in conference calls, in-person meetings, or other activities. Nevertheless, we will continually work with repository leadership to ensure that our research is as transparent as possible, that participants are frequently reminded about our ongoing project and its goals, that any participant concerns are addressed appropriately, and that assurances about confidentiality are communicated clearly, including the assurance that participants will not be individually identifiable in any products of our work.

Potential risks

The risks of this study are minimal. One potential risk is that some individuals may be uncomfortable expressing their opinions or find some questions difficult to answer. Participants are free to refuse to answer questions. Another potential risk is that some individuals may fear reprisal from superiors if they disclose

information about their biorepository, either because such information is considered proprietary or because it reflects negatively on the biorepository.

Provisions for protecting against potential risks

Participants will only be identified in transcripts and publications with unique study identification numbers or pseudonyms. Only investigators will have access to data files and original interview recordings. Only identification numbers will appear in analytic data sets. Audiotapes will be assigned case numbers; all tapes and study data will be stored in a locked file. In order to minimize the fear of reprisals as well as the risk for indirectly identifying participants, we will typically not identify biorepositories by name in publications and other presentations of our analyses, except when we have explicit permission to do so. In Specific Aim 3, we will purposively constitute focus groups in such a way as to minimize power imbalances, both to encourage open expression of opinions and to minimize fear of reprisals.

Why risks to subjects are reasonable in relation to potential benefits

Respondents will not be asked about any highly personal or threatening topics; they do not have to answer any questions they do not want to answer. We consider this project to involve no more than minimal risk as defined in 45CFR46.

INCLUSION OF WOMEN AND MINORITIES

Potential participants will be identified through their role as professionals or other stakeholders working in the area of biorepository research. Inclusion will therefore not be driven primarily by considerations of gender, race, ethnicity, or national origin. However, we do anticipate that these factors could influence perspectives on ethical and regulatory challenges in networked biorepositories. For this reason, we will, to the extent possible, utilize purposive sampling to maximize the diversity of our population in terms of gender, race, and ethnicity. Based on previous experience in this field, we anticipate the following representation of women and minority stakeholders among our sampled population:

1. Inclusion of minorities: We estimate that at least 25% of our interviews will include African-American, Hispanic/Latino, and other minority participants.

2. Inclusion of women: We estimate that at least half of our interviewees will be women.

OMB Number: 0925-0002

Planned Enrollment Report

Study Title: Semi-Structured Interviews (Specific Aim 1)

Domestic/Foreign: Domestic

Comments: Numbers provided are estimates. Actual recruitment will depend on the gender, race, and ethnicity of stakeholders working with networked biorepositories identified in Specific Aim 1a.

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	0	0	0	0	**0**
Asian	5	4	0	0	**9**
Native Hawaiian or Other Pacific Islander	0	0	0	0	**0**
Black or African American	4	4	0	0	**8**
White	38	37	4	4	**83**
More than One Race	0	0	0	0	**0**
Total	**47**	**45**	**4**	**4**	**100**

Study 1 of 2

Funding Opportunity Number: PA-14-276. Received Date: 2015-12-09T15:54:16.000-05:00

OMB Number: 0925-0002

Planned Enrollment Report

Study Title: Focus Groups (Specific Aim 3)

Domestic/Foreign: Domestic

Comments: Numbers provided are estimates. Actual recruitment will depend on the gender, race, and ethnicity of stakeholders working with case study repositories examined in Specific Aim 2.

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	0	0	0	0	**0**
Asian	3	3	0	0	**6**
Native Hawaiian or Other Pacific Islander	0	0	0	0	**0**
Black or African American	4	4	0	0	**8**
White	30	30	3	3	**66**
More than One Race	0	0	0	0	**0**
Total	**37**	**37**	**3**	**3**	**80**

Study 2 of 2

Funding Opportunity Number: PA-14-276. Received Date: 2015-12-09T15:54:16.000-05:00

INCLUSION OF CHILDREN

While children under the age of 21 may be represented in biorepositories as donors, they will not be represented in our sample. We are studying professionals and other stakeholders working in networked biorepositories, and do not anticipate children under the age of 21 will be serving in these professional roles. We also do not anticipate that stakeholders who are also donors, such as members of Community Advisory Boards, will be children under the age of 21.

MULTIPLE PD/PI LEADERSHIP PLAN

Drs. Brothers and Goldenberg have a strong working relationship, and a developing history of successful collaboration. They recently jointly planned a panel presentation on Genetic Exceptionalism at the conference *Genomics and Ethics in Research and Medical Decision-Making* in Cincinnati, Ohio. They have also served together on a number of advisory committees, and currently have two joint manuscripts in development. Through this shared work they have already developed strong lines of communication, staying in touch by e-mail, phone, or text nearly every day. The current grant application clearly delineates the areas of primary responsibility for each multiple PD/PI, and the budget clearly separates the funding for their respective institutions.

In addition to this strong collaborative relationship, there are two mechanisms to ensure effective leadership for the proposed research. First, the multiple PD/PIs and their respective teams from Louisville and Cleveland plan to have scheduled teleconferences every two weeks to discuss the project, as well as additional communications on an as-needed basis. Second, the investigators have developed an advisory panel comprised of experts in this area. In the unlikely event of a disagreement between the multiple PD/PIs, they will utilize this advisory panel to resolve conflict and build consensus.

Rationale for Multiple PD/PI Format

We have selected a two PI format for this study because (1) Drs. Brothers and Goldberg have complementary skills in the areas of normative analysis and empirical research methods, (2) their personal connections with networked biorepositories will facilitate study of a broader range of networks, and (3) this relatively ambitious and complex project will benefit from collaborative leadership.

BIBLIOGRAPHY AND REFERENCES CITED

1. *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease.* Washington DC: National Academy of Sciences; 2011.
2. Gottesman O, Kuivaniemi H, Tromp G, et al. The Electronic Medical Records and Genomics (eMERGE) Network: past, present, and future. *Genetics in Medicine.* Oct 2013;15(10):761-771.
3. Weinberg DS, Myers RE, Keenan E, et al. Genetic and environmental risk assessment and colorectal cancer screening in an average-risk population: a randomized trial. *Annals of internal medicine.* Oct 21 2014;161(8):537-545.
4. Brothers KB, Lynch JA, Aufox SA, et al. Practical Guidance on Informed Consent for Pediatric Participants in a Biorepository. *Mayo Clinic Proceedings.* November 2014;89(11):1471-1480.
5. Goldenberg AJ, Hull SC, Botkin JR, Wilfond BS. Pediatric biobanks: approaching informed consent for continuing research after children grow up. *Journal of Pediatrics.* Oct 2009;155(4):578-583.
6. Conley JM, Mitchell R, Cadigan RJ, Davis AM, Dobson AW, Gladden RQ. A trade secret model for genomic biobanking. *Journal of Law, Medicine & Ethics.* Fall 2012;40(3):612-629.
7. Rothstein MA. Expanding the ethical analysis of biobanks. *Journal of Law, Medicine & Ethics.* Spring 2005;33(1):89-101.
8. Haldeman KM, Cadigan RJ, Davis A, et al. Community engagement in US biobanking: multiplicity of meaning and method. *Public Health Genomics.* 2014;17(2):84-94.
9. Rothstein MA. Tiered Disclosure Options Promote the Autonomy and Well-Being of Research Subjects. *American Journal of Bioethics.* 2006;6(6):20 - 21.
10. Fabsitz RR, McGuire A, Sharp RR, et al. Ethical and Practical Guidelines for Reporting Genetic Research Results to Study Participants. *Circulation: Cardiovascular Genetics.* December 1, 2010 2010;3(6):574-580.
11. Goldenberg AJ, Maschke KJ, Joffe S, et al. IRB practices and policies regarding the secondary research use of biospecimens. *BMC Medical Ethics.* 2015;16:32.
12. Henderson GE, Edwards TP, Cadigan RJ, et al. Stewardship Practices of U.S. Biobanks. *Science Translational Medicine.* December 11 2013;5(215):215cm217.
13. Lunshof JE, Chadwick R, Vorhaus DB, Church GM. From genetic privacy to open consent. *Nature Reviews Genetics.* May 2008;9(5):406-411.
14. McGuire AL, Basford M, Dressler LG, et al. Ethical and practical challenges of sharing data from genome-wide association studies: the eMERGE Consortium experience. *Genome Research.* 2011;21(7):1001-1007.
15. Beskow LM, Clayton EW, Eisenberg L, et al. Model Consent Language. The Electronic Medical Records and Genomics (eMERGE) Network Consent & Community Consultation Workgroup Informed Consent Task Force; 2009:1-14.
16. Broder SM, Ponsaran RS, Goldenberg AJ. US public cord blood banking practices: recruitment, donation, and the timing of consent. *Transfusion.* Mar 2013;53(3):679-687.
17. Vaught J, Lockhart NC. The evolution of biobanking best practices. *Clinica Chimica Acta.* Oct 9 2012;413(19-20):1569-1575.
18. Kohane IS, Mandl KD, Taylor PL, Holm IA, Nigrin DJ, Kunkel LM. Reestablishing the Researcher-Patient Compact. *Science (New York, N.Y.).* May 11 2007;316(5826):836-837.
19. Haga SB, Beskow LM, Rao DC, Gu CC. Ethical, Legal, and Social Implications of Biobanks for Genetics Research. *Advances in Genetics.* Vol Volume 60: Academic Press; 2008:505-544.
20. Simpson CL, Goldenberg AJ, Culverhouse R, et al. Practical barriers and ethical challenges in genetic data sharing. *International Journal of Environmental Research and Public Health.* Aug 2014;11(8):8383-8398.
21. El Emam K, Rodgers S, Malin B. Anonymising and sharing individual patient data. *British Medical Journal.* 2015;350:h1139.
22. Hudson K, Lifton R, Patrick-Lake B, et al. *The Precision Medicine Initiative Cohort Program: Building a Research Foundation for 21st Century Medicine.* Bethesda, MD: National Institutes of Health; September 17 2015.
23. Clayton EW. Incidental Findings in Genetics Research Using Archived DNA. *Journal of Law, Medicine & Ethics.* 2008;36(2):286-291.

24. Murphy J, Scott J, Kaufman D, Geller G, LeRoy L, Hudson K. Public expectations for return of results from large-cohort genetic research. *American Journal of Bioethics.* Nov 2008;8(11):36-43.

25. Wolf SM, Crock BN, Van Ness B, et al. Managing incidental findings and research results in genomic research involving biobanks and archived data sets. *Genetics in Medicine.* 2012;14(4):361-384.

26. Marsolo K. Approaches to Facilitate Institutional Review Board Approval of Multicenter Research Studies. *Medical Care.* 2012;50:S77-S81.

27. Department of Health and Human Services. Federal Policy for the Protection of Human Subjects. *Federal Register.* 2015;80(173):53933-54061.

28. McCarty CA, Chapman-Stone D, Derfus T, Giampietro PF, Fost N. Community consultation and communication for a population-based DNA biobank: The Marshfield clinic personalized medicine research project. *American Journal of Medical Genetics Part A.* 2008;146A(23):3026-3033.

29. *Fact Sheet: President Obama's Precision Medicine Initiative.* Washington, D.C.: The White House, Office of the Press Secretary; January 30 2015.

30. Collins FS, Varmus H. A New Initiative on Precision Medicine. *New England Journal of Medicine.* Feb 26 2015;372(9):793-795.

31. Baker R, Boerwinkle E, Burke G, et al. *Building a Consortium of Cohorts – Cohort Identification and Participant Recruitment.* Bethesda, MD: National Institutes of Health;2015.

32. Department of Health and Human Services. Final NIH Genomic Data Sharing Policy. *Federal Register.* 2014;79(167):51345-51354.

33. Newborn Screening Saves Lives Reauthorization Act of 2014. Vol H.R. 1281. Washington, DC2014.

34. Hudson KL, Collins FS. Bringing the Common Rule into the 21st Century. *New England Journal of Medicine.* Oct 28 2015.

35. Mee B, Gaffney E, Glynn SA, et al. Development and progress of Ireland's biobank network: Ethical, legal, and social implications (ELSI), standardized documentation, sample and data release, and international perspective. *Biopreservation and biobanking.* Feb 2013;11(1):3-11.

36. Cadigan RJ, Lassiter D, Haldeman K, Conlon I, Reavely E, Henderson GE. Neglected ethical issues in biobank management: Results from a U.S. study. *Life sciences, society and policy.* Dec 1 2013;9(1):1.

37. Henderson GE, Cadigan RJ, Edwards TP, et al. Characterizing biobank organizations in the U.S.: results from a national survey. *Genome Medicine.* Jan 25 2013;5(1):3.

38. Brothers KB, Clayton EW. Parental Perspectives on a Pediatric Human Non-Subjects Biobank. *American Journal of Bioethics: Primary Research.* 2012;3(3):21-29.

39. Cadigan RJ, Easter MM, Dobson AW, et al. "That's a good question": university researchers' views on ownership and retention of human genetic specimens. *Genetics in Medicine.* Jun 2011;13(6):569-575.

40. Long MD, Cadigan RJ, Cook SF, et al. Perceptions of patients with inflammatory bowel diseases on biobanking. *Inflamm Bowel Dis.* Jan 2015;21(1):132-138.

41. Pope C, Mays N. *Qualitative Research in Health Care.* Malden, MA: Blackwell Publishing/BMJ Books; 2006.

42. Miles MB, Huberman AM. *Qualitative data analysis: an expanded sourcebook.* Thousand Oaks: Sage Publications; 1994.

43. Schensul SL, Schensul JJ, LeCompte MD. *Essential ethnographic methods: observations, interviews, and questionnaires.* Walnut Creek, Calif.: AltaMira Press; 1999.

44. Carey JW, Morgan M, Oxtoby MJ. Intercoder agreement in analysis of responses to open-ended interview questions: Examples from tuberculosis research. *Field Methods.* 1996;8(3):1-5.

45. Brothers KB, Clayton EW. 'Human Non-Subjects Research': Privacy and Compliance. *American Journal of Bioethics.* September 2010;10(9):15-17.

46. Jarvik Gail P, Amendola Laura M, Berg Jonathan S, et al. Return of Genomic Results to Research Participants: The Floor, the Ceiling, and the Choices In Between. *The American Journal of Human Genetics.* 2014;94(6):818-826.

47. Fullerton SM, Wolf WA, Brothers KB, et al. Return of individual research results from genome-wide association studies: experience of the Electronic Medical Records and Genomics (eMERGE) Network. *Genetics in Medicine.* 2012;14(4):424-431.

48. Brothers KB, Clayton EW. Biobanks: Too Long to Wait for Consent. *Science (New York, N.Y.).* 2009;326(5954):798.

49. Unpublished

50. Hammersley M. *Reading ethnographic research: a critical guide.* New York: Longman; 1990.
51. Emerson RM. *Contemporary Field Research: Perspectives and Formulations.* Prospect Heights, Ill.: Waveland Press; 2001.
52. Emerson RM, Fretz RI, Shaw LL. *Writing Ethnographic Fieldnotes.* Chicago: University of Chicago Press; 1995.
53. Schwandt TA. *The SAGE Dictionary of Qualitative Inquiry.* 3rd ed. Los Angeles: SAGE Publications; 2007.
54. Botkin JR, Goldenberg AJ, Rothwell E, Anderson RA, Lewis MH. Retention and research use of residual newborn screening bloodspots. *Pediatrics.* Jan 2013;131(1):120-127.
55. Denzin NK, Lincoln YS. *Handbook of qualitative research.* Thousand Oaks, Calif.: Sage Publications; 2000.

University of Louisville Research Foundation, Inc.

SUBRECIPIENT COMMITMENT FORM

All subrecipients are required to complete the Subrecipient Commitment Form and provide the signature of the authorized organizational representative, prior to submission of proposal.

SECTION A – CONTACT INFORMATION

Subrecipient Legal Name: Case Western Reserve University
Address: 10900 Euclid Avenue
City Cleveland State OH Zip 44106-4919
Phone: 216-368-4432 Email: medres@case.edu
Subrecipient PI Name: Aaron Goldenberg, PhD, MPH
Address where research will be performed 10900 Euclid Avenue
City Cleveland State OH Zip 44106-4976
Proposal Title: Addressing Ethical Challenges in Networked Biorepositories
Performance Period Begin Date: 07/01/2016 End Date: 06/30/2020
Subrecipient Funds Requested: $613,129 Subrecipient Congressional District OH-011
Subrecipient DUNS Number 07-775-8407 Subrecipent EIN 34-1018992
Is Subrecipient currently registered in the System for Award Management (SAM) No
U of L's PI Name: Kyle B. Brothers, MD, PhD
Prime Sponsor: National Institutes of Health

SECTION B – REQUIRED PROPOSAL DOCUMENTS

Statement of Work
Budget and Budget Justification in agency required format
■ Cost Reimbursable ☐ Fixed Price

SECTION C – CERTIFICATIONS

1. Facilities and Administrative (F&A) costs included in this proposal have been calculated based on the following:

   ■ Subrecipient's federally negotiated F&A rate for this type of work
   (If this box is checked please attach a copy of your current rate agreement or a URL link to the agreement)

   ☐ Other rates
   (Please specify the basis on which the F&A rate has been calculated in Section E Comments below)

   ☐ Not applicable
   (No F&A costs are requested by subrecipient)

2. Human Subjects ■ Yes ☐ No

   If **Yes**, please provide Institutional Assurance Number (FWA number) FWA00004428

3. Animal Subjects ☐ Yes ■ No

   If **Yes,** please provide IACUC Assurance Number _____

4. Cost-sharing ☐ Yes ■ No Amount: $_____

   (Cost-sharing amounts and justification should be included in the subrecipient's budget)

5. Conflict of Interest

Please check the appropriate response below

☐Not applicable because the project is not being funded by a sponsor that has adopted the federal financial disclosure requirements (AHA, etc.)

☒Subrecipient Organization certifies that it has an active and enforced conflict of interest policy at least as rigorous as 42 CFR Part 50, Subpart F "Responsibility of Applicants for Promoting Objectivity in Research" and 45 CFR Part 94 "Responsible Prospective Contractors." Subrecipient also certifies that, to the best of Institution's knowledge, (1) all financial disclosures will be made related to the activities that may be funded by or through a resulting agreement, and required by its conflict of interest policy, and (2) all identified financial conflicts of interest have or will have been satisfactorily managed, reduced or eliminated in accordance with subrecipient's conflict of interest policy prior to the expenditures of any funds under any resultant agreement and within a manner sufficient to enable timely FCOI reporting.

☐Subrecipient does not have an active and/or enforced conflict of interest policy and agrees to follow UofL's policy. (UofL's policy can be found at http://www.louisville.edu/conflictofinterest)

By signing below, Subrecipient certifies that the required training related to Conflict of Interest will be completed by all key personnel prior to engaging in any research related to any federally funded award. For those following UofL's policy, the training may be accessed by contacting coioff@louisville.edu.

6. Debarment and Suspension

Has the institution/organization, or any principal investigator or other person proposed to provide services for the proposed project ever been or is currently excluded, suspended, debarred, or otherwise deemed ineligible to participate in governmental healthcare, procurement, or other programs?

☐Yes ☒No **If yes, please explain in the Comments section below**

SECTION D – AUDIT STATUS

7. ☒Subrecipient is required to have an annual audit in accordance with OMB Circular A-133 or 2CFR200 as applicable.

Most recent fiscal year completed FY 2014

☐Subrecipient DOES NOT receive an annual audit in accordance with OMB Circular A-133 or 2CFR200 as applicable.

Subrecipient is a :

☒Non-profit entity (under federal funding threshold)
☐Foreign entity
☐For profit entity
☐Government entity
☐Other Explain:_____

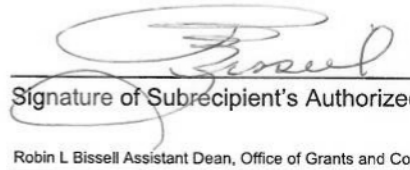
SECTION E – COMMENTS

current F&A rate agreement link - case.edu/research/media/caseedu/research/documents/Federal-IDC-acceptance-letter.pdf

current audit report link - http://www.case.edu/finadmin/controller/reporting.htm

APPROVED BY SUBRECIPIENT

The information, certifications and representations above have been read and approved by an authorized official of the Subrecipient named herein. The appropriate programmatic and administrative personnel involved in this application are aware of agency policy in regard to subawards and are prepared to establish the necessary inter-institutional agreements consistent with these policies. **Any work begun and/or expenses incurred prior to full execution of a subaward agreement are at the Subrecipient's own risk.**



Signature of Subrecipient's Authorized Official

12-2-2015

Date

Robin L Bissell Assistant Dean, Office of Grants and Contracts

Name and Title of Authorized Official

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SCOPE OF WORK – Case Western Reserve University

Dr. Aaron Goldenberg, Assistant Professor of Bioethics in the Department of Bioethics at Case Western Reserve University, provides expertise on ethical issues in clinical and public health genomics, biobanking, and pediatric ethics, and is experienced in both quantitative and qualitative research methods. A major focus of his work has been the ethical and social implications of collecting, storing, and using biological samples for future research.

Dr. Goldenberg will work with Dr. Kyle Brothers to lead the project team in the design and implementation of all study aims. More specifically, Dr. Goldenberg will take the primary lead in the qualitative data collection portions of Aims 1, and will co-lead aim 3, including oversight of the key informant interviews and discussion group processes. He will work with the larger research team to coordinate the recruitment and conduct of the in-depth interviews with Biorepository officials. He will also work with Dr. Brothers to code and analyze the interview/focus group data. Dr. Goldenberg will assist in the analysis of all project data and dissemination of findings. Dr. Goldenberg will help to assess and frame the ethical, normative, and policy implications of study results for newborn screening programs and the translation of results into recommendations for NBS program policy and practice. Finally, Dr. Goldenberg will participate in all monthly team meetings, yearly project meetings, and will help to translate findings for policy/practice recommendations.

University of Louisville Research Foundation, Inc.

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SECTION A – CONTACT INFORMATION

Subrecipient Legal Name: The University of North Carolina at Chapel Hill
Address: 104 Airport Dr. Ste. 2200 CB# 1350
City Chapel Hill State NC Zip 27599-1350
Phone: 919-962-3411 Email: resadminosr@unc.edu
Subrecipient PI Name: R. Jean Cadigan, PhD
Address where research will be performed 333 South Columbia Street, 343-A MacNider Hall
City Chapel Hill State NC Zip 27599-1350
Proposal Title: Addressing Ethical Challenges in Networked Biorepositories
Performance Period Begin Date: 07/01/2016 End Date: 06/30/2020
Subrecipient Funds Requested: $117,033 Subrecipient Congressional District NC-004
Subrecipient DUNS Number 608195277 Subrecipent EIN 56-600-1393
Is Subrecipient currently registered in the System for Award Management (SAM) yes
U of L's PI Name: Kyle B. Brothers, MD, PhD
Prime Sponsor: National Institutes of Health

SECTION B – REQUIRED PROPOSAL DOCUMENTS

Statement of Work
Budget and Budget Justification in agency required format
☐Cost Reimbursable ☐Fixed Price

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   ■Subrecipient's federally negotiated F&A rate for this type of work
   (If this box is checked please attach a copy of your current rate agreement or a URL link to the agreement)

   ☐Other rates
   (Please specify the basis on which the F&A rate has been calculated in Section E Comments below)

   ☐Not applicable
   (No F&A costs are requested by subrecipient)

2. Human Subjects ■Yes ☐No

   If **Yes**, please provide Institutional Assurance Number (FWA number) FWA-4801

3. Animal Subjects ☐Yes ■No

   If **Yes,** please provide IACUC Assurance Number _____

4. Cost-sharing ☐Yes ■No Amount: $_____

   (Cost-sharing amounts and justification should be included in the subrecipient's budget)

5. Conflict of Interest

Please check the appropriate response below

☐Not applicable because the project is not being funded by a sponsor that has adopted the federal financial disclosure requirements (AHA, etc.)

■Subrecipient Organization certifies that it has an active and enforced conflict of interest policy at least as rigorous as 42 CFR Part 50, Subpart F "Responsibility of Applicants for Promoting Objectivity in Research" and 45 CFR Part 94 "Responsible Prospective Contractors." Subrecipient also certifies that, to the best of Institution's knowledge, (1) all financial disclosures will be made related to the activities that may be funded by or through a resulting agreement, and required by its conflict of interest policy, and (2) all identified financial conflicts of interest have or will have been satisfactorily managed, reduced or eliminated in accordance with subrecipient's conflict of interest policy prior to the expenditures of any funds under any resultant agreement and within a manner sufficient to enable timely FCOI reporting.

☐Subrecipient does not have an active and/or enforced conflict of interest policy and agrees to follow UofL's policy. (UofL's policy can be found at http://www.louisville.edu/conflictofinterest)

By signing below, Subrecipient certifies that the required training related to Conflict of Interest will be completed by all key personnel prior to engaging in any research related to any federally funded award. For those following UofL's policy, the training may be accessed by contacting coioff@louisville.edu.

6. Debarment and Suspension

Has the institution/organization, or any principal investigator or other person proposed to provide services for the proposed project ever been or is currently excluded, suspended, debarred, or otherwise deemed ineligible to participate in governmental healthcare, procurement, or other programs?

☐Yes ■No **If yes, please explain in the Comments section below**

SECTION D – AUDIT STATUS

7. ■Subrecipient is required to have an annual audit in accordance with OMB Circular A-133 or 2CFR200 as applicable.

Most recent fiscal year completed FY 15

☐Subrecipient DOES NOT receive an annual audit in accordance with OMB Circular A-133 or 2CFR200 as applicable.

Subrecipient is a :
☐Non-profit entity (under federal funding threshold)
☐Foreign entity
☐For profit entity
■Government entity
☐Other Explain:_____

5. Conflict of Interest

Please check the appropriate response below

☐Not applicable because the project is not being funded by a sponsor that has adopted the federal financial disclosure requirements (AHA, etc.)

☒Subrecipient Organization certifies that it has an active and enforced conflict of interest policy at least as rigorous as 42 CFR Part 50, Subpart F "Responsibility of Applicants for Promoting Objectivity in Research" and 45 CFR Part 94 "Responsible Prospective Contractors." Subrecipient also certifies that, to the best of Institution's knowledge, (1) all financial disclosures will be made related to the activities that may be funded by or through a resulting agreement, and required by its conflict of interest policy, and (2) all identified financial conflicts of interest have or will have been satisfactorily managed, reduced or eliminated in accordance with subrecipient's conflict of interest policy prior to the expenditures of any funds under any resultant agreement and within a manner sufficient to enable timely FCOI reporting.

☐Subrecipient does not have an active and/or enforced conflict of interest policy and agrees to follow UofL's policy. (UofL's policy can be found at http://www.louisville.edu/conflictofinterest)

By signing below, Subrecipient certifies that the required training related to Conflict of Interest will be completed by all key personnel prior to engaging in any research related to any federally funded award. For those following UofL's policy, the training may be accessed by contacting coioff@louisville.edu.

6. Debarment and Suspension

Has the institution/organization, or any principal investigator or other person proposed to provide services for the proposed project ever been or is currently excluded, suspended, debarred, or otherwise deemed ineligible to participate in governmental healthcare, procurement, or other programs?

☐Yes ☒No **If yes, please explain in the Comments section below**

SECTION D – AUDIT STATUS

7. ☒Subrecipient is required to have an annual audit in accordance with OMB Circular A-133 or 2CFR200 as applicable.

Most recent fiscal year completed FY 14

☐Subrecipient DOES NOT receive an annual audit in accordance with OMB Circular A-133 or 2CFR200 as applicable.

Subrecipient is a :
☐Non-profit entity (under federal funding threshold)
☐Foreign entity
☐For profit entity
☒Government entity
☐Other Explain:_____

SECTION E – COMMENTS

APPROVED BY SUBRECIPIENT

The information, certifications and representations above have been read and approved by an authorized official of the Subrecipient named herein. The appropriate programmatic and administrative personnel involved in this application are aware of agency policy in regard to subawards and are prepared to establish the necessary inter-institutional agreements consistent with these policies. **Any work begun and/or expenses incurred prior to full execution of a subaward agreement are at the Subrecipient's own risk.**

Barbara Entwisle, PhD
Vice Chancellor for Research

Signature of Subrecipient's Authorized Official

12.2.15
Date

Barbara Entwisle, Vice Chancellor for Research
Name and Title of Authorized Official

The University of North Carolina at Chapel Hill, Office of Sponsored Research, 104 Airport Dr. Ste. 2200 CB# 1350
Address

Chapel Hill — City
NC — State
27599-1350 — Zip

919-9623411 — Phone
919-962-3352 — Fax
resadminosr@unc.edu — Email Address

SCOPE OF WORK – UNIVERSITY OF CAROLINA

Dr. Cadigan will work with Dr. Brothers and Dr. Goldenberg to ensure the successful completion of this project. She will bring her expertise in the ethical, legal and social implications of biobanking to examining the challenges inherent in networked biobanks. For the proposed project, Dr. Cadigan will use her prior experience searching online for U.S. biobanks to help create a systematic inventory of networked biorepositories in the United States and to develop and implement the key informant interviews with personnel and other stakeholders associated with these repositories (Aim 1). She will also serve as methodological lead on participant observations, including assisting with analysis of these data and conducting some of the participant observations of the biobanks (Aim 2). She will also work with the PI's to translate study findings into models for governance and practice (Aim 3). Lastly, she will provide expertise on the implications of these data for policy and practice within biorepositories and help to disseminate study findings.

University of Louisville Research Foundation, Inc.

SUBRECIPIENT COMMITMENT FORM

All subrecipients are required to complete the Subrecipient Commitment Form and provide the signature of the authorized organizational representative, prior to submission of proposal.

SECTION A – CONTACT INFORMATION

Subrecipient Legal Name: Mayo Clinic
Address: 200 First Street
City Rochester State MN Zip 55905-0001
Phone: 507.284.4715 Email: researchadmin@mayo.edu
Subrecipient PI Name: Dr.Richard Sharp
Address where research will be performed 200 First Street
City Rochester State MN Zip 55905-0001
Proposal Title: Addressing Ethical Challenges in Networked Biorepositories
Performance Period Begin Date: 7/1/2016 End Date: 6/30/2020
Subrecipient Funds Requested: $183,637 Subrecipient Congressional District MN-01
Subrecipient DUNS Number 006471700 Subrecipent EIN 1416011702A1
Is Subrecipient currently registered in the System for Award Management (SAM)
U of L's PI Name: Kyle B. Brothers, MD, PhD
Prime Sponsor: National Institutes of Health

SECTION B – REQUIRED PROPOSAL DOCUMENTS

Statement of Work
Budget and Budget Justification in agency required format
■Cost Reimbursable ☐Fixed Price

SECTION C – CERTIFICATIONS

1. Facilities and Administrative (F&A) costs included in this proposal have been calculated based on the following:

   ■Subrecipient's federally negotiated F&A rate for this type of work
   (If this box is checked please attach a copy of your current rate agreement or a URL link to the agreement)

   ☐Other rates
   (Please specify the basis on which the F&A rate has been calculated in Section E Comments below)

   ☐Not applicable
   (No F&A costs are requested by subrecipient)

2. Human Subjects ■Yes ☐No

   If **Yes**, please provide Institutional Assurance Number (FWA number) _____

3. Animal Subjects ☐Yes ■No

   If **Yes,** please provide IACUC Assurance Number _____

4. Cost-sharing ☐Yes ■No Amount: $_____

   (Cost-sharing amounts and justification should be included in the subrecipient's budget)

5. Conflict of Interest

Please check the appropriate response below

■ Not applicable because the project is not being funded by a sponsor that has adopted the federal financial disclosure requirements (AHA, etc.)

☐ Subrecipient Organization certifies that it has an active and enforced conflict of interest policy at least as rigorous as 42 CFR Part 50, Subpart F "Responsibility of Applicants for Promoting Objectivity in Research" and 45 CFR Part 94 "Responsible Prospective Contractors." Subrecipient also certifies that, to the best of Institution's knowledge, (1) all financial disclosures will be made related to the activities that may be funded by or through a resulting agreement, and required by its conflict of interest policy, and (2) all identified financial conflicts of interest have or will have been satisfactorily managed, reduced or eliminated in accordance with subrecipient's conflict of interest policy prior to the expenditures of any funds under any resultant agreement and within a manner sufficient to enable timely FCOI reporting.

☐ Subrecipient does not have an active and/or enforced conflict of interest policy and agrees to follow UofL's policy. (UofL's policy can be found at http://www.louisville.edu/conflictofinterest)

By signing below, Subrecipient certifies that the required training related to Conflict of Interest will be completed by all key personnel prior to engaging in any research related to any federally funded award. For those following UofL's policy, the training may be accessed by contacting coioff@louisville.edu.

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☐ Yes ■ No **If yes, please explain in the Comments section below**

SECTION D – AUDIT STATUS

7. ■ Subrecipient is required to have an annual audit in accordance with OMB Circular A-133 or 2CFR200 as applicable.

Most recent fiscal year completed FY 2014

☐ Subrecipient DOES NOT receive an annual audit in accordance with OMB Circular A-133 or 2CFR200 as applicable.

Subrecipient is a :

☐ Non-profit entity (under federal funding threshold)
☐ Foreign entity
☐ For profit entity
☐ Government entity
☐ Other Explain:_____

SECTION E – COMMENTS

APPROVED BY SUBRECIPIENT

The information, certifications and representations above have been read and approved by an authorized official of the Subrecipient named herein. The appropriate programmatic and administrative personnel involved in this application are aware of agency policy in regard to subawards and are prepared to establish the necessary inter-institutional agreements consistent with these policies. **Any work begun and/or expenses incurred prior to full execution of a subaward agreement are at the Subrecipient's own risk.**

Janice S. Grace acting for David M. Moertel

Signature of Subrecipient's Authorized Official

12/1/2015
Date

David M. Moertel
Name and Title of Authorized Official

200 First Street
Address

Rochester
City

MN
State

55905-0001
Zip

507.284.4715
Phone

507.284.4288
Fax

researchadmin@mayo.edu
Email Address

SCOPE OF WORK – MAYO CLINIC

Dr. Sharp will work with Dr. Brothers and Dr. Goldenberg to ensure the successful completion of this project. He will bring his extensive experience in the ethical, legal and social implications of biobanking to bear on this effort to examine the challenges inherent in networked biobanks. He will participate in data analysis and communication of research findings in published reports and at national conferences. Dr. Sharp will also assist Drs. Brothers and Goldenberg in developing recommendations for managing ethical, legal and social issues in biobank oversight and governance. Dr. Sharp will participate in weekly research meetings via videoconference and travel to Louisville for twice yearly in-person research meetings. In year 4, Dr. Sharp will assist with planning and leading a national symposium at which best practices for biorepository oversight will be developed.