UTAH RESOURCE FOR GENETIC & EPIDEMIOLOGIC RESEARCH (RGE)

RGE Guidance for creation of an IRB/RGE application to access the UPDB

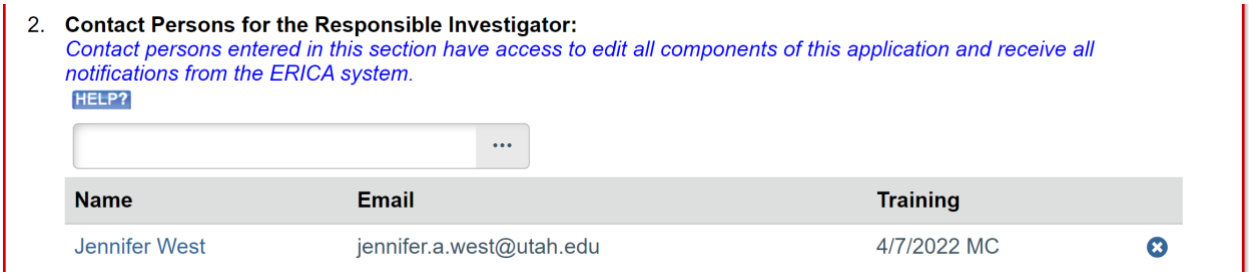
IRB Application

SECTION 1: Contacts and Title

Question 2:

Contacts should include anyone needing access to edit the IRB/RGE applications, such as a study or regulatory coordinator. Coinvestigators, or study team members engaged in the research, should be added in Section 2 under the specific site(s) with which they are affiliated.

**Tip: add Jennifer West, Sr Research Manager at RGE, as a contact person if you would like to allow her access to edit the application.*


2. **Contact Persons for the Responsible Investigator:**
Contact persons entered in this section have access to edit all components of this application and receive all notifications from the ERICA system.
HELP?

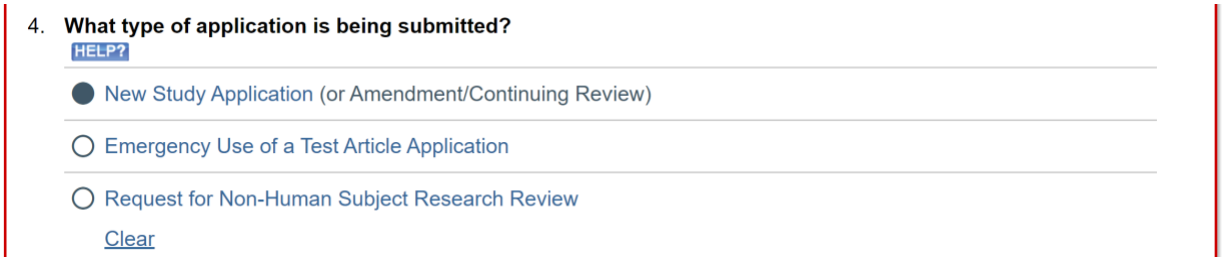
Name	Email	Training
Jennifer West	jennifer.a.west@utah.edu	4/7/2022 MC

Question 3:

Guests can view the whole application in ERICA but do not have access to edit.

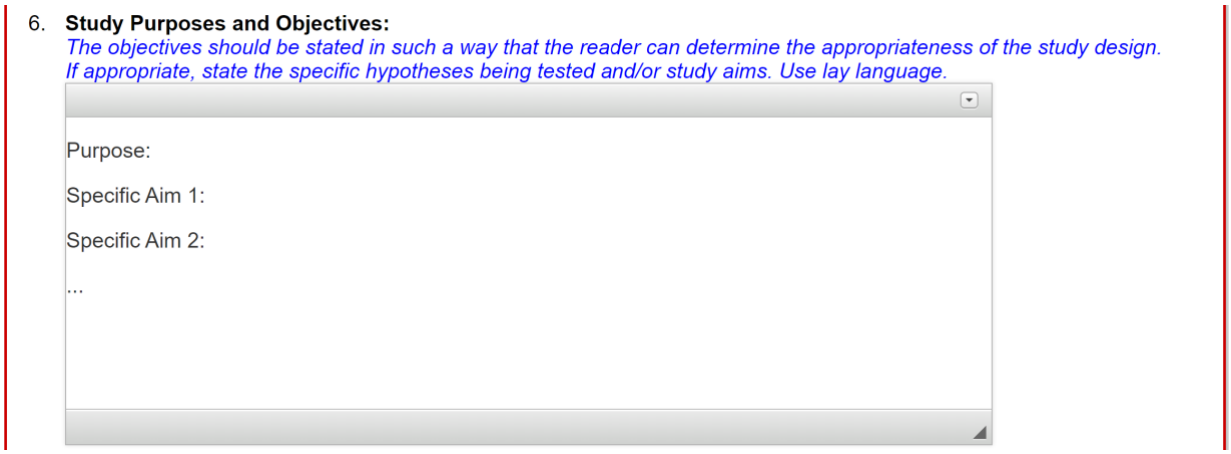
Question 4:

For studies using the Utah Population Database (UPDB), we recommend a New Study Application. Please only select a Request for Non-Human Subject Research Review after consulting with RGE staff. RGE applications would rarely, if ever, be Emergency Use of a Test Article Application.



Question 6:

The RGE Committee expects to see the overall purpose of the study and numbered specific aims. For consistency, these aims should be referenced by number in the study procedures and statistical methods detailed in Section 4, Questions 6 and 9.

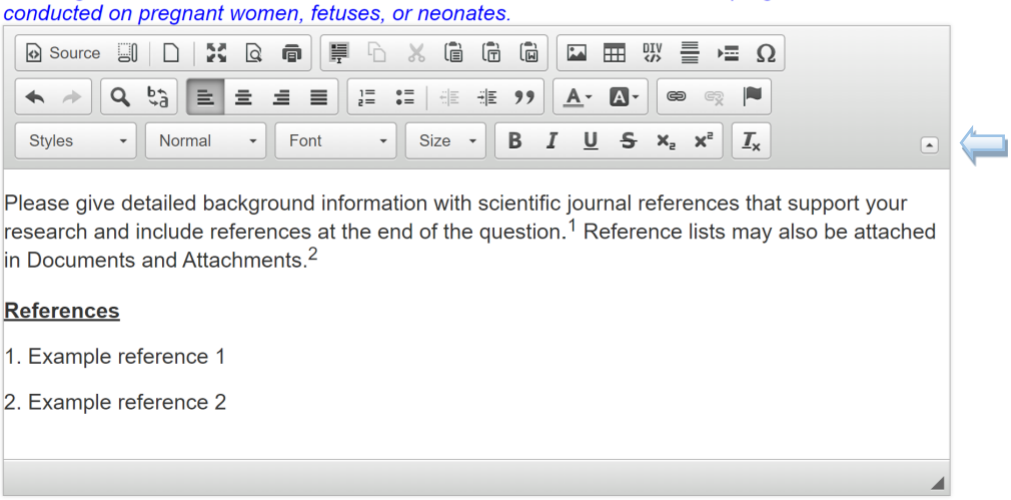


Question 8:

The RGE Committee requires detailed background information with scientific journal references that support your research and include references at the end of the response. Reference lists may also be attached in IRB Documents and Attachments.

**Tip: The top right arrow of the text box may be selected to allow for easier formatting.*

8. **Background and Introduction:**
Identify the research area being studied and provide a review of the literature that provides the basis for understanding the objectives of the study. This review should be written such that scientists outside the investigator's area of expertise can understand the issues involved. Any information about previous research related to this study involving animals and/or humans should be summarized. Include studies on pregnant animals if the research is conducted on pregnant women, fetuses, or neonates.



SECTION 2: Study Location and Sponsors

Question 1:

Members of the study team who are engaged in research and affiliated with the University of Utah (UU), Intermountain Primary Children's Hospital (PCH), the Veterans Affairs SLC Health Care System (VAMC), or Shriners Hospitals for Children Intermountain should be added under their specific study site(s) as either the Principal Investigator or site staff/sub-investigators.

Other study sites with their own IRB oversight can be added to the response for Section 8, Question 3. Study team members at other sites can be added in RGE Section 7.

If you include participant enrollment goals for consenting/observation/intervention at each site, the total of these sites should be included in the total number of participants listed in Section 3, Question 4.

**Tip: Requesting a Single IRB for a multi-site study triggers an additional review process with the UU IRB. We recommend contacting the IRB for further guidance.*

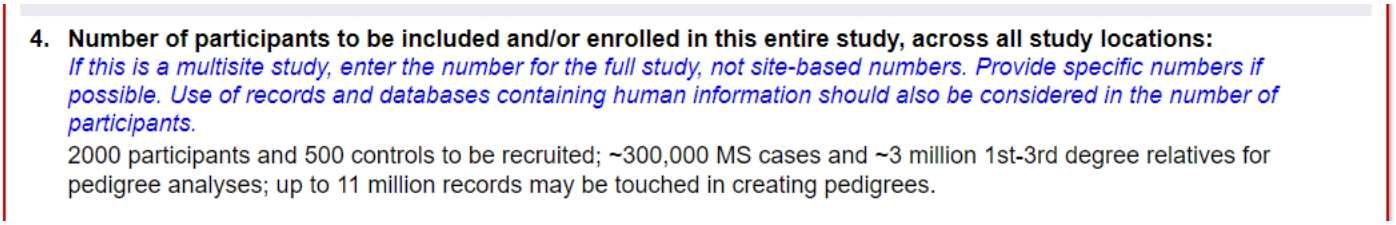
SECTION 3: Participants

Question 4:

Use of records and databases containing human information should be included in the number of participants.

Please include the number of cases/participants and the number of controls (if applicable). If requesting data for relatives, the approximate number of relatives should be included. The total number of participants across all study sites should include the number of participants expected for each site in IRB Section 2. Please make sure that numbers for participants are consistent throughout the IRB and RGE applications.

**Tip: The box for participant number is a text field, allowing for a description of the cohort if necessary.*



4. Number of participants to be included and/or enrolled in this entire study, across all study locations:
If this is a multisite study, enter the number for the full study, not site-based numbers. Provide specific numbers if possible. Use of records and databases containing human information should also be considered in the number of participants.
2000 participants and 500 controls to be recruited; ~300,000 MS cases and ~3 million 1st-3rd degree relatives for pedigree analyses; up to 11 million records may be touched in creating pedigrees.

Questions 5 & 6:

Please provide details for both cases/participants and controls (if applicable). Please include any ICD codes used for inclusion/exclusion criteria.

SECTION 4: Study Information

Question 3:

RGE recommends at least 5 years to account for approval, data collection, analyses, and publication.

Question 4a:

Please select “Written or electronic review” when using the UPDB. Other methods should be selected if applicable.

Question 4b:

Please provide a description of how participant selection, even if there is no recruitment.

If the study includes chart review, please clarify who on the study team is responsible for completing the chart review and at what point the review occurs. If there are plans to use the University of Utah Health (UUH) EDW’s Warthog tool, please reference it. You may use some of the language from the following paragraph if necessary:

The study will utilize the "Warthog" Targeted Chart Review Tool, a web-based self-service query tool that allows researchers to quickly run targeted text note audits using Boolean search terms to help answer questions about each patient in a specified cohort. The user can choose a cohort and search through text documents, retrieve the actual results of these queries, annotate notes on the fly, and export the resulting dataset. Warthog allows researchers to define inclusion/exclusion criteria based on structured as well as non-structured clinical data, annotate and perform quick quality assessment of clinical notes, find co-morbidities, etc. Warthog also allows researchers to create and answer questions on the fly, integrate their answers with the rest of the dataset, and maintain research data as tables in the application, rather than in spreadsheets. Finally, Warthog maintains a patient and clinic-note level logs of patient records that were accessed by researchers during the study, which allows detailed auditing.

If participants in the UUH EDW are linked to the UPDB, please include the following sentence:

The study will utilize the Master Patient Index that links the demographic records from the UUHSC EDW to the UPDB under IRB_00045234, “*Master Subject Index between the Utah Population Database and the University of Utah Health Sciences Center*.”

If participants in the Intermountain Health EDW are linked to the UPDB, please include the following sentence:

The study will utilize the Master Linkage File that links records from the Intermountain Health EDW to the UPDB under IRB_00023676, “Utah Population Database and Intermountain Linkage Project.”

Question 5:

Most studies using data from the UPDB use a Waiver of Consent if the study is not contacting participants for recruitment.

Question 6:

All procedures should be detailed here. Each specific aim listed in Section 1, Question 6 should be referenced here as applicable.

**Tip: UPDB data should be broadly and briefly described in this section and referenced by data source.*

6. **Describe all the procedures chronologically, from screening/enrollment through study closeout, which will be completed in the research project.**
The investigational activities, treatments, or procedures must be clearly detailed as to how and when they will be performed. For clinical studies, this includes study visits, drug treatments, randomization, and the procedures that are part of standard of care. For clinical studies, a distinction should be made between the procedures for treatment evaluation versus procedures for safety evaluation. Treatment endpoints must be defined as well as interim procedures for dealing with adverse events.

Specific Aim 1

Cohort will be assembled as described in Question 4b using the UUH EDW and data held in the UPDB, including death certificates and Utah Department of Health and Human Services (UDHHS) healthcare facility data (inpatient, ambulatory surgery, and emergency department data). Basic demographic details will be pulled. Birth date and diagnosis dates provided to study team will be month/year only.

Specific Aim 2

Comorbid conditions will be pulled for participants, controls, and family members using the UUH EDW and data held in the UPDB, including death certificates, Utah Cancer Registry (UCR) records, and UDHHS healthcare facility datasets (inpatient, ambulatory surgery, and emergency department data).

Specific Aim 3

Distance to healthcare facility will be calculated by UPDB staff using addresses from birth certificates, death certificates, driver license records, and voter registration records. Addresses will not be released to the study team.

If UPDB Kinship Analysis Tools are used in the selection of high risk pedigrees to examine familiality, please use the following statement:

Kinship Analysis Tools (University of Utah, Salt Lake City, Utah) software was developed to estimate the magnitude of familial risk using the familial standardized incidence ratio (FSIR) based on this genealogy database (Kerber,1995). Use of the FSIR requires a large genealogic database and a linked population-based disease registry. The FSIR is based on the ratio of the observed to the expected incidence of a disease occurring in a pedigree, multiplied by the kinship-weighted coefficient (Kerber,1995). This statistic measures the excess relative risk attributable to familial factors. The UPDB is population based, and the linkage to the UPDB meets the criteria for analysis using the FSIR.

Kerber, RA. Method for Calculating Risk Associated with Family History of a Disease (1995). Genetic Epidemiology 12:291-301.

Full dates (birth, death, or diagnosis) and identifiable geographic variables must include scientific justification. If time of events is necessary for the study, the RGE Committee prefers month/year and the UPDB staff can provide sequence of events within a given month. The UPDB staff can also provide time intervals if necessary.

All ICD/CPT codes may be provided in either this response or in the applicable RGE Sections (3C-3F). A code template document is available to facilitate importing and querying requested codes by the UPDB staff.

Question 9:

Please provide a thorough response for planned statistical methods that addresses all specific aims.

**Tip: Staff at UPDB can help with statistical analysis plans.*

Request for Waiver of Consent:

Most studies using data from the UPDB use a Waiver of Consent if the study is not contacting participants for recruitment. Please include a list of all identifiers from the RGE application. If data are being requested from PCH, please include UPDB IDs as identifiers.

Consent Form:

If your study is obtaining consent to link participants to the UPDB, please include the following language in the Consent Document:

"We may link your information to the Utah Population Database (UPDB). The UPDB is a University of Utah research resource and is an extensive research database of demographic information linked to other data, such as family history and medical information. This linkage will allow information about you and your family to be updated and evaluated for this study in the future."

SECTION 5: Data Monitoring

Question 1:

RGE requires that access to data is the minimum necessary to accomplish the research. Please select: “The collection of information about participants is limited to the amount necessary to achieve the aims of the research, so that no unneeded information is being collected.” Other precautions should be selected if applicable.

Question 2:

RGE requires the following to be selected for all studies: “Storing research data on password protected computers or in locked cabinets or offices.”

If the study includes identifiers, please select: “Participant identifiers will be stored separately from the coded, participant data.”

If the study is using Safe Harbor de-identified data, please select: “Complete de-identification of study data.”

Please review definitions of potentially (personally) identifying information, Limited Data Sets, and Safe Harbor de-identified data sets.

If the study is sharing data outside the University of Utah, please select: “All data that will be transferred or transported outside of the institution will be encrypted.”

Other precautions should be selected if applicable.

Question 6:

RGE recommends annual monitoring of the study data and documentation. More frequent monitoring may be appropriate for some studies.

SECTION 6: Risks and Benefits

Question 1:

Please include in your response that there are some potential privacy risks, such as breach of data, re-identification of research participants, etc.

SECTION 7: HIPAA & the Covered Entity

Question 1a:

Please review definitions of potentially (personally) identifying information, Limited Data Sets, and Safe Harbor de-identified data sets. If your data set includes more identifiers than a Limited Data Set, please select a Waiver of Authorization.

**Tip: A Waiver of Authorization is required for all studies requesting PCH Intermountain Health data. Please include UPDB IDs as identifying information in the Waiver.*

Question 1b:

Investigators are encouraged to use the existing links between the UPDB and the EDWs when UUH medical record numbers (MRNs) or Intermountain Health Enterprise Master Member Index (EMMI) numbers are available. If MRNs or EMMI numbers are not available, it may be necessary to link project demographic records directly to the UPDB. The UPDB is NOT part of the covered entity. Please review the IRB guidance on Consent and Authorization Requirements for studies using the UPDB.

SECTION 8: Resources and Responsibilities

Question 1:

The IRB recommends that you provide a short paragraph outlining the qualifications of the study staff. You do not need to name investigators.

Question 3:

Investigators not affiliated with the University of Utah should be listed by name and institution and you should clearly state the level of data to be accessed (De-identified, Limited, or Identifiable data). You should also state if a Material Transfer Agreement (MTA) or Data Transfer Agreement (DTA) is signed or in process. Please indicate if investigators are covered by their own IRB.

ANCILLARY APPLICATION (RGE Application):

SECTION 2: Data Security

Question 2:

The RGE Committee prefers that study teams use VPN remote access to either HCI servers or Center for High Performance Computing – Protected Environment (CHPC-PE). If you need to use a data storage location that is not listed, please click the "ADD" button to enter your location and complete with requested details. Please note that storage location(s) not previously approved by RGE may require additional time for review and approval.

If you are storing data obtained through RGE on a server and you also download data to a local computer to run software for statistical analysis, pedigree drawing, etc., please add each local computer as a storage location. You may group local computers with the same data security measures into one entry, as long as all buildings and room numbers where the computers are located are included in the response.

**Tip: Any questions regarding this section can be directed to the RGE Data Security Analyst at RGE.Security@utah.edu.*

Question 3:

For disposition of data, RGE generally recommends that investigators select "Data will be returned to RGE for long-term storage and all data stored on project computers will be destroyed after the data are returned to RGE." Please review requirements of your institution and/or sponsor.

RGE recommends that the anticipated end date be 5-10 years from the study start date. The RGE Committee may require justification for anticipated end dates greater than 10 years.

**Tip: The anticipated end date should be consistent with the study length entered in IRB Section 4, Question 3.*

SECTIONS 3A-3G:

In these sections you are required to select the data sources and elements necessary for your study. These selections vary greatly depending on the study. Specific data elements and scientific justification are required responses. RGE requires that access to data is the minimum necessary to accomplish the research.

SECTION 3A: Demographic & Family Relationships

Demographic Information

- Birth date and death date information should be selected in demographics, not from birth and death certificates.
- Full dates (birth, death, or diagnosis) must have scientific justification. If time of event is necessary for the study, RGE prefers month/year and the UPDB staff can provide sequence of events within a given month. The UPDB staff can also provide time intervals if necessary. Please note that requesting months and years is classified as a Limited Data Set.
- Most studies need last date known living in Utah / follow-up date for full analyses.
- RGE recommends keeping the date format requests consistent. For example, if you are requesting birth month/year, please request last month/year known living in Utah.

Family Relationship Information

- Please use this section to identify the information the study needs about family relationships.

Genealogy Record Details

- Data elements should only be selected if the study needs baptism and endowment dates as a proxy measure of healthy lifestyle and/or social integration.

SECTION 3B: Vital Records

Birth Certificate Details

- Please review the available fields before completing this section.
- To contact potential research participants using birth certificates, the Office of Vital Records and Statistics sends letters to individuals meeting inclusion criteria. For more information, please contact Linda Wininger.

Death Certificate Details

- Please review the available fields before completing this section.
- If your study is using death certificates, most analyses require cause of death and manner of death.
- To contact potential research participants using death certificates, the Office of Vital Records and Statistics sends letters to individuals meeting inclusion criteria. For more information, please contact Linda Wininger.

SECTION 3C: Cancer

Utah Cancer Registry (UCR)

- UPDB includes a subset of UCR data:
    - Primary site
    - Histology
    - Stage
    - Grade
    - Survival Months
    - Behavior
    - Laterality
    - Address information for geospatial analysis
- For additional UCR data, including treatment data, please contact the UCR Research Manager.
- Please review UCR information for researchers.
- Requests for UCR data are generally based on SEER Site Recodes.

- To contact potential research participants using UCR records, UCR staff sends letters to individuals meeting inclusion criteria. Only those individuals who agree to be contacted about the study are provided to the study team. For more information, please contact the UCR Research Manager.

SECTION 3D: DHS, UBDN, URADD, DLD, Voter, Census

DHS

- Please contact Jennifer West for more information.

UBDN

- Please see Utah Birth Defect Network for more information.
- To contact potential research participants using UBDN records, UBDN sends letters to individuals meeting inclusion criteria. For more information, please contact Amy Nance.

URADD

- Please see Utah Registry for Autism and Developmental Disabilities for more information.
- To contact potential research participants using URADD records, URADD sends letters to individuals meeting inclusion criteria. For more information, please contact Colin Kingsbury.

DLD (Driver License Data), Voter Registration, and U.S. Census Data for Utah

- Please see UPDB-Other Records for more information.

SECTION 3E: APCD & Healthcare Facility

All Payer Claims Data (APCD)

- The Department of Health and Human Services (DHHS) requires submission of a Variable Request Worksheet for all APCD requests.

- The completed Variable Request Worksheet must be attached in this section for review by the RGE Committee and the DHHS Data Use Subcommittee.
- Access to APCD Medicaid data requires submission of a separate application that may be attached in this section.
- Limited Medicare data are available from APCD.
- Please note that APCD data cannot be used to identify individuals for contact.

Healthcare Facility Data (Hospital Inpatient Discharge Data, Ambulatory/Outpatient Surgery Data, and Emergency Department Data)

- DHHS requires submission of a Variable Request Worksheet for all Healthcare Facility Data (HFD) requests.
- The completed Variable Request Worksheet must be attached under each requested data source (inpatient, ambulatory surgery, and/or emergency department) for review by the RGE Committee and the DHHS Data Use Subcommittee.
- Please note that HFD data cannot be used to identify individuals for contact.

SECTION 3F: UU Health & Intermountain Health

UU Health Master Subject Index/Enterprise Data Warehouse

- For questions about access to UU Health, please contact DataScienceServices@hsc.utah.edu.

Intermountain Health Master Linkage File/Enterprise Data Warehouse

- Intermountain Health (IH) requires a separate application to the Intermountain IRB through the iRIS system for access to data for individuals 18 and older. You need a Principal Investigator authorized to submit an IH IRB application. The IH IRB application does not need to be approved but should at least be started by the time the ERICA application is submitted.
- The IH collaborator should be listed in Section 8.3 of the IRB application and as Other Study Personnel in RGE Section 7 if the collaborator is not affiliated with the University of Utah.
- All new projects must have an initial approval from the IH Scientific/Operations Committee. Please contact Jennifer West for an introduction to the IH Scientific/Operations Committee.

- Studies using IH data may need a Material/Data Transfer Agreement.

SECTION 3G: Geographic Groupings

Please contact Jennifer West with questions about geographic groupings.

SECTION 5A: Identifying Info Requested from UPDB

Question 1a:

This section is intended to summarize the identifying information requested directly from the UPDB.

Question 1c:

If you need assistance with the approximate number of records to be accessed, please contact Jennifer West.

Question 1d:

The RGE Committee evaluates the period of access to identifiable information based on the project design. The time period should be kept to the minimum necessary.

SECTION 5B: Identifying Info from Data Sources Linked to UPDB

Question 1a:

This section is intended to summarize the identifying information requested from sources linked to the UPDB. This could include identifiers used for chart review of electronic health records, recruitment, or identifying information collected by the research project.

SECTION 6: Linking Project Records

Investigators are encouraged to use the existing links between the UPDB and the EDWs when UUH medical record numbers (MRNs) or Intermountain Healthcare Enterprise Master Member Index (EMMI) numbers are available. If MRNs or EMMI numbers are not available, it may be

necessary to link project demographic records directly to the UPDB. Please review the charges for record linking and other available UPDB Services.

The UPDB is NOT part of the covered entity. Please review the IRB guidance on Consent and Authorization Requirements for studies using the UPDB.

Please contact Jennifer West if you intend to link project records to the UPDB.

SECTION 7: Project Personnel

Investigators and Other Study Personnel

- Please click on "Update" for each individual and provide the following information:
  - Study-specific activities/duties.
    - Please include detailed responses for specific activities or duties on this project. Avoid generic responses based on roles or job, such as co-investigator, clinician, study coordinator or lab assistant. [Identifying the Intermountain Health principal investigator or data analyst is acceptable.]
    - Here are some common activities and duties:
      - obtain informed consent
      - collect biospecimens from research participants
      - process lab samples
      - perform lab experiments
      - clinical exams
      - clinical phenotyping
      - refer patients
      - review patient charts or health records
      - IT/computer support
      - oversee/supervise study staff
      - collect/enter data
      - analyze data
      - evaluate data analysis results
      - write manuscripts
  - Access to RGE data (aggregated, de-identified, or potentially identifiable).
  - Current version of the RGE confidentiality agreement if one is not already attached in ERICA.
    - Electronic signatures are only accepted through DocuSign. Please send name(s) and email address(es) of individuals who need a confidentiality agreement through DocuSign to Jennifer West.

- Human Subjects Training certification.
  - Training certifications that have been reported to the IRB are displayed in the last column. The date represents the last date the training was completed. CITI and GCP trainings expire every 3 years. If trainings need to be updated in ERICA, please submit CITI completion certificates to the IRB. The letters represent the modules.
    - Training module codes
      - CITI – Social and Behavioral (S)
      - CITI - (Bio)Medical (M)
      - NIH (N)
      - CITI - VA (V)
      - UUIRB (U)
      - Exemption Umbrella (E)
      - Central (Single) IRB (C)
      - Good Clinical Practice (G)
  - For other study personnel with access to individual level data, RGE accepts documentation of Human Subjects or privacy training. Documentation can be attached to the study team member in ERICA in RGE Section 7. Documentation does not need to be attached if the training dates and codes are already present. Please contact Jennifer West with questions.
- Any relationships with for-profit companies relevant to the research.
  - Please review RGE's policy on for-profit companies.

SECTION 8:

Responsible Investigator

RGE requires the Responsible Investigator to sign a Statement of Assurances and Data Security Assurances. Electronic signatures are accepted only through DocuSign. Please contact Jennifer West for DocuSign forms.

Principal Investigator (if different from Responsible Investigator)

If this is a multisite study, the Principal Investigator at each site should also sign a Statement of Assurances and Data Security Assurances.

Material Transfer Agreements (MTA) and/or Data Transfer Agreements (DTA)

If the study team includes investigators who access individual level data and who are not affiliated with the University of Utah, a Material/Data Transfer Agreement must be executed through the University of Utah Partners for Innovation, Ventures, Outreach & Technology (PIVOT) or the Office of Sponsored Projects (OSP). This includes investigators at other institutions who access data on University of Utah servers.

**Tip: The RGE Committee expects that necessary MTA(s)/DTA(s) and/or additional necessary IRB applications (e.g., Intermountain Health) have been initiated at the time of application submission.*

Other RGE Documents

You may attach supporting documents for your RGE application in this section. Documents requiring IRB approval should be attached in Documents and Attachments in the IRB application. Consent forms, recruitment materials, surveys/questionnaires, reference lists, and CVs should still be uploaded in the IRB Documents and Attachments Section.

You may attach IRB approval documentation from other institutions for this project. Other examples of RGE-specific documents may include flow charts, diagrams, figures, variable spreadsheets, etc.