PERSONALIZED MEDICINE COALITION

January 26, 2026

Martin A Makary M.D., M.P.H.
Commissioner
U.S. Food & Drug Administration
Department of Health and Human Services
10903 New Hampshire Ave
Silver Spring, MD 20993

Re: Reclassification of Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product; Proposed Amendment; Proposed Order; Request for Comments [Docket No. FDA-2025-N-4622]

Dear Commissioner Makary:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising nearly 200 institutions from across the health care spectrum, thanks the U.S. Food & Drug Administration (FDA) for the opportunity to submit comments on the recent proposal to reclassify certain post amendment class III nucleic acid-based test systems indicated for use with a corresponding approved oncology therapeutic product (product codes OWD, PJG, PQP, and SFL) from class III (premarket approval) into class II (special controls), subject to premarket notification.[i] Current companion diagnostics (CDx) regulations and those for test systems included in drug labels are intended to protect patients by ensuring quality and consistency of treatment-guiding biomarker testing in clinical trials and clinical practice. However, these same regulations have had unintended negative consequences on innovation, implementation, and accessibility of precision medicine.[ii] The proposed reclassification order would shift many current and future oncology-based CDx tests and tests systems that are included in drug labels but not considered essential to a more efficient path to market while maintaining high diagnostic quality. PMC generally supports the least burdensome approach detailed by the FDA in the proposed reclassification order but urges special controls that are sufficiently clear, specific, and consistently applied to serve as the primary mechanism for assuring patient safety, effectiveness, and clinical reliability. If finalized, the reclassification order should improve access to diagnostics that provide important information to guide cancer treatment.

PMC defines personalized medicine as an evolving field in which physicians use diagnostic tests and individual details about a person's health to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health. By combining data from diagnostic tests with an individual's medical history, circumstances, and values, health care providers can develop targeted treatment and prevention plans with their patients.

Personalized medicine is helping to shift the patient and provider experiences away from trial-and-error toward a more streamlined process for making clinical decisions, which will lead to improved patient outcomes, a reduction in unnecessary treatment costs, and better patient and provider satisfaction. PMC and its members are leading the way in personalized medicine and in developing evidence showing how patients and the health care system can benefit from appropriate testing and tailored treatment as soon as possible during their clinical experiences.

Statement of Neutrality

Many of PMC's members will present their own responses to the recent FDA proposal to reclassify certain post amendment class III nucleic acid-based test systems indicated for use with a corresponding approved oncology therapeutic product (product codes OWD, PJG, PQP, and SFL) from class III (premarket approval) into class II (special controls), subject to premarket notification 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 adversely impact the ability of individual PMC members, alone or in combination, to pursue separate comments with respect to the proposal.

Importance of Companion Diagnostics (CDx) to Personalized Medicine in Oncology

Cancer is known to be a complex disease in which the same cancer type can behave differently in different populations. The consequence of these individual differences is that within a population of patients suffering from the same cancer, the mainstay therapy fails to achieve efficacy in many patients.[iii] CDx assess the biochemical basis of a disease to determine the response to a particular therapy or drug. Over the past 25 years, CDx have facilitated a fundamental change in cancer therapeutics with several important cancer drugs using these assays to identify eligible patients.

A personalized medicine approach enhances treatment efficacy, minimizes adverse effects, and contributes to more efficient clinical trials by focusing on defined patient populations. Many CDx utilize advanced technology like the next-generation sequencing of DNA for comprehensive genomic profiling to analyze hundreds of disease-related genes at once using either a tissue biopsy or a liquid biopsy of blood or other body fluids. CDx often supply critical information to a healthcare provider as to whether a therapy can work for a particular patient, so these tests must be of high quality with demonstrated ability to provide accurate and reliable results.

As the application of CDx in oncology therapeutic development and clinical care has increased, so too has regulatory uncertainty. The FDA has long acknowledged difficulties that come with CDx development, including heavy evidentiary requirements and challenges aligning timelines with review of a therapeutic. In a recent survey diagnostic business leaders reported that regulatory uncertainty complicates long-range strategic planning and called for a balanced regulatory approach that upholds high standards for clinically deployed diagnostics, without unnecessarily stifling innovation.[iv]

Test systems that are not CDx but referenced in a therapy's labeling to provide information about patient risks and benefits also have value to personalized medicine. While biomarkers identified by these types

of test systems may not be a prerequisite to therapeutic use, they help providers understand response rates or overall survival in indicated patients.

Impact of the Proposed Reclassification Order

PMC understands that the reclassification order proposed by the FDA on November 24, 2025, would move certain nucleic acid-based test systems for use with a corresponding approved therapeutic product into Class II. We appreciate that the proposal is intended to decrease regulatory burden by allowing use of the 510(k) pathway for review. It is important to distinguish the future 510(k) pathway from current Premarket Approval (PMA) requirements. The move to reclassify oncology CDx into a Class II framework should ensure that special controls are sufficiently clear, specific, and consistently applied to serve as the primary mechanism for assuring patient safety, effectiveness, and clinical reliability. This requires articulating special controls with adequate operational specificity, including expectations related to clinical performance, lifecycle oversight, and post-market change management, to promote predictable implementation, protect patient safety, and preserve provider and payer confidence in FDA-authorized companion diagnostics while continuing to support innovation and patient access.

Tissue-based biopsy tests make up the majority of approved CDx, but liquid biopsy tests have emerged as important tools in precision medicine. Liquid biopsy-based technologies are especially valuable in advanced oncology to address the needs of patients who are too medically fragile to submit to tissue biopsy, when tissue biopsy materials have been depleted, and when tissue biopsy testing would be inappropriate because new mutations arising during tumor progression are being investigated. Liquid biopsy assays have been approved as CDx using the product codes proposed by the FDA for reclassification. PMC joins with BLOODPAC and other stakeholders in requesting the addition of liquid biopsy to the definition detailed in the proposed reclassification order to provide clarity and help expedite the availability of these critical technologies.

The 510(k) pathway is generally more cost-effective and typically results in shorter premarket review timelines for both FDA and industry. It will allow the focus to be on meeting the bar for equivalence with other approved tests that have established biomarkers and the flexibility to use predetermined change control plans, rather than another 510 (k) submission, for future modifications. With nearly 200 approved or cleared CDx available today,[v] the reclassification proposal may enable more manufacturers to develop these types tests such that patients would benefit from increased access to appropriately safe and effective tools.

Conclusion

Thank you for your commitment to ensuring that patients can access high-quality diagnostics to help inform their treatment. We look forward to working with you and your colleagues at FDA to facilitate timelier availability of these and other advances in personalized medicine. If you have any questions about the content of this letter, please contact me at 202-499-0986 or cbens@personalizedmedicinecoalition.org.

Sincerely,

Cynthia A. Bens
Senior Vice President, Public Policy

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[i] U.S Food & Drug Administration. *Immunology and Microbiology Devices; Reclassification of Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product; Proposed Amendment; Proposed Order; Request for Comments [Docket No. FDA-2025-N-4622].* November 25, 2025. https://www.federalregister.gov/documents/2025/11/25/2025-21071/immunology-and-microbiology-devices-reclassification-of-nucleic-acid-based-test-systems-for-use-with (accessed January 20, 2026).

[ii] Oliner, Kelly S., et. al *Challenges to Innovation Arising from Current Companion Diagnostic Regulations and Suggestions for Improvements.* Clin Cancer Res (2025) 31 (5): 795–800**.** March 1, 2025. https://doi.org/10.1158/1078-0432.CCR-24-2729 (accessed January 20, 2026).

[iii] McBrearty N, Bahal D, Platero S. *Fast-tracking drug development with biomarkers and companion diagnostics.* J Cancer Metastasis Treat. 2024;10:3. January 17, 2024. http://dx.doi.org/10.20517/2394-4722.2023.134 (accessed January 20, 2026).

[iv] Hersey, Sarah. et. al. *Precision medicine: What is so difficult? The interplay and complexities of pharmaceutical and diagnostic partnerships to deliver the promise of precision medicine.* The Journal of Precision Medicine. December 17, 2025. https://doi.org/10.1016/j.premed.2025.100027 (accessed January 20, 2026).

[v] U.S Food & Drug Administration. *List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools.* December 17, 2025.https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools (accessed January 20, 2026).