

The CETT Program's Guidelines for Data Collection and Sharing

Summary of Action

The overarching goal of the CETT program is to stimulate the sound development of clinically available tests for rare disorders while leveraging the opportunity to improve knowledge and understanding of the disorder. It is hoped that this two-pronged approach will lead to improved clinical care and better management outcomes for those with rare genetic conditions.

CETT Program participants contribute clinical testing results to a common public database to improve understanding of the disorders being tested and the interpretation of results (benign, pathogenic, or VOUS) associated with clinical phenotype information collected at the time testing is requested.

Although the samples are originally collected solely for clinical care, they can be made available for research purposes in a Health Insurance Portability and Accountability Act (HIPAA)-compliant manner to stimulate additional discovery.

If the future research use of the data is consistent with the October 16, 2008, Office for Human Research Protections (OHRP) "Guidance on Research Involving Coded Private Information or Biological Specimens" [<http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf>], the National Institutes of Health (NIH) can make clinical data available for research purposes and publicly display these data through the databases maintained by the National Center for Biotechnology Information (NCBI). Of primary importance is ensuring that patients and guardians are appropriately informed **and** have ample education about their rights to opt out of this use.

The CETT program supports these activities by:

Sponsoring the development of appropriate educational materials for clinicians, patients, and genetics professionals on the strengths and limitations of the specific test ordered, the opt-out process for data removal from public databases, and a description of a patient's access to clinical research.

Providing electronic clinical data collection forms that contain the opt-out feature and description of later-date opt-out processes.

Providing a HIPAA-compliant, secure data collection and storage facility to receive and manage the data from the electronic forms.

Encouraging the inclusion of the opt-out processes to accompany the report of testing results.

CETT Program Policy

To facilitate the widest access for these data, CETT collaborative teams agree to the following principles:

1. CETT Collaborative Teams will follow de-identification procedures as defined within the NIH Genome-Wide Association Studies (GWAS) Policy [http://grants.nih.gov/grants/gwas/gwas_ptc.pdf].
2. CETT Collaborative Teams will develop procedures and educational/informational documents, consistent with the previous points, for notification to the tested subjects or their legally authorized representative that:

De-identified clinical data will be submitted and stored at the NIH for future distribution for research purposes

- b) Educational/informational materials are available about future research (including the potential benefits and risks of research) to patients or their surrogates at the point of clinical care and subsequently to public databases (see <http://cettprogram.org/resources.aspx#3Cett>)
- c) There is a process for individuals to decide that their clinical data will not be submitted to NIH for research sharing, that is, an “opt-out” procedure, and for their individual data to be removed from future distributions should they decide to opt out at a later date. The materials for each of the participating laboratories will be shared and discussed with the CETT staff education coordinator as they are developed.

All educational and informational materials and laboratory results reports from each of the CETT Collaborative Teams will contain language similar to the opt-out model provided below:

Sample language for the clinical submission form:

The requested clinical information is important for interpreting your patient’s test result. Collected clinical information and test results will be included in a HIPAA-compliant public database as part of the National Institute of Health’s effort to improve diagnostic testing and understanding of this disorder. Access to de-identified information allows researchers, clinicians, and other stakeholders to find relationships between genetic changes and clinical symptoms. Confidentiality of each sample will be maintained. Patients may have their data withdrawn from database use at any time by contacting our laboratory at XXX-XXX-XXXX. Refusal for inclusion in public de-identified databases may be indicated by checking this box. _____ If the box is not checked the data will be anonymized and used.

Sample language for the educational materials:

Patient/health professional version

What happens to the information and the sample from my child’s test?

Understanding your child’s test results: Your physician will include a form about your child’s clinical symptoms with the blood sample. This information will help the laboratory understand your child’s test result. The University of Chicago Genetic Services Laboratory keeps patient samples indefinitely for quality control and other internal purposes.

Understanding the condition: After removing your child's name and all identifying information, your child's clinical symptom information and test results are kept in a public database. Confidentiality of your child's information is maintained. Information from many children with this condition will increase what we know about it and the genetic test. Researchers may use this information to find relationships between genetic changes and clinical symptoms.

Your options: You may choose to refuse (opt out) to include your child's information in public databases by telling your physician to check the box on the clinical form at the time the sample is collected. If the box is not marked the anonymized data will be used. You may withdraw the data from present and future inclusion at anytime by contacting our laboratory at xxx-xxx-xxxx. You may call the laboratory if you have any questions.

Geneticist version

Use and retention of patient clinical information and test samples

Patients' clinical information will be used by the laboratory to interpret test results. The laboratory will keep a blood sample for test validation and other purposes. The clinical information will have all identifying information removed ("de-identified") and be kept, along with the test results, in public databases. Researchers may use this information to increase what we know about the condition and find relationships between genetic changes and clinical symptoms.

Patients can opt out of having their (or their child's) information in the public databases at any time. To opt out at the time the test is ordered, the physician will need to check the appropriate box on the test order form. If the box is not checked, data will be anonymized and used. If patients wish to remove their data from this use at any other time, they can contact the laboratory directly at XXX-XXX-XXXX.

Sample language for inclusion with the report:

LABORATORY NAME retains patient samples indefinitely for validation, education purposes, and/or research. Submitted clinical information and test results are included in a HIPAA-compliant public database as part of the National Institute of Health's effort to improve diagnostic testing and understanding of this disorder. Access to de-identified information allows researchers, clinicians, and other stakeholders to find relationships between genetic changes and clinical symptoms. Confidentiality of each sample is maintained. Patients may have their sample removed from storage and withdraw their data from present and future database use by contacting our laboratory at XXX-XXX-XXXX.

3. Genetic data that CETT Collaborative Teams will contribute to NIH will include:

The name of the test

The testing method used

The reference sequence AND build version of the gene used for test interpretation

The Online Mendelian Inheritance in Man (OMIM) number of the disorder

The OMIM numbers of any known allelic variants using current [HGVS nomenclature](#)

f)

The testing results including

a.

The Human Genome Variation Society (HGVS) name of any variants identified

b.

Assessment of the clinical consequence based on the American College of Medical Genetics guidelines on reporting Ultra-Rare Diseases 7.1.1.

g)

The laboratory's threshold protocols used to report findings (thresholds). Tests with both positive and negative findings will be included.

h)

All Pub Med ids and other sources used as references in the test interpretation for annotation

Privacy Safeguards for Publicly Shared Data

All data samples will include the name of the testing laboratory and a laboratory-provided random code for the individual sample. No HIPAA identifiers for the tested individual or information regarding the ordering physician will be included in the data submission. The omission of these fields is hard coded in the electronic form. However, laboratories also retain the right to remove any fields OR individuals whose identification they believe cannot be adequately safeguarded under HIPAA. The NCBI will never be provided with the keys to the codes.

Data Collection Processes at the Clinical Laboratory

1.

Clinical information will be requested at the time of sample submission. An online clinical information submission form will be available to the clinician as part of the test-ordering process. The form will include information about the opt-out processes that can remove data from current deposits for public use and will refer to the additional information available from (2) below.

2.

Information and opt-out procedures about the submission of de-identified molecular results and clinical information being contributed to public databases will be posted on:

a.

Clinical testing laboratory Web sites along with test-ordering information.

b.

All educational and informational materials associated with the specific test.

c.

When possible, the patient advocate Web site, list serve, and/or other mechanisms of communication the patient advocate collaborative partner uses to maintain contact with the patient community.

3.

The clinical testing laboratory will discuss samples with a positive finding or a finding of unknown significance (VOUS) with the ordering clinician and additional clinical information may be requested from the clinician. Use of the online submission form will be an option.

4.

The policies guiding the posting of de-identified information will be discussed directly with the ordering clinician when contact is made for item #3. The availability of an opt-out option will be fully described for the clinician to appropriately advise the patient or the patient's guardian.

1.

Tested samples with a negative result will be returned to the clinician without direct contact by the laboratory although information about the opt-out procedures AND access to clinical research will accompany the negative report to the ordering clinician (see #6, below).

All test reports will be accompanied by a statement about the submission of de-identified molecular and clinical information to NCBI and subsequent distribution for research purposes along with information about how to opt out.

All test reports will include a statement about the desire to collect both clinical and molecular data along with instructions for how to provide such information online.

De-identified, coded data will be securely transferred to NCBI under appropriate data security protocols.

Data Use at NCBI for Restricted Access Users

1.

Authorized researchers present data access requests, including a brief research proposal, through the NCBI's database of genotypes and phenotypes (dbGaP) data access process (as for other array comparative genomic hybridization [aCGH] or GWAS studies in dbGaP).

Researchers publish research results from the data. Published work forms the basis of future clinical decisions by the community per usual professional practices.

In the event a researcher wishes to locate specific individuals whose samples are in the database to invite them to participate in an Institutional Review Board (IRB)-approved research protocol, the researcher must (and can only) contact the submitting testing laboratory. In turn, the testing laboratory can contact the ordering physician and convey the request. The ordering physician can then determine whether they feel it is appropriate to contact the patient with the request. The researcher is never given the patient's contact information. The researcher's contact information is given to the patient, mediated by the ordering physician. If the patient decides to participate in the research study, they contact the researcher directly and the informed consent process for the research protocol is conducted at that time.

There is no expectation of return of research results to the patient.

However, as with other dbGaP studies, a researcher may contact the testing laboratory directly. The testing laboratory can contact the ordering physician whose patient carried the variant of interest to the researcher if the testing laboratory is satisfied that the research is *bona fide*. The ordering physician is then responsible for directly contacting the patient, identifying the proposed research contact, and providing the researcher's contact information to the patient if the ordering physician agrees such communication is warranted.

Submission Data Flow

Data Request Flow – to dbGaP and to request research follow up