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To: Genetic Testing Registry (NIH/OD/OSP)
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Creation of a readily available source to identify the various laboratory tests for genetic markers of germline or somatic cell mutation is a laudable goal. Many in the genetics community have made great use of the laboratory and test listing offered by "GeneTests". That voluntary listing of laboratories, tests offered, and whether their assays are being used for research or clinical testing along with the laboratory's permit or license status under the federal Clinical Laboratory Improvement Amendments (CLIA) or other relevant regulatory program (NYS) has been valuable.

It is NOT clear to this commentator how creation of another VOLUNTARY repository of laboratory and test menu information will be of any advantage.

Regarding what "tests" to include the registry should clearly segregate those tests intended to detect markers for inherited disease/trait/ or risk factor from those tests designed to detect acquired markers for somatic cell mutation or change in gene expression associated with various cancers or other disease states. While there may be some overlap in the populations to be tested, the frequency of testing a particular individual, and the predictive values of germline genetic markers and acquired somatic cell changes argue for a clear distinction.

It is true that the existing resource of GeneTests does not attempt to qualify the assays or genetic tests listed as to their analytical or clinical validity or clinical utility. However, these terms are little understood by the consumer stakeholders and poorly understood by the medical providers who might access this resource. Therefore the clear definition of each term to be included must be prominently displayed and regularly repeated so as to be very available to the information submitter and the end user. Inclusion of any of the additional data elements without the submission of the data to support the claim and a means of independent review of that submission to verify the claims of the submitter cannot be expected to provide reliable claims for aiding the provider in selecting an appropriate laboratory or test.

Having been responsible for review of the validation materials submitted by laboratories offering genetic tests performed on specimens collected in New York State for the past 30 years, I must emphasize that the quality of data supporting claims of analytical or clinical validity of the offered tests varies greatly. This suggests that there are many laboratory directors who also struggle with the definitions of the suggested data elements. There are also several laboratory directors who appear to have little or no appreciation of the essential nature of assay validation prior to offering such assays for clinical case identified reporting for health care decision making. Establishing the assay performance characteristics and making certain the assay offered is reproducible, accurate, and establishing reference ranges or cut off values is not always understood. Providing the data to suggest the assay is known to distinguish between persons affected or at risk of the target disease or condition and the unaffected individual or calculating positive and negative predictive values is often overlooked. The NYS program does not ask the submitting laboratory to describe clinical utility of the test as offered as this is too often a matter of the perception of the ordering health care provider or the patient themselves and not easily ascertained or documented by the laboratory. If described by the laboratory it is likely to represent marketing claims with little scientific support.

The registry must be mandatory. If the NIH does not have the authority to require registration of the offered assays then the registry should be the responsibility of the FDA or CMS (CLIA) under their regulatory authority.

The documentation of the stated data elements must be submitted to an appropriately resourced review process for review. Only independently reviewed data elements should be included in the registry.

If both laboratories and assay vendors are to participate, then their submissions should be kept in separate files in the database. There is no certainty that the laboratory will implement and use the assay as designed

by the vendor or that the ordering health care provider will order the test or use the result as intended by the vendor or the performing laboratory.

Thank you for the opportunity to submit these comments.

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