COLLEGE of AMERICAN PATHOLOGISTS

February 4, 2019

Scott Gottlieb, M.D.
Commissioner
US Food and Drug Administration (FDA)
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Developing and Labeling In vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products; Draft Guidance for Industry; Availability [Docket No. FDA-2018-D-3380]

Submitted via Electronic Submission to www.healthIT.gov

Dear Dr. Gottlieb:

The College of American Pathologists (CAP) appreciates the opportunity to comment on the Food and Drug Administration draft guidance entitled, Developing and Labeling In vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products; Draft Guidance for Industry. As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. As physicians specializing in the diagnosis of disease through laboratory methods, pathologists have a long track record of delivering high quality diagnostic services to patients and other physicians and have a keen interest in ensuring that access to these services is not unduly restricted. The CAP supports the FDA's effort to broader evidence-based indications for oncology companion diagnostics.

The CAP strongly believes that the label should indicate the biological pathway or target of testing rather than a specific test or test process and that the label should not restrict testing methodologies to only FDA approved or cleared devices but rather specify the analyte to be tested. The information derived from appropriate testing provides extensive clinical information regarding the specific analyte; prescription of the drug; and clinical outcome. Broadening the label will allow patient access to valuable tests and ensure the pathologists" ability to provide the most thorough evaluations for their patients. Further, implementation of the guidance may allow the incorporation of new scientific evidence of disease pathobiology and technical advances in device methodology.

SPECIFIC COMMENTS ON THE DRAFT GUIDANCE QUESTIONS
Please describe any specific challenges with developing the evidence needed to identify in labeling a companion diagnostic for use with a specific group or class

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of oncology therapeutic products, rather than a specific therapeutic product. For example, please describe any challenges resulting from industry or business practices, including business agreements. What actions can FDA take to address the challenge(s)?

The CAP believes one challenge for oncology therapeutics within the same group or class is of having different performance characteristics and potentially different indications. For example, osimertinib is approved for T790M-positive NSCLC, whereas erlotinib, gefitinib and afatinib are not. Likewise, erlotinib is recommended for patients with leptomeningeal involvement by NSCLC. So, the package insert may have to account for the varying performance characteristics and indications for each of the drugs.

Please describe any specific challenges with submitting a premarket approval (PMA) supplement to FDA to expand the labeling for an approved companion diagnostic for use with a specific group or class of oncology therapeutic products. What actions can FDA take to address the challenge(s)?

Some FDA approved companion diagnostics may not necessarily detect all the relevant variants for a specific group of drugs. For instance, at least one FDA-approved BRAF assay doesn't detect all the variants that predict response to the group of BRAF therapeutic oncology products. The FDA could potentially provide guidance on all the variants that need to be detected in order to be labeled more broadly.

Please describe any additional actions FDA can take to facilitate or encourage broader, evidence-based labeling that supports the use of a specific group or class of oncology therapeutic products with a companion diagnostic.

The guidance notes that variations in defined cut-points established for specific biomarkers for companion diagnostics can lead to challenges in implementing broader labeling for a specific group or class of oncology therapeutic products. Are there actions that FDA, or the broader scientific community, can take to facilitate standardization in this area?

We recommend when broadening the companion diagnostic label each test submission should include sufficient details of the biological basis for the test and its performance characteristics such that these could be used as benchmarks for comparison with other tests. Also, for broader labeling, establishing minimum performance characteristics of the assay(s) may need to be considered.

The FDA could potentially require each approved companion diagnostic to detect variants at or above a specific allelic frequency, such as 5%. The updated molecular testing guideline for selection of lung cancer patients for treatment with targeted TKIs, recommends only deploying assays capable of detecting EGFR T790M mutations in as little as 5% of EGFR alleles.

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Thank you for the opportunity to submit these comments. The CAP looks forward to working with the FDA to ensure patients' care is guided by the best test available. Please direct questions on these comments to Helena Duncan at (202) 354-7131 or hduncan@cap.org.

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