



November 12, 2010

Francis Collins, MD, PhD
Director
National Institutes of Health
Department of Health and Human Services
9000 Rockville Pike
Bethesda, Maryland 20892

Re: Genetic Testing Registry

Dear Dr. Collins:

The College of American Pathologists (CAP) appreciates the opportunity to comment on the proposed Genetic Testing Registry. The CAP is a national medical specialty society representing more than 17,000 physicians who practice anatomic and/or clinical pathology. College members practice their specialty in clinical laboratories, academic medical centers, research laboratories, community hospitals and federal and state health facilities.

The October 8, 2010 *Federal Register* Notices states that the goals of the GTR are to promote transparency by encouraging test providers to share information about the purpose and validity of their tests; provide a resource for the public including health care providers, patients, and researchers—to locate laboratories that offer particular tests; and facilitate genomic data sharing for research and new scientific discoveries. The College does not believe that a single interface can meet the goals for all stakeholders. The prototype interface presented at the November 2nd public meeting may indeed be useful to researchers but will be difficult for patients and providers to get helpful information.

In addition, it is clear to CAP that the registry's definition of genetic testing goes well beyond what most think of as genetic. There will be unintended consequences from the intended definition. We believe a very structured and deliberate approach should be pursued to make this registry truly useful.

CAP Response to NIH Questions on the proposed Genetic Testing Registry

1. Based on an analysis of RFI comments and other operational issues, NIH is considering a phased approach to developing the GTR in which some types of tests would be eligible for early entry in the GTR and other types of tests would be added later. If NIH adopts this approach, what criteria should be used to determine which genetic tests should be included in the first phase of the GTR, and what types of tests would meet these criteria?

CAP has a long record of working to ensure the quality of diagnostic tests. As the major hospital laboratory accrediting organization in the United States, we have confidence that all tests, including genetic tests, performed in CAP accredited laboratories achieve the highest standards required of a clinical test. Our program of laboratory inspection, proficiency testing,

and standards development is designed to accommodate novel technical and biological innovations as needed to advance clinical care.

There are some kinds of tests, however, that fall outside the purview of the CAP Laboratory Accreditation Program. We increasingly encounter tests performed by sole source laboratories that do not avail themselves of the extensive professional peer review and inspection processes available through the College's Accreditation Program.

Many of these tests are "genetic" often utilizing novel technologies, and not infrequently claim to portend the future of personalized medicine. If they remain outside the traditional clinical testing processes, such tests will remain problematic. Consequently, we suggest that this test registry focus initially on tests that fall outside the traditional clinical laboratory oversight systems.

We believe these are the tests that are in greatest need of demonstrated quality assurance, of demonstrated clinical utility, and indeed, if they are as forward reaching as some claim, would be the tests of greatest research interest. We would consider in this category those tests performed by one or few laboratories (sole source tests) in such a manner that eludes the level of safeguards established by the CAP Accreditation Program. We include in this category tests whose interpretation is dependent on proprietary information, including Genome Wide Association Studies (GWAS) that is not available for professional peer review and critique. We include in this category tests which are performed without the kind of medical oversight of usage and interpretation that is required of the laboratory Medical Director by CAP standards (e.g. DTC tests).

Development of a registry that can accommodate these tests would immediately address many of the concerns that have been raised about genetic tests (e.g. tests offered without adequate quality assurance or proficiency testing), but which we do not believe are in question for the vast majority of tests already in clinical use.

We would suggest that after this initial phase, due consideration can be given the gradual and logical introduction of other test categories into the registry in a manner that will be useful, and not duplicate programs already in place.

2. Several RFI responders, who are potential data submitters, noted that it makes more sense for clinicians and genetics professionals to be the source of clinical utility evidence rather than test developers and/or test providers. Given that data submitters are unlikely to have clinical utility information, how is this data element best addressed in the GTR?

The development, understanding and vetting of clinical utility evidence is a multidisciplinary process that encompasses laboratory professionals, researchers, and the clinicians who order these tests for their patients. Their experiences and observations, whether structured or anecdotal, are captured in the medical scientific literature, where they are presented for insight, comment, critique, and the ever present challenge of validation and refinement (or rejection). Clinical validity and clinical utility are linked to the various clinical contexts in which a test may have relevance. Any model whereby each individual lab is required to submit "clinical utility" evidence would be absolutely unworkable. Furthermore, it will be difficult, if not impossible, to capture this dynamic process in any single index or entry, and, indeed, it is critical that this process not be diminished by oversimplification. It is problematic for clinicians and genetic professionals to be the sole source of clinical utility evidence.

3. Among responders to the RFI question about including a data element for test cost, half were in favor of including cost information and half were opposed. What are the benefits, risks, and challenges of including cost information in the GTR?

It is impractical to attempt to include the cost or "price" in the GTR for multiple reasons. The "price" of a test is determined by the health care institution that the laboratory serves, the clinical context, negotiated coverage agreements, and other factors of which the laboratory has no knowledge.

4. What safeguards can be put in place to prevent GTR users from misunderstanding, misinterpreting, or misusing the information in the Registry?

Misunderstanding, misinterpretation, and misuse of any information in the GTR are of great concern to the College of American Pathologists. The Medical Directors of clinical laboratories have responsibilities that extend from appropriate test selection for a patient's specific clinical context to correct interpretation and reporting to the ordering physician. Test directories and registries can be an important tool in that process, but unless these are constructed in such a manner and with sufficient safeguards, there is potential that misunderstanding, misinterpretation and misuse could compromise patient safety, or indeed, create harm. That possibility gives us pause. We strongly recommend that NIH establish appropriate monitors to document that such misunderstandings, misinterpretations, misuses, or other harms are not occurring through the use of this registry.

5. What mechanisms can be used to provide materials that explain the GTR's data elements to audiences with varying technical expertise?

The College of American Pathologists and a number of other professional organizations have relayed to NIH the opinion that a single test registry may be incapable of serving the various audiences envisioned. Certainly during the development phase, we recommend that the endeavor be divided into separate directories whose designs are guided by the specific audiences and functions they are intended to serve. The Centers for Disease Control and Prevention and the Agency for Healthcare Research and Quality have successfully demonstrated this approach. In the future, these separate projects could be linked or amalgamated as appropriate for their function, assuring their efficacy and minimizing risk to patients.

It would be helpful if NIH included a glossary of terms and specified data elements, paying particular attention to the differences between somatic and germline mutations. NIH could make free workshops, presentations and webinars available to any health practitioner and to the general public, but we feel it will be extremely difficult to develop one set of materials that will be appropriate for all audiences. NIH should consider developing separate material for clinicians and the general public. Users need easily understandable peer-reviewed literature and an explanation of methodologies such as PCR, sequencing and mass spectroscopy.

The College of American Pathologists is pleased to have the opportunity to comment on these issues and appreciates your consideration of these comments. Please direct questions regarding this letter to Fay Shamanski at (202) 354-7113 (fshaman@cap.org).

Sincerely,

College of American Pathologists