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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rom. 1061
Rockville, Maryland 20852
FDA-2016-D-1233-0001

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The American Association for Clinical Chemistry (AACC) welcomes the opportunity to provide input to the Food and Drug Administration (FDA) regarding its draft guidance *"Use of Public Human Genetic Variant Databases to Support Clinical Validity for Next Generation Sequencing (NGS)-Based In Vitro Diagnostics."* Although AACC supports greater accumulation and sharing of genetic data, we believe the current public-private partnership under the Clinical Laboratory Improvement Amendments (CLIA) remains the appropriate means for advancing and overseeing this innovative field.

AACC is a global scientific and medical professional organization dedicated to clinical laboratory science and its application to healthcare. AACC brings together more than 50,000 clinical laboratory professionals, physicians, research scientists, and business leaders from around the world focused on clinical chemistry, molecular diagnostics, mass spectrometry, translational medicine, lab management, and other areas of laboratory science to advance healthcare collaboration, knowledge, expertise, and innovation.

AACC agrees that electronic databases can serve as an invaluable resource for professional laboratory scientists, clinicians, genetic counselors and researchers seeking greater information about variants associated with differing disease conditions and interpretations. We would caution the FDA, however, in placing too much reliance on these data repositories. There are a number of limitations associated with archived data, including:

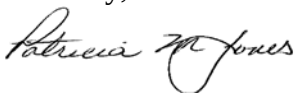
- the age of the information;
- limited accumulated data; and
- varying interpretations.

Further, while human genetic variant databases can be an effective tool for assisting healthcare professionals interpret genetic test results, they are not a replacement for professional judgment. Medical judgment incorporates multiple pieces of evidence, including patient-specific factors, which are essential to determining the pathogenicity of a variant. We are concerned that patient health and safety could be compromised if a new regulatory approach is adopted that limits the ability of healthcare professionals to use their judgment in classifying variants.

AACC recommends that if the agency moves forward with this guidance it clarifies whether data submissions from multiple independent investigators would be accepted as confirmatory evidence of clinical utility in lieu of requiring multiple published accounts of the same genetic variant - clinical phenotype relationship. Scientific journals are hesitant to publish confirmatory studies (they want original findings) and it's challenging to substantiate all claims about the variants.

We look forward to continuing to a dialogue with the FDA on this important issue. If you have any questions, please email Vince Stine, PhD, AACC Director of Government Affairs, at vstine@aacc.org.

Sincerely,



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