

## **Request for Information (RFI) on the NIH Plan to Develop the Genetic Testing Registry (NOT-OD-10-101)**

**From: The University of North Carolina Center for Genomics and Society, Ethics and Policy Group**

On behalf of the University of North Carolina's Center for Genomics and Policy (CGS) and the CGS Ethics and Policy Group, we respectfully submit our comments to this RFI. The CGS, directed by Dr. Gail Henderson, is an NIH/NHGRI designated Center of Excellence in Ethical, Legal, and Social Implications of Genetic Research (CEER). The CGS Ethics and Policy Group, led by Don Bailey, Lynn Dressler and Dan Nelson, provides ELSI education and consultation in the areas of genomic research and the development of relevant research policy and public policy.

**General Comments:** The overall concept for the Genetic Testing Registry (GTR) is commendable- a public resource of information regarding availability and validity of genetic tests, including tests marketed by direct-to-consumer industry. However, we have several areas of general concern:

- Laboratorians have confidence in the information on GENETEST, in part because of their confidence that clinicians (i.e. actual users of the information) are intimately involved in the curation of the information. What mechanisms for oversight of content and curation will exist for GTR? How will confidence be engendered with GTR? This will be essential to ensure continued use of GTR by stakeholders.
- Although the website indicates that the GTR will not be replacing "GENETESTS" website, what is the interface between GTR and GENETESTS? For example, will GTR be providing information that GENETESTS will not or vice versa? Are the DTC tests the unique feature of GTR not currently shared with GENETESTS?
- What is the incentive for stakeholders to post information regarding availability and validity of the tests? How will GTR deal with the obvious and inherent conflicts of interest among those who will be posting their tests on the website?
- What type of model is GTR following for gauging relative value of tests? Will there be something similar to WIKI-with comments/evaluations posted by consumers of the site sharing their experiences ordering/interpreting the test? How will consumer evaluations be displayed? Some consumer evaluations may focus on factors such as turn around time and price and these may be more persuasive than other more important elements of test quality such as sensitivity and specificity. How will this be addressed?
- How will the measures of analytic and clinical validity, clinical utility and personal utility be standardized across sites prior to uploading in the database and how will it be presented? What is the mechanism, if any, to address the quality of data being submitted-for example, how the positive predictive value was derived-e.g.,

retrospective or clinical data vs. compared to existing data vs. estimated by a computer algorithm? This is especially challenging for the concept of clinical utility, which has a substantial subjective component.

- Will the registry also have a plain language version of the information for the public, consumers, patients, other stakeholders who may not have a technical/medical background? There is concern that a “one size fits all” website that caters to all audiences may ultimately serve none of them well. Will the registry explain or interpret measures of validity so they can be useful to all stakeholders?
- What recommendations will be made regarding the need for genetic counseling for accurate interpretation of results? This has become a standard recommendation and appears on most genetic testing laboratory reports.

### **Specific Comments:**

1. If submitters are “solely responsible for the content and quality of the data they provide to GTR” (Questions and Answers, Genetic Testing Registry. <http://www.ncbi.nlm.nih.gov/gtr/>),
  - a. How will the GTR be a service to the consumer/public, etc, except to provide information on availability of the test?
  - b. Even if published work is cited for the assertions of validity, what type of education materials/modules will be available to consumers to facilitate use of the registry? For example, will GTR provide consumers with information regarding how to distinguish between a “good” PPV and a “bad” PPV?
  - c. If there are no checks on the quality of the data being submitted, will GTR provide any means of evaluation of the information that is collected?
2. Having the NIH associated with the database can automatically be associated with a “stamp of approval”. Will the NIH have any disclaimers on the site and/or associated with the information that it does not endorse any of the tests in the GTR?
3. In addition to providing information on how to order tests, will the GTR also offer:
  - a. How to interpret test results? Will there be a recommendation that testing be done through a health care provider/genetic professional? Many genetic testing laboratories prefer that testing requests not originate from a patient/consumer as labs have neither the resources nor the desire to interact directly with the public. The way that laboratory reports are currently written would make it very difficult for an untrained consumer (and even many physicians) to interpret correctly.
  - b. Help the consumer distinguish between tests for conditions that are clearly genetically determined (e.g. Mendelian) compared to those tests from complex disorders that have unclear inheritance patterns, such as tests based on information derived from GWAS or other methodologies?

- c. The searching methods of health care providers/genetics professionals would be expected to be quite distinct from those of consumers. How will these differences be accommodated?
  - d. Direct link to the website of the company? This can also be construed as endorsement if this link exists. How will this be addressed?
- 4. Definition of genetic test: suggest the following additions:
  - a. variations in chromosome, gene or protein FUNCTION
  - b. inclusive language to ensure that all possible “omics” are covered (including microbiome)
  - c. include epigenetic tests
- 5. Standard definitions for validity measures: suggest using CDC definitions from ACCE effort.
- 6. Along the continuum of tests that are experimental to those that are standard of care, how will the GTR distinguish and/or update for the consumer/user of GTR? If this information is being considered in the common data elements, what standard of reference will be used?
- 7. How will the GTR obtain data on personal utility and how will this be measured and reported? How will common data elements be developed for this measure?
- 8. How will pleiotropy be addressed, especially with respect to intent of test or recommended patient population? Will this information be captured in the data elements?
- 9. Include in limitations of test: the population in which the test was evaluated.
- 10. Include in specimen requirements: frozen or formalin fixed paraffin embedded tissue (FFPE)
- 11. Include in test methodology, the guidelines for test interpretation and how those guidelines were derived (high/low cut point derivations; positive/negative interpretation of the test)
- 12. For consumer, describe the differences in regulatory clearance (PMA v 510k) and why that is important regarding level of scrutiny by the FDA.
- 13. Agree it would be helpful to reference other resources, such as SACGHS, USPSTF, EGAPP etc. But also to provide a plain language summary for public.

14. If possible, helpful to industry to look at the format data was provided to FDA or CMS and use of similar format to facilitate uploading data and not have to develop this anew.