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Sent: Monday, August 02, 2010 6:10 PM
To: Genetic Testing Registry (NIH/OD/OSP)
Subject: Comments regarding GTR

NIH GTR RFI Comments
National Institutes of Health
Office of Science Policy
6705 Rockledge Drive, Room 750
Bethesda, MD 20892

NOTE: These comments are being provided by the individual author listed below and should not be considered an official stance by any entity associated with Mayo Clinic.

This letter is in response to the NIH RFI regarding development of a Genetic Test Registry (GTR). It is important to recognize that the NIH already has an outstanding, peer reviewed genetic testing resource at www.genetests.org. That resource is utilized on a daily basis by patients, physicians, researchers, genetic counselors, pathologists, and laboratorians. Genetests has been developed over several years with expert input and is updated on a regular basis. It is very important that the funding for this resource not be diverted to develop a new Genetic Test Registry. Finally, it would seem that GeneTests already meets the broad criteria set out for the GTR: "...a centralized public resource that will provide information about the availability, scientific basis, and usefulness of genetic tests." It would seem that the visionary team that has developed GeneTests over the years would be the team to tackle what would be needed to add to the resource to accomplish the goals set out for the GTR.

The stated goal for the GTR is to provide "transparent access" to "information about the validity and usefulness of these tests" to "enable informed decision making by patients, caregiver, health care providers, clinical laboratory professionals, payers, and policymakers." Although laudable, it is very doubtful that the collection of data elements listed would meet that goal. Comments regarding some of those Data Elements are listed below.

Finally, I agree that all patients should have access to quality testing. The question becomes how to adequately inform patients without providing information that can be misinterpreted or misleading to someone that does not have an adequate scientific knowledge or the background to make such an assessment.

It is hoped that these comments will be taken into consideration in considering both the need for and development of a Genetic Test Registry.

Sincerely,

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DATA ELEMENTS:

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

If the goal is to provide a testing database that would be most useful to the public, it would seem that a laboratory testing registry would be of much more widespread utility. Then, after working out which data elements are most informative for the general public, that experience could be further developed to build out the database to include genetic testing. This would also provide the public with the background for interpretation of data from simple testing prior to progressing to the complexities of genetic testing.

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?

Currently, laboratory testing is tied to the medical oversight for a particular patient. The physicians work with their pathologists and laboratorians to obtain the most appropriate testing for that patient. The disconnect often comes from the system as a whole which tends to reward lowest cost testing as opposed to quality testing. The question would be even if the patient, armed with information from the GTR, would be able to direct where their testing would be performed.

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?

There would need to be a clear distinction between testing performed in a laboratory with ongoing CLIA and CAP certification from laboratories performing testing on a research basis.

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?

Some general concerns would include: misinterpretation of quality data, forced release of proprietary information for view by competitors, use of public information for questionable marketing purposes

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?

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?

- 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 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)
- 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
 - 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)

a. through k. is information readily available and would be best provided if it could be electronically transferred in current formats.

- l. The laboratory only provides testing available through a health care provider or public health mandate. Performance characteristics all already required by CLIA. n. Clinical validity - It may be very difficult to determine clinical validity for rare genetic disorders, and, yet does that make having the test available for patients any less important? For example, is identification of a rare genetic disorder in and of itself enough clinical validity to offer testing even though no clinical intervention is possible? Who determines that?

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

Validation records should not be made publically available for view by competitors.

Clinical sensitivity and specificity for rare genetic disorders is not always available and can vary by target population. Price can vary and can be sensitive to competitive market forces. Many of the variables listed above for testing, performance, utility, specificity & sensitivity, etc. can be interdependent and variable depending on ethnicity, specimen handling, fixatives, cell viability, tissue type etc.. As more information is required of the submitting laboratories, the complexity and likelihood of errors rises exponentially, whereas the ability and enthusiasm of participants to keep information up to date fails in inverse proportion.

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?

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)?

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)?

The ability to submit all data electronically is a must. Integrity of the submitted data vs the online data must be verified. It would be best if information provided to other regulatory agencies such as NY State, FDA, etc. did not have to be recapitulated.

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?

A major incentive would be to ensure that participation truly guaranteed availability of testing of higher quality for patients and appropriate use of that testing by health care providers for better patient care.

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

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

professional efforts?

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

A lot of the data elements that are suggested would not be available to be transferred electronically. This would be expensive and resource intense to build. However, much of this information is currently made available to healthcare providers when requested.

It is very important that those individuals staffing the registry be knowledgeable (ie. hands on experience) about laboratory testing for genetic disorder. Partnering with the team at GeneTests is strongly recommended and preferred.