NCATS ENACT

Cohort Discovery, Research on De-identified Aggregated Data (RDAD) and Enclave Research

Human Subjects Research Determinations

Purpose and objectives:

The goals of the National Clinical and Translational Science Award (NCATS) Evolving Next-Generation Accrual to Clinical Trials (ENACT) project, formerly Accrual to Clinical Trials (ACT), are to enable the federated network made up of sites from the Clinical and Translational Science Award (CTSA) Consortium, to accelerate clinical research through Cohort Discovery and Research on De-identified Aggregated Data (RDAD) and to utilize the patient-level data collected across the federated network in safe**,** secure, Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant environment. ENACT takes advantage of the widespread implementation of electronic health records (EHRs) and the well-established extensive informatics and regulatory expertise within the CTSA Consortium.

A. Cohort Discovery and RDAD

ENACT involves cohort discovery across the federated network. All participating ENACT sites have an independent underlying data repository containing select patient information. Data types available for query include patient demographics, diagnoses, clinical procedures, visit dates, lab results, and some medication data. The data is harmonized to a common representation (e.g., common values for patient race-ethnicity) across all sites to assure valid patient counts.

ENACT's harmonized network can effectively identify the number of patients per site who meet specific query criteria. These de-identified patient counts can be used to determine a) whether there is sufficient sample size across the federated network to address a research question b) the distribution of the patient population across the network.

1. **Procedures used to gather information:** The authorized user with site-specific approved access logs into the secure web-client portal. Authorized users are required to sign a User Terms of Data Access agreement prior to accessing the network.
2. **Description of data gathered:** The disease specific queries return a de-identified patient count for each network site or an aggregated de-identified dataset.
3. **Human Subjects Research:** ENACT Cohort Discovery and RDAD are not considered human subjects research.

   For an activity to constitute human subjects research it must meet the definition of research and involve human subjects.

   i. RESEARCH is defined as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 46.102(d)].

- Cohort Discovery and RDAD may be considered a systematic investigation. A complex detailed plan being implemented to carry out the case queries.
- Cohort Discovery is not designed to develop or contribute to universally applicable knowledge. It is designed to identify potential research sites by providing a de-identified patient count from each network site based on the case query.
- Cohort Discovery does not constitute research.
- RDAD is likely designed to develop or contribute to universally applicable knowledge.
- RDAD constitutes research.

ii. HUMAN SUBJECT is defined as a living individual about whom an investigator conducting research: (1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens [45 CFR 46.102(e)(1)].

- The authorized user will not intervene or interact with individuals to obtain information or biospecimens to use, study or analyze.
- The authorized user will not obtain identifiable private information or identifiable biospecimen to use, study or analyze.
- Neither Cohort Discovery nor RDAD involve human subjects.

B. Enclave Research

ENACT provides access to patient-identifiable data generated from the harmonized network to address important health questions. The dataset is maintained in a HIPAA-compliant, "safe" cloud environment for a specified, limited time with restricted access. The dataset cannot be copied, printed, or transferred.

1. **Procedures used to gather information:** The authorized user with site-specific approved access logs into the secure web-client portal. Authorized users are required to sign a User Terms of Data Access agreement prior to accessing the network.
2. **Description of data gathered:** Specific patient-identifiable data are sent to a secure HIPAA-compliant cloud environment for analysis. Access to the data is controlled and time to conduct data analysis is limited.
3. **Human Subjects Research:** ENACT Enclave Research may be considered human subjects research

   For an activity to constitute human subjects research it must meet the definition of research and involve human subjects.

   i. RESEARCH is defined as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 46.102(d)].

- Enclave Research is considered a systematic investigation. A detailed plan to address specific question(s) will be designed and a query will be implemented to generate a dataset for evaluation with the intent to develop or contribute to generalizable knowledge.
- Enclave Research activities are designed to develop or contribute to universally applicable knowledge. The intent is to study important health questions using data maintained across the federated network
- Enclave Research constitutes research.

ii. HUMAN SUBJECT is defined as a living individual about whom an investigator conducting research: (1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens [45 CFR 46.102(e)(1)].
    - If the dataset contains identifiable private information about living patients, and the authorized user will obtain, use, study, or analyze the identifiable private information the activity involves human subjects.

If the ENACT Enclave Research dataset constitutes research and involves human subjects, the activity would qualify as Human Subjects Research. IRB approval is required.

Expedited, Category 5: Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

A Waiver of Informed Consent and a Waiver of HIPAA Research Authorization are required. Requirements for IRB reliance between ENACT sites for performing human subject research using data from those sites will depend on the nature of the research and the types of data that will be imported into enclaves, such as de-identified datasets or datasets that include PHI.