

August 2, 2010

Thank you for providing us the opportunity to respond to comments for the planned Genetic Testing Registry (GTR). New York State's Clinical Laboratory Reference System has been reviewing analytic and clinical validity for genetic tests since 1990 and somatic variations since 1994. In recent years the types of technology and the breadth of available tests has expanded greatly. We are concerned about several aspects of the proposed new registry, based on our own experience.

We believe the small niche labs providing important services in the field of rare disorders will not be able to enter the data required, either because they do not have the required information or they lack the resources to keep the GTR current with necessary updates. The ultimate failure of the registry would be closure of the few laboratories that can provide these services to individuals because their test information is no longer available in an easily accessible form.

Without staffing, who is responsible to curate the registry? For example, tests have rapidly evolved in a very short time frame from a targeted panel of a few mutations in a major disease gene to many mutations in many genes, to exon sequencing, to full gene analysis, including DNA sequence and deletion/duplication analyses of extensive panels of genes. How can laboratories be expected to keep up with changes in the registry for each test, when some laboratories offer hundreds of such genetic tests?

Many large laboratories advertise extensive test menus, however much of the testing is contracted out to other laboratories. In such cases, whose responsibility is it to enter the various data elements the GTR is requiring, and which laboratory is accountable for the data provided? Many large laboratories own smaller ones, or have testing available in different laboratories across the country; again, which entity is accountable for the information provided to the GTR?

In our experience there is much confusion from test providers and clinicians in their understanding of the definitions of analytical and clinical validity, and clinical utility. A laboratory entering these data, without any oversight or juried review of the claims and/or the data is left with their advertising/marketing materials to cite for validity. What transparency will be provided for validity in different populations, for example? While this is covered under "Recommended Patient Population", we believe this will still lead to inappropriate ordering and interpretation. For example, a cystic fibrosis test has many variations; someone looking for such a test will need some basis for comparison. That is, a health care provider needs to understand whether they are looking for a laboratory to test for CFTR-related disease, congenital bilateral absence of the vas deferens, or classical cystic fibrosis. In the simplest sense, the test name (commercial name, gene name, analyte name, method name) can be a major source of confusion. The clinical validity and utility are dependent on the population being tested, the purpose for which the test is being ordered, and other factors that cannot be easily captured in a data field. In some cases, this information isn't available, so the data will not be useful for clinical decision-making.

Here are some specific concerns on the individual data elements requested. The intended use of the test “e.” is an area of confusion. The same test can be used for screening of newborns, for carrier screening, and for diagnosis (asymptomatic [prenatal and pre-implantation] and symptomatic). Without an understanding of the limitations of the various applications of the test result, we believe tests will be ordered incorrectly. We believe, since the proposed registry will be housed under the auspices of the NIH, it will be afforded enhanced credibility. That is, the users will assume there is some form of oversight, data management, and/or hierarchical classification system. If users are misled in this regard, we feel NIH's reputation will suffer.

Another source of confusion is the term "Analyte" as stated in “i.”. If a genetic sequence is being ordered, is the gene being completely sequenced? Is only the coding region covered? Is the regulatory region covered? How about intron sequences, etc.? This is an important concern in our experience classifying tests for our New York State permitted population.

The term “availability, ‘k.’, (is the submitter the sole provider of the test or are there multiple providers)” is another source of confusion. This information will not be useful for clinicians if the laboratory offering the test is responsible for filling in this data field.

Point “l., accessibility (through health care provider, public health mandate, etc.)” is subject to state and local laws, and should not be included in the registry.

The last point, “p. cost (price of the test and health insurance coverage)” will be out of date before it is useful. It will be impossible for laboratories with large test menus that market across the country to keep this information accurate and up to date because rates vary depending on the payer and on contractual arrangements. Insurers’ contracts with testing laboratories and test costs are in a constant state of flux. In addition, the cost of a test must be considered along with details that are in the best interest of the patient, the least expensive test may not be the best for a particular purpose.

We recommend the formation of a study group consisting of geneticists and others from the Department of Health and Human Services, including NIH, CDC, FDA, and CMS. Representatives from New York State's Program will be happy to participate in any capacity. Similarly, this group should also have participation from the various sectors of the laboratory community. In order for the GTR to be of maximal value there will need to be staff available to monitor the input of data, to properly classify tests, and to monitor data quality. This approach has worked well for the GeneTests database, which is used extensively by the genetics community at present.

Respectfully Submitted,

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