



**Response from:**

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**The NIH is seeking input and advice on the following items:**

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

All tests that make some sort of utility claim should be included, also those that are not overtly connected to health (e.g. Child IQ, sports performance, baldness, etc). One aim of the GTR should be to create confidence in genetic testing and help protect against false or exaggerated claims. To have one single reliable (worldwide I hope) location where anyone, scientist, medic, consumer, journalist, business partner, etc can go to would be very helpful. If we end up with fragmented GTRs for different areas it will be less useful. Although run by NIH the criteria should include more than just strictly health applications

Further, the GTR should go beyond “testing” – it should cover all services, especially interpretation services which will become the main area of “personal genetics” as the testing part itself becomes routine.

**2. What are the potential uses of the GTR for**

- a. **Researchers** – find collaborators and suppliers. ELSI researchers will benefit from a central mass of information
- b. **Patients/consumers** – find reputable suppliers, education
- c. **Health care providers** – find reputable suppliers, education
- d. **Clinical laboratory professionals** – deposit information on own services, find suppliers / partners / customers, information on competitors(!)
- e. **Payers** – education and information to help make decisions on utility and reimbursement. Maybe they will learn more about the opportunities for prevention and will be kept aware of specific ethical/legal problems regarding health insurance
- f. **Genetic testing entities/data submitters** – information on available tests & services. Depending on how the database is structured it may offer the possibility of collaborative data sharing
- g. **Policy makers** – education, awareness of services available, consumer attitudes (if consumer input is allowed)

- h. **Electronic health records** – depends on the scope of the GTR and the database structure but there is a potentially very interesting opportunity to explore using standard language to enable genetic interpretation information to be incorporated into EHR.

**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?**

Genes, SNPs, dbSNP rs numbers, claims that are made with clear links to how they arrived at the claims/advice/interpretations from the scientific literature. Full bibliography. It would be useful to have independent assessments of each service as well – either by professionals (like a journal editorial board and peer review) or via moderated comment, or both

- 4. What are the potential benefits and risks associated with facilitating public access to information about the:**
- a. **Availability and accessibility of genetic tests?**
  - b. **Scientific basis and validity of genetic tests?**
  - c. **Utility of genetic tests?**

**Benefits:**

A central reliable source of tests available, with some independent professional assessments of validity and utility will encourage consumer confidence, will allow the choice of relevant tests and will hopefully steer consumers away from untrustworthy services. The information will also help to decide whether healthcare professional involvement may be useful either before or after testing. Healthcare professionals also count as consumers, such a resource would be very helpful to determine what tests to use and how to integrate with clinical decision making.

**Risks:**

a) Depends on how the GTR is set up. If not presented well it could increase confusion and damage the uptake of genetics in health. If public access is to be given it will need to be pitched at the various levels expected to use it, from uninformed layperson to genetics expert. It has to be more consumer friendly than <http://www.ncbi.nlm.nih.gov/> (not a criticism of NCBI, which is obviously excellent for professionals!).

b) The way the tests/services are presented, it has to be clear that simply being present on the registry is not an endorsement of the claims of the services offered.

c) A dedicated genetic testing registry is required but it should not foster so-called “genetic exceptionalism”. It should not encourage that idea that common genetic variations associated with traits are deterministic of disease independent of environmental variables

- 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?**

Best way is to state the reason for the absence of data. There may be no data, it may be restricted for personal or commercial confidentiality, it may be conditionally available, e.g. for research, etc.

- 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, LOINC<sup>ii</sup>))**
- 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**
- 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 characteristics<sup>i</sup>**
  - 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<sup>i</sup>**
  - 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)**

All of the above. Accuracy of testing via historical data of control samples, allele frequencies stratified for population etc. Clinical validity to include odds ratios, relative risks, lifetime risks – in a way that is understandable by lay people. Modifiers are important, almost all risk assessments will be modified by environmental parameters and it is important that this is clear.

Clinical and personal utility is sometimes straightforward but often is hard to quantify. This section needs to be explanatory, figures and percentages will not be very helpful most of the time

Other info: most tests will involve the use of software in their interpretation. It will be important to give as much information as possible on this. For risk calculations the precise methods need to be supplied, for interpretations of gene x gene and gene x environment interactions and the advice generated, descriptions of the algorithms should be supplied. Also the validation procedures of the software should be detailed – how it is controlled to be sure that the correct advice/results are given for the various input results. What level of standard was used in the creation of the software and in the programming of the rules?

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

While some software details should be given it will clearly be difficult to submit full algorithms etc, and other commercial secrets.

**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?**

No further comments

**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)?**

No comment

- 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)?**

No comment

- 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?**

Submission to the GTR should become a “required” step by any service provider. Not necessarily enforced but essential in the sense that if it is not there then it is suspect. Service providers would benefit from a GTR logo that they could use on their websites to link to their own submissions. It should become a commercial risk not to submit to the GTR. With the help of press, social media, conferences etc, the GTR should be widely publicised, easily accessible (and easy to understand/navigate, especially for journalists)

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

Keep it up to date. Ensure an adequate budget, keep it publicised, regularly report on results, benefits, effects, etc of the GTR including in scientific papers

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

Submitting tests and services, reviewing other tests and services, commenting on them (preferably on the GTR site itself).

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

As mentioned above, a review mechanism would be useful. A sort of peer review as used by scientific journals, with editorial board etc. There should be areas for comments by other users, maybe via comments or a wiki type system. Most service providers will have nothing to fear but there are already too many very dubious services and the GTR can help weed them out either via their absence from the registry or by critical analysis on the site. In addition it would be useful to have space for comment of tests which are available but which are not on the registry. Many of these will likely be dubious and are absent to avoid scrutiny – they should be

scrutinised anyway. Others may well be valuable but have not been submitted for various reasons (time & resources, ignorance of the registry, etc)

The most valuable thing that the GTR can achieve is clarity and transparency...many services *will* be direct to consumer but both healthcare professionals and consumers alike will suffer if the genetics/genomics service industry becomes as opaque and exploited as the supplement industry.