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**Sent:** Thursday, July 22, 2010 8:48 AM  
**To:** Genetic Testing Registry (NIH/OD/OSP)  
**Cc:** Roderick Rowan McInnes, Dr; Roderick McInnes  
**Subject:** ASHG Comments on GTR

7/19/10

The American Society of Human Genetics (ASHG) is making comments regarding the Genetic Testing Registry after consultation with the Board of Directors and several other thought leaders in our community. ASHG is the primary professional membership organization for human genetics specialists worldwide. The Society's nearly 8000 members include researchers, academicians, clinicians (including genetic counselors), and laboratory practice professionals. While the content and management of the proposed Genetic Testing Registry may more directly affect our members performing patient related activities, our researchers would also use the registry. We have four major areas of concern regarding the GTR as it is currently proposed to address, as we believe it is premature to respond to many of the specific questions listed in the RFI.

The four areas can be introduced as:

1. Current registries are working, and ANY replacement must be of comparable or higher quality;
2. The complexity of genetic testing may predispose naïve users to potential harms;
3. The imprimatur of the NIH will imply some quality level of all tests registered;
4. The human genetics community has not been appropriately involved in the initiation of such an important project.

*First*, the most fundamental concern expressed by the community is the lack of quality control of the content of the GTR as presently envisaged, a situation that stands in sharp contrast to the extant GeneTests site that is used literally daily in many clinics around the world. The total reliance on contribution of data by providers, and the expectation that all test providers will contribute honestly, state the risks of the test, address the generally weak data related to the clinical validity and utility of many tests, and remain up to date all seem to us to be unworkable and highly unlikely. The direct links and straightforward information about tests and disorders in GeneTests, GeneClinics and GeneReviews remain a valued resource because the data are curated in such a way that clinicians can depend on its quality. This relates both to the oversight provided, and the current focus on disorders with a major single gene effect.

Several leaders of the ASHG community have argued against any immediate effort that tries to address the performance characteristics and clinical validity of tests for more complex traits because they do not believe it is possible to do a good job at this time and with the current data. The associations and complex risks, especially for predictive tests for complicated disease phenotypes, cannot be display in a straightforward manner in a registry format. These issues are especially relevant for physician and lay consumers who do not deal with predictive risk calculations on a regular basis. We believe that the NIH should not associate itself with something that cannot be done well. In keeping with the stated goals of the GTR, we believe that the mission of such a registry or database must expand to include more

complex clinical and genetic situations, but that test accuracy, validity and clinical relevance must take priority over the speed and ease of resource development.

*Second*, the community is concerned about potential harms to patients, harms that could include over-testing, the misinterpretation of test results and the quality of the communication of test results to individuals and their families. The establishment of an enormous database containing inconsistently described tests will not address these issues. We wish to emphasize that the interpretive process in medicine is gray and simply cannot be captured in a 0/1 format. We remain concerned that these clinical issues are not fully appreciated as there has been so substantive information regarding these issues, and contingencies and processes that we are aware of that are currently under consideration will not be able to address these problems.

*Third*, the ASHG is convinced that both clinical and public audiences will infer that all GTR-registered tests have the approval of the NIH and the government, even with the disclaimers that will be included. The clout of the NIH, with national and international audiences dependent upon the accuracy and integrity of information from the agency, cannot be overestimated in this context. One can readily envisage a general practitioner thinking “This a registered NIH test and, therefore, should be safe (no harm), accurate (and readily interpretable), and appropriate for use in health care and planning.” Such perspectives must be anticipated by the NIH. We are left with substantive concerns that the current vision of the GTR team fails to accommodate fully this critical issue.

We are sensitive to the concern of the NCBI that the programming infrastructure of current genetic test registries need major overhaul or a clean start, and that the GTR could achieve this and more. It has been assured that the GTR would be linked to extensive resources, including GeneReviews. We understand that voluntary information from providers, both public and private, would address the NIH mandate of full access to the data and comprehensive informational resources related to the tests. However, these potential benefits of the GTR are outweighed by the more important issue, that quality control of the tests in the GTR would, in the current model, be totally dependent upon the individual or company that submitted the test to the GTR. Comprehensiveness should not trump the quality of content, and the two are not mutually exclusive.

*Fourth*, we assert that the GTR must be subject to comprehensive and continuing consultation and advisory processes with appropriate medical genetics input. We believe it is at the point of input into a database that standards should be met; after a test is publicly registered, it is too late for anyone (NIH or others) to remove the information, and the potential for harm will have been created. The onus should be on a laboratory or company to get a test of high quality in a registry, rather than on the NIH to get a registered test of inferior quality out. To begin this process, we suggest a two-step process with an initial workshop of invited laboratory leaders and clinical geneticists could who could begin the process of suggesting the parameters for the GTR. Then, a Working Group could be gathered to set parameters for content of the registry. We would be happy to suggest geneticists who would be informed contributors to the workshop and the working group or a longer-term advisory committee. If you wish, we could describe in detail what the genetics community would see as an appropriate group for making some *a priori* decisions about definitions and guidelines for a GTR. We are encouraged and challenged by this possibility.

This high-profile initiative will receive tremendous scrutiny, and early stumbles will introduce both barriers and biases that may limit the ultimate success of the GTR; the fallout could extend to the broader field of genetic medicine. The challenges of rolling this out in a manner that is both robust and responsive to the immediate needs of diverse stakeholders are formidable, but we think that both the

NIH and the broader genetics community are up to the task. Our impression is that the GTR surely will be developed, but that the ASHG stakeholder community can and should be directly and centrally involved in developing and maintaining it.

Respectfully submitted,  
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