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GeneDx

Good morning. My name is Sherri Bale and I am a Board-Certified Medical Geneticist. Since March of 2000 I have been the President and Clinical Director of GeneDx, a clinical diagnostic laboratory specializing in the development and performance of molecular diagnostic testing in rare hereditary disorders. GeneDx serves the community of patients with rare disorders through their geneticists and other physicians.

My comments will address points 2 and 4 on the Question List.

As a lab providing testing, GeneDx is a potential submitter of data to the GTR, and it is of significant concern to us that the curation of submissions that is currently being performed by board-certified clinical geneticists and genetic counselors associated with GeneTests be maintained as GeneTests is inactivated and its data transitioned into the GTR.

The GTR will be most useful to all stakeholders if the high quality of information currently available through GeneTests, and inclusion of only tests that are valid for the purpose of diagnosis of hereditary disease in the medical setting, is maintained. Thus it is my opinion that information about the clinical validity of a submitted test is best obtained, evaluated, and determined by an appropriate professional review panel consisting of board-certified genetics professionals, rather than test developers and/or test providers. It is critical that only those tests that achieve the highest level of utility for the diagnosis of patients with genetic disease are represented in the GTR. As this information is expected to be used for the clinical management of patients and that impact the some of the most important decisions a family will ever make, only the highest quality medically-relevant genetic tests should be represented in the Registry.

Thus, those tests that are based solely on associations (as defined in the epidemiologic/statistical sense) and identified through retrospective population case/control or cohort studies, should not be listed in the GTR, unless there is prospective data available that support the hypotheses generated by the association studies that can be evaluated by appropriately trained and board-certified genetics professionals. These reviewers should be responsible for evaluating the utility of the test in the diagnosis, management, and genetic counseling of patients with genetic disorders. The exclusion of tests from the GTR that fail to meet the criteria of high clinical utility and validity is essential. While this level of stringency may lead to the exclusion of many Direct-to-Consumer tests that are currently on the market and are based solely on population risk analyses, animal studies, or in vitro functional assays, their inclusion could lead to the incorrect assumption by the non-cognoscente that these tests have specific medical implications for a specific tested individual, when that is a false conclusion.

I propose that three levels of genetic tests exist for the purpose of this discussion:

- 1) Medically-relevant genetic tests with high clinical validity and utility, as determined by qualified Board-certified genetics professionals. Such tests should be included in the GTR.
- 2) Tests that are being offered by a non-CLIA certified laboratory in support of on-going research about the relationship of a disease to a gene. Such tests should be clearly labeled in the GTR (as they are currently identified in GeneTests) as Research level testing.
- 3) Tests based solely on population risk, animal, or in-vitro functional studies should NOT be included in the GTR.

Caveat emptor is not appropriate when dealing with the genetic health of patients and families.

Thank you.