



February 8, 2019

Scott Gottlieb, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20857

Sent electronically

Re: Docket No. FDA-2018-D-3380-0001: Developing and Labeling In vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products; Draft Guidance for Industry

Dear Commissioner Gottlieb:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 230 institutions and individuals across the health care spectrum, appreciates the opportunity to submit comments on the U.S. Food and Drug Administration (FDA)'s draft guidance titled *Developing and Labeling In vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products*.ⁱ The draft guidance represents a positive step forward. PMC respectfully asks, however, that FDA address some issues we have with the draft before finalizing this guidance.

PMC and its members recognize personalized medicine as an evolving field that uses diagnostic tools to identify specific biological markers to help determine which interventions will be best for each patient. By combining this information with an individual's medical history, circumstances, and values, personalized medicine allows doctors and patients to develop targeted prevention and treatment plans. Companion diagnostic tests are a vital part of personalized medicine that can yield crucial information necessary for guiding therapeutic treatment decisions and unlock the potential of targeted therapeutics to serve their desired populations.

Personalized medicine is advancing rapidly and enabling more accurate diagnoses, better prediction of individual susceptibility to disease based on genetic or molecular factors, improved detection of disease at early stages, greater use of targeted treatments, and greater efficiency and effectiveness for the health care system. Since 2014, the number of personalized medicines approved by the FDA annually has topped 20 percent. Of the 59 treatments approved in 2018, PMC classifies 25 of them, or 42 percent, as personalized medicines. We applaud the agency for facilitating the rapid pace of personalized medicine innovation.

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PMC provided comments to the FDA in 2011 on the first draft guidance issued by the agency related to the development of companion diagnostics. Under that paradigm, FDA has approved and cleared companion diagnostics to detect variants in individual genes that are indicated for directing treatment with a specific drug.ⁱⁱ We appreciate your own recognition via the release of this draft guidance that the current environment for developing and labeling companion diagnostics may not be ideal to patient care since it requires that physicians order individual companion diagnostic tests and/or obtain additional biopsies from patients in order to unlock additional treatment options.ⁱⁱⁱ We applaud you for issuing this draft guidance to begin a dialogue with stakeholders on regulatory changes that could improve the status quo for providers, patients and industry.

Statement of Neutrality

Many of PMC's members will present their own responses to FDA and will actively advocate for those positions. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance, and are not intended to impact adversely the ability of individual PMC members, alone or in combination, to pursue separate comments on this draft guidance.

Overall, the draft guidance represents a positive step forward in bringing standardization to molecular testing methods in oncology and provides developers with a streamlined pathway for pursuing class labeling for companion diagnostics that address more than one oncology treatment. PMC respectfully asks FDA to consider the following comments.

I.) Considerations in Seeking Class Labeling for Companion Diagnostics

FDA details a number of factors in the draft guidance that developers should consider when seeking to expand a companion diagnostic label beyond that for an approved individual therapy. The recommendations relate to whether a specific group of oncology treatments can be defined; whether there is enough clinical experience with at least two treatments for the same biomarker-defined disease indication; and whether there is demonstrated analytical validity across a range of biomarkers and clinical validity in the intended disease areas. PMC appreciates the flexibility shown by the FDA in noting in this draft guidance that these data can be produced not only from new studies, but also from data in published literature. Not immediately requiring developers to generate additional clinical evidence will add efficiency to the process of achieving class labeling for diagnostic tests. PMC urges the FDA to retain this flexibility in the final guidance.

We believe that FDA can take further action to encourage broader, evidence-based labeling. In describing the clinical validity requirements, the draft guidance specifies that a future companion diagnostic sponsor could either perform concordance studies with a previously approved companion diagnostic or choose to perform a clinical study establishing the link between the result of the companion diagnostic and patient outcomes for that indication. PMC proposes that final guidance address the possibility of utilizing real-world data (RWD) as additional evidence to help establish such a link. Additionally, RWD can be effectively used toward post-market commitments requiring clinically relevant data.

II.) Continued Engagement with Stakeholders on Outstanding Issues

The draft guidance recognizes that in an evaluation of clinical validity, the defined cut-off for a specific companion diagnostic is important to consider in the context of broader labeling because different cut-offs

may identify different groups of patients. The *Federal Register* notice for this draft guidance issued a call to facilitate standardization of defined cut-point variations. PMC recommends that FDA hold meeting or workshop including thought leaders from relevant professional societies to ensure that there is robust stakeholder input on standardization.

The *Federal Register* also requested examples of business practices that present challenges to developing the evidence needed for labeling a companion diagnostic for use with a specific group or class of oncology therapies, rather than an individual therapy. By doing this, FDA acknowledged that regulatory changes alone might be insufficient. The labeling for a companion diagnostic and its associated treatment can have important implications for promotion and marketing, patenting, and reimbursement, among other considerations.

Current business arrangements between diagnostic manufacturers and therapeutic sponsors have facilitated close collaboration that has been valuable throughout the development and use of approved products. These partnerships have been vital to novel companion diagnostic development that has transformed the oncology space. In cases where therapies and companion diagnostics are co-developed in partnership, the data generated on the companion diagnostic may be proprietary. Many of our members have asserted in the past that these proprietary data should not be opened to a general class labeling claim because it could have a deleterious effect on innovation. We ask that you continue to engage with the broader stakeholder community as you finalize this guidance so that it has the intended effect of relieving some commercial challenges to diagnostic development, as opposed to inadvertently stifling novel companion diagnostic and therapeutic development.

III.) Future Applicability of the Draft Guidance to Other Therapeutic Areas

PMC advocates for personalized medicine to prevent and treat diseases beyond oncology. We understand that the current draft guidance is limited to companion diagnostics and treatments in oncology, but we believe that personalized medicine has the potential to successfully treat patients with diseases with unmet need in the future. We know FDA shares this vision.

In 2018 the agency approved two new therapies targeting treatments for some patients with HIV and is increasing approvals each year for specific patient populations that have rare and undiagnosed diseases. We hope the agency will recommend that developers of therapeutic products and associated companion diagnostics collaboratively consider development programs that may result in broader labeling of companion diagnostics outside of oncology. FDA should address similar situations that may occur outside of oncology and how any final guidance issued in oncology would apply to other diseases that may benefit from class labeling for companion diagnostics in the future.

Conclusion

Thank you for considering these comments. PMC welcomes the opportunity to serve as a resource to FDA as this guidance on in vitro companion diagnostic devices for a specific group or class of oncology therapeutic products is revised and finalized. If you have any questions about the content of this letter, please contact me at 202-589-1769 or cbens@personalizedmedicinecoalition.org.

Sincerely,



Cynthia A. Bens
Senior Vice President, Public Policy

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ⁱ Food and Drug Administration. *Developing and Labeling In vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products*. December 2018 <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-afda-gen/documents/document/ucm627805.pdf> Last accessed: February 2, 2019.

ⁱⁱ Food and Drug Administration. *In Vitro Companion Diagnostic Devices. Guidance for Industry and FDA Staff*. August 2014. <https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm262327.pdf> Last accessed: February 2, 2019

ⁱⁱⁱ Food and Drug Administration. December 2018. *Statement from FDA Commissioner Scott Gottlieb, M.D., on the FDA's new effort for developing and class labeling of in vitro companion diagnostics for classes of oncology therapeutic products* <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm627745.htm> Last accessed: February 5, 2019