



NIH Request for Information on Genetic Testing Registry  
Submitted by Genetic Alliance  
[www.geneticalliance.org](http://www.geneticalliance.org)

August 2, 2010

### **Executive Summary**

Genetic Alliance strongly believe the NIH proposal for a voluntary Genetic Testing Registry (GTR) is an imperative step in the right direction towards increased transparency and accuracy of the information available on genetic tests to consumers and all stakeholders. It will advance the appropriate use of genetic tests by consumers to improve health. It is our recommendation that, in conjunction with major proposals we have made to FDA regarding the oversight of genetic testing, that the registry be made mandatory.

The GTR should make the inclusion of genetic tests that indicate something about health a priority; such tests and their results have the most potential to positively impact patients' lives. The GTR empowers patients/consumers to be proactive in their healthcare, and the transparency of quality, validity, and utility data is an essential stride towards the further integration of genetic tests into clinical practice. The registration of tests increases industry self-regulation by increasing standards; however, until the genetic testing registry is mandatory, information will remain incomplete at the expense of consumers and the healthcare system. We firmly believe that the genetic testing registry must be mandatory to maximize its legitimacy and power.

The significance of each category of information provided by the GTR varies by stakeholder, yet the ability for all stakeholders to access the same data promotes transparency and increases informed decision-making across all parties. The GTR will supply researchers with data on the availability and quality of a test to reduce duplication of tests, while providing insight into tests that require improvements. Patient/consumer accessibility to the GTR promotes an active role for patients in their healthcare, as they become better informed to play a key role in deciding which tests are most relevant to their health needs. With patients and healthcare providers having access to the same information, there will be common grounds for discussion and healthcare providers will be better prepared to discuss test results. Further, payers will also be able to use the information to accelerate technology assessment. Genetic testing entities/data submitters will have the opportunity to review data from other labs and use this to improve the quality of tests, which will raise industry standards.

T: 202.966.5557  
F: 202.966.8553

4301 Connecticut Ave., NW  
Suite 404  
Washington, DC 20008-2369

[info@geneticalliance.org](mailto:info@geneticalliance.org)  
[www.geneticalliance.org](http://www.geneticalliance.org)

Categories of data that affect clinical decision-making are of highest importance for the GTR. Contact information for the laboratory providing the test, including location of laboratory, website, telephone number, and e-mail addresses, is critical to ensure access to the laboratory so that questions are answered and errors are addressed in a timely manner. Testing companies should provide the test name as well as providing details about specific variants detected by the test. The purpose of the test must be articulated and descriptions must clearly distinguish between tests that are to be used for screening, diagnostic, predictive, carrier status, and pharmacogenomic purposes. In addition, known limitations of the tests for specific subpopulations and any known lack of treatment options should be stated. Information on the availability of tests will increase efficiency, as patients/consumers and providers can determine the best method and location to obtain a particular test. Accessibility of a test should be made clear, and whether or not a patient needs to go through a health provider or can order the test direct-to-consumer should be stated in the registry. Data on the analytic and clinical validity are imperative to consumers, health care providers, and payers in determining the appropriateness of receiving a test, given its validity, cost, and impact on clinical decisions. Reported ranges of test results will at least reveal the confidence intervals of each test. The cost of the test will inform consumer and payer decisions, as well as promote competition among testing companies. Some data elements will be less pertinent to consumers, but very important to researchers and laboratories. Providing information about laboratory certifications, regulatory clearances, test methodology, analytes, specimen requirements, performance characteristics, and method used for proficiency testing will allow researchers and laboratories to remain competitive in the market.

Test developers can easily provide most of the information already discussed. Clinical utility, on the other hand, requires consideration that is largely qualitative and its meaning varies from individual to individual. We believe that a mechanism that allows providers and individuals to evaluate the utility of a genetic test and to aggregate evidence can help define clinical utility in the GTR. Clinical utility refers to the ability of a genetic test to inform clinical decision making, yet test results may have utility for patients beyond treatment that are important to consider. Therefore, it is not appropriate to hinder access if a patient may see value in a test beyond its clinical implications. Groups, such as EGAPP, have taken on the task of determining the clinical utility of particular tests; however, EGAPP has only evaluated a handful of tests in its five years. This suggests, and perhaps begs for, the need for an alternate method for a timely evaluation of the utility of a test. Further, the GTR may allow other recommendation categories than those currently employed by EGAPP, for example, a 'use with discretion' category. Allowing individuals to determine utility for themselves is one solution with many benefits. An evaluation tool that reinforces the other data provided in the GTR and asks questions about ethics, cost-effectiveness, benefits, harms, and consequences of getting the test will provide patients with insight for direct-to-consumer tests, and patients by facilitating involvement in clinical decision-making.

The more information made available by the GTR, the better; it promotes an open discussion among stakeholders that increases the efficiency and effectiveness of genetic testing. However, it is important to note that the inability to provide data pieces should not preclude a test from being added to the registry. In many cases, information, such as the positive and negative predictive value, clinical specificity, clinical sensitivity, prevalence, and penetrance, will not be easily obtainable, particularly for rare genetic conditions. Such tests should note what

information is not available and provide specific reasons to ensure that consumers and/or clinicians adequately consider the risks of pursuing the test.

The system must require registrants to update test information as information becomes available so the registry remains valid and up-to-date. This process could be facilitated by a required annual review of registered tests. It is important that penalties for not updating the GTR do not negatively impact patients/consumers. Removing a test from the market as a penalty would hinder a patient's ability to obtain a test that benefits his or her health. The updating process may remain open to loopholes until the registry is mandated. While the testing registry is not mandatory, test developers will lack an incentive to constantly and consistently update test information. Making data entry into the registry as easy as possible will be important for encouraging compliance. With that being said, there is a copious amount of information for testing companies to maintain, and a system that links data collected by other agencies, for example the FDA and CMS, can streamline the process. Additionally, the Genomic Applications in Practice and Prevention Network (GAPPNet) which aims to accelerate and streamline the use of validated genomic knowledge and applications into clinical and public health practice, is establishing a network of genetic tests in the research and development phase and collecting data on these tests. The data collected by GAPPNet can be transferred to the GTR database once the test is ready for use by the general population. This will reduce the burden of maintaining the GTR to researchers, and facilitate the uptake of the GTR. Additionally, electronic health records can feed data into the registry and facilitate the continuous collection of information on each test.

As genetic testing becomes more frequently used in clinical practice, it is essential that all stakeholders can depend on a reliable source of data on the use, validity, and utility of all available genetic tests, whether offered direct-to-consumer or prescribed by a clinician. This system will increase access and quality of genetic tests by offering a place for all stakeholders to compare information on available genetic tests. The genetic testing registry asks a great deal of test developers therefore, it is imperative that the system is usable. This requires taking advantage of systems already in place and encouraging providers and consumer involvement in the evaluation of utility. Until the genetic testing registry is mandatory, the system will remain incomplete and lack utility itself. Further, the development of technology systems to gather data from test developers and laboratories is critical. Required registration of tests in genetic testing registry facilitates the necessary collaborations by all parties to improve genetic tests and how they are used in practice.

Thank you for the opportunity to provide comments on this important development. Genetic Alliance will continue to remain involved in the development and implementation of the genetic testing registry to maximize its benefits to the entire healthcare ecosystem.

Specific comments on the questions outlined in the RFI:

### **III. Request for Comments**

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

- No. Initially one could make an argument that only health related tests should be included, excluding, for example, a genetic test for curly hair. But even as more associations emerge it will be critical to include all genetic tests.

#### **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) policymakers, and (8) electronic health records?**

- By providing comprehensive information about all genetic tests in a single registry, the GTR will make the ordering of genetic tests much easier for healthcare professionals. Up to date information on the data elements provided in question six will decrease the time burden HCPs experience from having to search multiple disjointed sites or even call genetic testing companies directly. With an online format, healthcare professionals can access this information wherever and whenever they need it to provide the best medical care.
- Patients/consumers will be able to be more engaged in their own health care by providing the GTR as a public resource. If roll-overs or general descriptions of the terminology utilized in the data fields are provided, patients will be able to increase their genetic literacy. The GTR will allow patients to ask questions of their healthcare providers, which will promote more conversation around the topic of genetic testing. Additionally, they will be able to see if it's necessary to order the test in partnership with their physician or if it can be ordered independent of a provider.

#### **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) policymakers, and (8) electronic health records?**

- The data elements mentioned in question six are critical to include for health care providers and patients/consumers.
- Categories of data that affect clinical decision-making are of highest importance for the GTR
- Keeping track of data generated by the tests will be important for researchers. For multiplex testing especially, when you are not necessarily ordering a test to receive the results for everything that it can detect.

#### **4. What are the potential benefits and risks associated with facilitating public access to information about the:**

##### **a. Availability and accessibility of genetic tests?**

###### **Benefit:**

- Understand if they have more than one company to choose from, which may not always be presented in clinic
- Understand that if the test is denied through one company by their insurer, they may have other options
- Know how they can pursue certain testing
- Patient/consumer accessibility to the GTR promotes an active role for patients in their healthcare, as they become better informed to play a key role in deciding which tests are most relevant to their health needs.
- May help to decrease incorrect orders by healthcare providers

###### **Risks:**

- It will be said that consumers cannot process this information effectively. We believe that an ecosystem will develop around the registry to help consumers understand what they are seeing. Genetic Alliance and its GAPPNet project with partners CDC and the University of Michigan will be creating systems that help consumers understand what is in GTR, and also determine what associated tools are needed to make it most useful.

##### **b. Scientific basis and validity of genetic tests?**

###### **Benefit:**

- Patients and their families often become the experts on their condition. As open access to information expands, patients will become increasingly interested in asking questions and understanding more of the details about genetic tests.

###### **Risk:**

- Tests in early development, with limited evidence for clinical validity could be said to be harmful. We contents that they will be exposed as such in the registry and increase consumer confidence in the industry and utility for providers.

##### **c. Utility of genetic tests?**

###### **Benefit:**

- Consumers will be able to ask questions about these tests of their health care providers
- Can use this information to appeal denial of genetic testing by insurance companies

**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? How important is this distinction for enhancing transparency, including for the purpose of identifying research opportunities?**

- It is very important to distinguish what fields are left blank to not having data versus not filling it in for other reasons. For the former, perhaps include a checkbox that says “No data currently available.”
- Depending on how the registry is set up, empty fields could be color coded based on the reason why the information is missing.
- Some information that may be applicable for quantitative tests may be non-applicable for qualitative tests so this should be clear as well, both when asking laboratories to provide information and when presenting it in the GTR.

**6. To describe adequately and accurately 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?**

- We believe all of these are important, with the caveat that when they are missing, there needs to be a reason indicated – i.e., information not available vs. information withheld or forgotten.

**a. Contact information (e.g., location, name of the laboratory director, and contact information for the laboratory performing the test)**

- Including email, web site, and if they have genetic counselors or genetic information specialists on staff

**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, LOINC ii))**

**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)**

- Reflex testing
- The intended use field may need to be open to allow for the selection of more than one option. Some tests may to serve as a screening test in some cases and confirm a diagnosis in others.

**f. Recommended patient population**

- We see this as an area of special interest to the rare disease community and to consumers in general. This will be augmented by special populations themselves.

**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?)**

- Any known lack of treatment options should be stated

**h. Test methodology**

- Detailed information about methodology may be proprietary.

**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?)**

- This would have to be determined by an automated function in the GTR.
- Need to determine what it means to be a “sole provider” of a test, whether it’s based on methodology or what it detects or both.

**l. Accessibility (e.g., accessible through a health provider, public health mandate, and/or direct-to-consumer)**

**m. Performance characteristics**

- 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**

**n. Clinical validity**

- 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)**
- r. Special notes (e.g. test run twice a week, preferences for shipping, etc.)**
- s. Amount of time until results will be available**
- t. How results will be disclosed (e.g., phone, fax, mail, email, online portal)**
- u. Clearly delineate those tests that are available on a research only basis and those that are available on a clinical basis**
- v. Data field that shows when the entry was originally created and when it was last updated**

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

- Utility might be difficult for the laboratories to provide because the utility of some tests may really vary depending on the patient's situation and the laboratory does not get that information.
- Performance characteristics may be difficult for tests that are for rare conditions because they don't have a large enough pool of samples to be able to provide numbers and answers for the questions around clinical and analytic validity.
- The inability to provide data pieces should not preclude a test from being added to the registry. In many cases, information, such as the positive and negative predictive value, clinical specificity, clinical sensitivity, prevalence, and penetrance, will not be easily obtainable, particularly for rare genetic conditions

**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?**

- Advantage: The name of a test is not always a clear indicator of what variants are specifically detected by this method.
- Disadvantages: It will be important to consider that certain tests may generate information that is not reasonable to report based on the indication for testing. Multiplex testing is a good example of this. It may be disadvantageous to include details of detection for these tests but it should be said that information generated by these tests should not be disregarded. Development of registries to maintain records of the

extraneous information generated by these tests will be critical for the development of systems to manage unexpected and incidental findings.

**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)?**

- The GTR should include links to published recommendations from professional societies, SACGHS, USPSTF, EGAPP, and other federal agencies. These recommendations should be provided on the pages of the appropriate tests, as well as on a single page of all recommendations. This will provide another great service to those involved in genetic testing by being able to access all of the recommendations in a single place.
- Consider linking to GeneReviews and GeneClinics, as those are valuable resources to the clinical community as well. Since those resources are now managed by NCBI, a seamless integration between those resources and the GTR will be greatly appreciated by the clinical community.
- Because this work is being done through NCBI, it'd be great to pull through articles related to research that has utilized the tests as well.
- Information regarding certifications and regulatory clearances and what they entail would increase transparency. It should be able to answer questions like "What does it mean that a laboratory is CLIA certified?" "Why would I order an FDA approved test over one that is not?"

**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)?**

- In order to make the submission of data as easy as possible, researchers and companies should be able to link to data that has already been submitted to other agencies. Additionally, the data should be subdivided into categories, so that it is easy to navigate to the data fields one is looking for when changes need to be made to particular data items. To the extent that it's possible, data fields should consist of check boxes or drop down boxes to decrease the amount of free text that needs to be included. This will not only make it easier to submit data but also make it easier for the users of the GTR to have a clear sense of when tests have similar criteria in common instead of extrapolating from free test answers.
- GAPPNet is establishing a network of genetic tests in the research and development phase and collecting data on these tests. The data collected by GAPPNet can be transferred to the GTR database once the test is ready for use by the general population
- Many labs have their own electronic databases that have information about the tests that they provide. If possible, the GTR should be able to link into these as well.

**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?**

- Researchers, test developers, and manufacturers may hesitate to submit their data to the GTR because for the first time, healthcare professionals, patients, and the general public will be able to compare tests directly using easily accessible data. The individuals involved in the discovery, development, and production of genetic tests worry that the time and resources needed to populate the GTR will negatively impact their other priorities. Therefore, the GTR will need to be developed in a manner that automatically pulls in data that is available in other sources, decreasing the amount of information that must be entered in multiple databases. By providing data about their tests in the GTR, new, smaller companies will have another avenue to educate the community about the availability of their test(s).
- The difficulties of linking the information systems in the labs, particularly laboratories that are offering a larger number of tests, will probably be a significant hurdle.

**12. What are the most effective methods to ensure continued stakeholder input into the maintenance of the GTR?**

- The GTR staff must report a summary of the comments received from the community and what steps it will take to implement suggestions and address concerns raised in both the short and long term. The NIH should, however, understand the special interests of those making the comments, and make intelligent decisions about which to accept, modify and reject. This includes these comments.
- GTR staff must continue to provide a means for open communication with interested stakeholders. Responses provided will need to be tailored to the questions and comments raised in the inquiry, and not follow the templates responses that have been shared with the community questioning the GTR so far.
- Throughout the rollout of the GTR, the GTR staff should solicit feedback from stakeholders through opportunities for open, honest communication at scientific meetings. One aspect that they could comment on could be the ease of navigation of the GTR, which will no doubt be of great concern.
- The GTR should consider an advisory committee of various stakeholders representing wide interests. These could include geneticists, genetic counselors, informatics specialists, consumers, laboratorians, and researchers.
- An additional suggestion would be to constitute an advisory board that consists of representatives of the stakeholder community internal and external to NIH:

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

- Genetic Alliance looks forward to the GTR as a resource for our community. We expect to integrate it into the GAPPNet effort that we are coordinating. In addition, we will make it part of our Disease InfoSearch resource. Further, we will provide access to it in our work with Gateway to Rare and Neglected Disease Therapeutics (GRANDRx).

Finally, in our work to understand appropriate oversight for genetic testing, we look forward to the registry becoming mandatory and integrated as a first level or class for a new FDA designation – advanced diagnostics.

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

- While the initial phase of data submission to the GTR is voluntary, we strongly advocate for submission being required.
- Because of fear and questions related to genetic discrimination, the GTR should provide links to information about GINA and other applicable laws such as [ginahelp.org](http://ginahelp.org)
- Consider the implementation of an automated system, where companies and researchers have to provide updates to their listing at least annually. A balance must be found between burdening the companies with requests for updates and making sure the information is current for the benefit of the user.
- Be transparent about who is working on the GTR staff. Some of the stakeholders think that there are no clinically-trained staff involved and think this is a major downside of the GTR.
- The need for an alternate method for a timely evaluation of the utility of a test. Allowing individuals to determine utility for themselves is one solution with many benefits. An evaluation tool that reinforces the other data provided in the GTR and asks questions about ethics, cost-effectiveness, benefits, harms, and consequences of getting the test will provide patients with insight for direct-to-consumer tests, and patients by facilitating involvement in clinical decision-making

Sharon F. Terry, MA  
President and CEO  
[sterry@geneticalliance.org](mailto:sterry@geneticalliance.org)

Genetic Alliance  
4301 Connecticut Avenue NW - Suite 404  
Washington DC 20008-2304  
Telephone: 202.966.5557  
Fax: 202.966.8553  
[www.geneticalliance.org](http://www.geneticalliance.org)