ASSOCIATION FOR MOLECULAR PATHOLOGY
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October 13, 2016

Division of Dockets Management (HFA-305)
US Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2016-D-1703-0001 for "Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product; Draft Guidance for Industry and Food and Drug Administration Staff."

Submitted electronically at www.regulations.gov

To Whom It May Concern:

On behalf of the Association for Molecular Pathology (AMP), thank you for the opportunity to submit written comments on the draft guidance entitled "Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product."

AMP is an international medical and professional association representing approximately 2,300 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Membership includes professionals from the government, academic medicine, clinical testing laboratories, and the in vitro diagnostics (IVD) industry.

Optimized patient care relies on test design that evolves and is modified upon elucidation of new discoveries and technologies. In the draft guidance, FDA states that a companion diagnostic should be granted a *de novo* request, clearance, or approval contemporaneously with the approval of a corresponding therapeutic product. We are concerned that FDA's current regulatory approach does not allow FDA to keep pace with how fast the science is progressing and that as a result, some patients would not receive the most appropriate care. This could arise because FDA anticipates that "approval of the therapeutic product could be delayed until an appropriate IVD companion diagnostic received marketing authorization" even if there is one or more well-validated laboratory developed testing procedures (LDPs) offered by CLIA authorized laboratories. In addition, patient care may be compromised because of outdated testing parameters cemented into place upon FDA clearance or approval. The concept that the only appropriate test is the one co-developed with the drug, or developed with studies using likely unobtainable specimens from patients being treated with that drug, would hinder the application of new technologies and improvements to current tests over the decades the drug is in use.

AMP strongly recommends that the term "companion diagnostic" not be used in any regulatory policy and instead that the Agency replace the term with "targeted biomarkers" to more accurately reflect that many valid tests may enable physicians to make decisions regarding the use of a specific treatment for a patient. The single test, single drug paradigm as described by the term "companion diagnostic," is obsolete as new technologies allow for the testing of multiple analytes simultaneously with greatly reduced per-analyte costs.

As FDA acknowledges in the recently released guidance[1] on one of these new technologies, next generation sequencing, an ideal tool to help ensure accuracy and reliability as tests and technologies advance is standard reference materials. AMP strongly recommends that standard reference materials be created for targeted therapies, whether produced in a public-private partnership such as Pharma-NIST or through Pharma-funded private mechanisms.

In the "Prescreening for Eligibility for Therapeutic Product Clinical Trials" section, FDA incorrectly suggests assurances cannot be made about the performance of LDPs, referred to as "local tests" in the draft guidance. In actuality, the CLIA program at the Centers for Medicare & Medicaid Services, in addition to state level requirements and third party reviewers are readily verifying that LDPs are both accurate and precise. Building off this regulatory foundation, standards developed through collaborative efforts between professional organizations and various government entities, which could include FDA, would provide laboratories with the ability to ensure that agreed upon thresholds for analytical validity were met without the need for burdensome and costly FDA premarket review.

Furthermore, while we appreciate that the guidance does not specifically reiterate FDA's thoughts on the inclusion of a branded test on labeling materials, AMP believes that drug labels should not specify the brand name of diagnostic tests. We recommend FDA use this guidance document to update their thinking on the subject.[2]

Once again, we appreciate the opportunity to provide these comments on the present draft guidance. If we can provide additional information, please feel free to contact Tara Burke at 301-634-7962 or tburke@amp.org.

Sincerely,

Charles E. Hill, MD, PhD
AMP President

[1] Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germline Diseases, Draft Guidance for Stakeholders and Food and Drug Administration Staff. 2016. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM509838.pdf. Accessed August 12, 2016.

[2] In Vitro Companion Diagnostic Devices, Guidance for Industry and Food and Drug Administration Staff. 2014. http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm262327.pdf. Accessed August 12, 2016.