

1. Are there any types of genetic tests that should not be included in the GTR?

Genetic tests with clinical application in the practice of medical genetics should be included. Genetic tests which are marketed directly to the public should NOT be included, particularly those which purport to provide risk assessment for complex disorders or recommend lifestyle interventions based on test results. Genetic testing for ancestry or parentage determination or forensic purposes should not be included. Zygosity testing should be included as this test is sometimes clinically useful.

2. What are the potential uses of the GTR for (1) researchers, (2) patients/consumers, (3) health care providers, (4) clinical laboratory professionals, (5) payers, (6) genetic testing entities/data submitters, (7) policy makers, and (8) electronic health records?

1. **Researchers: genotype/phenotype correlation, contacting affected individuals and their providers, literature review, identifying other studies/reports in progress**
2. **Patients/consumers: contacting other affected individuals through providers, contacting experts, enrolling in clinical trials or case series, learning about the condition, learning about available resources**
3. **Health care providers: genotype/phenotype correlation, diagnostic information, management and surveillance guidelines, aiding with literature review, contacting experts, genetic mechanisms and pathogenesis information, genetic counseling information**
4. **Clinical laboratory professionals: interpreting results, pricing other tests, contacting other laboratories, literature review, clinical information**
5. **Payers: shopping around to select preferred laboratories, contacting laboratories**
6. **Genetic testing entities/Data submitters: standard data entry, obtaining clinical information, shopping around, assessing test sensitivity, comparing techniques used by various labs**
7. **Policy makers: Education, standardization of genetic testing and counseling offered thereafter**
8. **Electronic health records: Electronic link from patient record (electronic lab report) to relevant page**

3. What data elements are critical to include for use by (1) researchers, (2) patients/consumers, (3) health care providers, (4) clinical laboratory professionals, (5) payers, (6) genetic testing entities/data submitters, (7) policy makers, and (8) electronic health records?

1. **Genetic loci information, pathophysiology functions, latest literature updates**
2. **Resources for support groups, patient support information associated with particular birth defects, centers of excellence, local provider access**
3. **All of the above plus clinical summary and all of below as well as key clinical features, differential diagnosis, diagnosis CPT codes**
4. **Testing: who does it and where, sensitivity, mutation database updated, is the testing complete, does it include whole gene as well as intragenic deletion/duplication testing**

5. **Testing sensitivity, indications for testing family relatives,**
 6. **Same as 4 plus links to other allelic disorders**
 7. **CPT coding for disease AND testing information**
 8. **Electronic links to paperwork, ability to complete on line, and send simultaneously to originating and destination institution**
4. What are the potential benefits and risks associated with facilitating public access to information about the:
- a. **Availability and accessibility of genetic tests?**
 - i. **Risks**
 1. **Public may order or request incorrect or inappropriate testing**
 2. **Risk of testing minors may be increased (loss of autonomy)**
 3. **Genetic clinics may be overwhelmed with questions/visits from individuals (patients and providers) who had/ordered incorrect testing, inappropriate testing, or test results (both positive and negative) that they do not understand. This time will be taken away from families that truly need genetic counseling/genetic evaluation.**
 4. **When non-genetic providers order testing, patients may not get the genetic counseling and full genetic evaluation that is needed.**
 5. **Informed consent may not be obtained.**
 - ii. **Benefits**
 1. **Better understanding among all providers as well as the public to the vast number of genetic conditions that testing is available for.**
 2. **Potentially, could increase the awareness and needs of the genetic tests that are not currently available.**
 3. **Potentially, could provide the grounds of a competitive environment for labs offering testing. Thus making genetic testing more affordable for families.**
 4. **Brings awareness of genetic testing/genetic conditions and the need for funding/research.**
 - b. **Scientific basis and validity of genetic tests?**
 - i. **Risks**
 1. **Laboratories and possibly genetic clinics may have to deal with answering many calls from the public about what the information means.**

ii. **Benefits**

1. **Empowers public**
2. **Brings awareness to Insurance companies regarding the need to provide coverage for genetic testing.**
3. **Brings awareness of genetic testing/genetic conditions and the need for funding/research.**

c. **Utility of genetic tests?**

i. **Risks**

1. **Laboratories and possibly genetic clinics may have to deal with answering many calls from the public about what the information means.**

ii. **Benefits**

1. **Empowers public**
2. **May help non-genetic providers to more appropriately recommend testing.**
3. **Brings awareness to insurance companies regarding the need to provide coverage for genetic testing.**

d. **Brings awareness of genetic testing/genetic conditions and the need for funding/research.**

5. What is the best way to distinguish between data fields left blank because of an absence of data/evidence and those left blank for other reasons? **If left blank because data is unavailable I would suggest entering “unknown.”** How important is this distinction for enhancing transparency, including for the purpose of identifying research opportunities? **It is important to indicate ‘unknown’ when collecting data so that improvements can be made in how the data was collected in the first place...so that the right questions are asked to get the information needed.**
6. To adequately and accurately describe a genetic test, which of the following data elements should be included in the GTR? Are there other data elements that should be added? What information is necessary to represent adequately each data element?
 - a. Contact information (e.g., location, name of the laboratory director, and contact information for the laboratory performing the test)
 - b. Laboratory certifications (e.g., Federal or State certification of the laboratory that performs the test)
 - c. Name of the test (e.g., common test name, commercial name, marketing materials about the test and/or genetic testing entity, standard identifier (e.g. CPT codes, LOINCⁱⁱ))

- d. Regulatory clearances (e.g., for tests reviewed by the Food and Drug Administration, the 510(k) or premarket approval (PMA) number)
- e. Intended use of the test (e.g., diagnosis, screening, drug response)
- f. Recommended patient population **Indications for testing family members**
- g. Limitations of the test (e.g., is the test validated only for certain subpopulations or limited to particular uses such as screening but not diagnostic testing?)
- h. Test methodology
- i. Analyte(s)—What is being measured in the test (e.g., genetic sequence)
- j. Specimen requirements (e.g., blood, saliva, tissue samples, amniotic fluid)
- k. Availability (e.g., is the submitter the sole provider of the test or are there multiple providers?)
- l. Accessibility (e.g., accessible through a health provider, public health mandate, and/or direct-to-consumer)
- m. Performance characteristicsⁱ
 - i. Analytical sensitivity
 - ii. Analytical specificity
 - iii. Accuracy
 - iv. Precision
 - v. Reportable range of test results
 - vi. Reference range
 - vii. Method used for proficiency testing (e.g., formal PT program, alternative assessment) and score **is testing “complete”, i.e. gene and intragenic del/dup testing**
- n. Clinical validityⁱ
 - i. Clinical sensitivity
 - ii. Clinical specificity
 - iii. Positive and negative predictive value
 - iv. Prevalence
 - v. Penetrance
 - vi. Modifiers
- o. Utility (e.g., clinical and/or personal utility) or outcomes
 - i. Benefits
 - ii. Harms
 - iii. Added value, compared with current management without genetic testing
- p. Cost (e.g., price of the test, health insurance coverage)

7. What types of information might be difficult for test providers to submit and why?

8. What are the advantages and disadvantages of collecting and providing information on the molecular basis of genetic tests, such as detailed information about what the test detects and the specific methods employed? **Advantages: knowing the specific methods used, such as methylation-sensitive PCR, quantitative PCR, or MLPA aids in choosing laboratories to send testing as well as in interpretation of test results once they are available. Knowing whether deletion/duplication analysis is available, for example, helps in choosing which laboratories to send sequencing tests. Then the ordering provider then knows adding on deletion/duplication analysis after negative sequencing results is available. Knowing detection rates is also helpful when selecting which laboratory to send testing. Disadvantages: I can think of no disadvantages for providing the specific methods employed nor for including what the tests detect. Inclusion of these details aid in both selecting laboratories for molecular testing and in interpretation of results.**
9. In addition to the data elements, would it be helpful to reference other resources, and if so, which ones (e.g., published studies, recommendations from expert panels such as the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children, U.S. Preventive Services Task Force, or Evaluation of Genomic Applications in Practice and Prevention Working Group)? **Yes I think it would be helpful to reference expert panel recommendations as were listed in the question and also including care guidelines that may have positions on benefits and risks related to genetic testing from ie ACMG or ACOG etc. I would also suggest offering resources for the general public to contact for more information ie. National Society of Genetic Counselors or AMBG for a provider in their area.**
10. As the GTR is being designed, what are the important processes to consider to make the submission of data as easy as possible for the data provider (e.g., the capability of linking to information that has been submitted to other agencies, such as the Food and Drug Administration and the Centers for Medicare and Medicaid Services, or a master file of data common to particular tests)? JB
11. Which potential benefits and risks would be most likely to affect the decisions of researchers, test developers, and manufacturers on whether to submit data to the GTR, and what factors will best encourage submission of complete and accurate data? MAF
12. What are the most effective methods to ensure continued stakeholder input into the maintenance of the GTR?

- 1. Make it user-friendly:**
-Fast (server capacity)
-Self-explanatory data entry and retrieval
-Few fields
-Easy login
-Well-organized

- direct link to labs and order forms
- 2. Make the data immediately and freely available
- 3. Allow cost and service (molecular technique) comparisons on the site
- 4. Require frequent updates
- 5. All clinical synopses should be peer-reviewed
- 6. Allow incorporation of photographs and other media
- 7. Standard format
- 8. Free
- 9. Unique identifiers to prevent duplication
- 10. ABMG certification required for data entry

13. For what purpose(s) would you use the Registry to support your professional efforts? MEP

14. Are there any other issues that NIH should consider in the development of the GTR? MEP

<http://www.nih.gov/news/health/mar2010/od-18.htm>

<http://www.ncbi.nlm.nih.gov/gtr/qa/>