

**PMC Policy Committee Meeting**  
**Tuesday, April 24, 2018, 12:00 p.m. ET**

## **Business Meeting Materials Packet**

### **Contents:**

1. PMC Comment Letter on “Proposed Medicare Coverage Decision Memorandum for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer” (submitted January 17, 2018)
2. Rep. Swalwell’s Dear Colleague Letter Requesting Co-Sponsors for “Advancing Access to Precision Medicine Act” (H.R. 5062)
3. PMC’s Outside Witness Testimony on FY19 FDA Appropriations
4. PMC FY 2019 Appropriations Talking Points
5. Patient Advocacy Organization Working Group Overview
6. Pharmaceutical and Diagnostics Working Group Overview
7. Federal Register Notice – Tissue Agnostic Therapies in Oncology: Regulatory Considerations for Orphan Drug Designation; Public Workshop; Request for Comments
8. Abstract: Cost-Effectiveness of Multi-Gene Panel Sequencing (MGPS) for Advanced Non-Small Cell Lung Cancer (aNSCLC) Patients (accepted by ASCO)

### **Separate:**

1. 2018 BIO International Convention: Personalized Medicine and Diagnostics Track Agenda



January 17, 2018

Tamara Syrek Jensen, J.D.  
Director, Coverage & Analysis Group  
Centers for Medicare & Medicaid Services  
Mailstop S3-02-01  
7500 Security Blvd.  
Baltimore, MD 21244

Sent electronically

**RE: Proposed Medicare Coverage Decision Memorandum for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450N)**

Dear Ms. Syrek Jensen:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 200 institutions across the health care spectrum, appreciates the opportunity to submit comments regarding the Centers for Medicare & Medicaid Services (CMS)' Proposed Medicare Coverage Decision Memorandum for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer.

Personalized medicine is an evolving field that uses diagnostic tools to identify specific biological markers, often genetic, to help determine which medical treatments and procedures 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.

Personalized medicine is helping to shift the patient and provider experience away from trial-and-error and 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. As noted above, PMC's members are leading the way in personalized medicine and recommend that patients who may benefit from this approach undergo appropriate testing and tailored treatment as soon as possible during their clinical experiences.

In recent years, NGS technologies have played an essential role in advancing our understanding of altered genetic pathways involved in human cancer. PMC appreciates CMS' recognition that NGS is an important technology for identifying

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cancer patients who may benefit from a specific treatment path, and we applaud CMS' work with the Food and Drug Administration (FDA) to accelerate coverage for the FoundationOne CDx (F1CDx) through the Parallel Review Process. We commend the agencies on their approval and preliminary coverage for the F1CDx. High quality, validated genomic profiling assays accelerate patient access to precision approaches to cancer diagnosis and treatment. PMC supports timely finalization of the National Coverage Determination (NCD) for the F1CDx and encourages CMS to continue allowing product developers to pursue Parallel Review as a voluntary process.

We sense growing enthusiasm for the diagnostic innovation upon which personalized medicine depends. In order to capitalize on this opportunity, stakeholders must work toward agreement on a framework that lays out clear paths to coverage and payment, which in turn will encourage the investment that the field requires. Those policies will accelerate the pace of advancement in both diagnostics and personalized medicine. We appreciate therefore CMS' interest in putting in place guidance that will shape an industry with great potential to improve patient care and make the health system more efficient.

We are concerned, however, that the scope of the proposed decision memo for this National Coverage Analysis (NCA) interferes with current established care pathways and removes the flexibility some test developers have to quickly bring NGS technologies to market outside of the Parallel Review Process. We believe that both allow patients and providers to benefit from personalized medicine technologies. Our comments pertain to how the proposed policy, as written in the decision memo, would affect coverage for clinical testing services already employed in patient care and those that will be developed in the future, as well as the potential burden patient, providers, and product developers will face under the proposed coverage with evidence development (CED) requirements. PMC respectfully asks that you consider the following comments as you finalize this proposed decision memo and we would be honored to serve as a resource to CMS as you contemplate the implementation of broader coverage policies for diagnostic laboratory tests using NGS.

### **Statement of Neutrality**

Many of PMC's members will present their own responses to CMS 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 with respect to the proposed decision memo on NGS for Medicare beneficiaries with advanced cancer or related issues.

### **Criteria for National Coverage**

Under Section A of the proposed decision memo, to be granted full coverage patients must have recurrent, metastatic, or advanced stage IV cancer; cannot have been previously tested using the same NGS test; and must have decided to seek further cancer treatment. This language does not address coverage for NGS testing in patients with cancer at earlier stages. However, use of NGS-based testing,

including liquid biopsies, in patients with earlier stage cancer may have an even greater impact on survival, outcomes, and quality of life. If CMS moves forward with finalizing the NCA for other diagnostic laboratory tests using NGS in addition to the FICDx test, the agency should consider broadening the NCA to include coverage of testing performed in patients facing earlier stages of cancer and allow more than one test in an individual's lifetime to account for potential recurrence.

Section A of the proposed decision memo also describes the criteria for full coverage of a diagnostic laboratory test using NGS. PMC understands that the NCA will only extend full coverage to tests if they are FDA-approved companion in vitro diagnostics; are used in cancers with FDA-approved companion diagnostic indications; and provide FDA-approved reports of test results to the treating physicians specifying FDA-approved treatment options. We agree that tests meeting these criteria should receive full coverage but also acknowledge concerns raised by the American Medical Association and others in the medical community that the proposed national coverage criteria are restrictive and run counter to processes firmly established in medical practice.

Current local coverage determinations are based on the clinical usefulness of proven biomarkers independent of test methodologies and the status of their regulatory approval for marketing and labeling. Clinicians rely on research findings to help them assess and understand a given patient's disease and to guide treatment decision-making. Thus, in practice, new clinical oncology data often prompts guideline revisions and spontaneous adoption prior to FDA-indicated approval to allow physicians to provide patients with the best care based on the most up-to-date findings. The NCA will supersede these existing local coverage determinations, which currently provide coverage for clinically valid and medically necessary testing services. In addition, the criteria requiring an NGS-based test to have FDA approval for companion diagnostic indications would limit the ability of providers to use NGS tests that are recommended in clinical guidelines.

Diagnostic tests performed in clinical laboratories are reviewed using well-accepted processes for determining the analytical and clinical validity of tests and are subject to ongoing review by accreditation bodies and through statute. They are often included in prevention, screening and treatment guidelines for specific conditions that are developed by professional societies, the Agency for Healthcare Research and Quality (AHRQ), and the United States Preventive Services Task Force (USPSTF). If the proposed scope of coverage is not modified, the NCA will lead to blanket non-coverage determinations for many of these tests and services moving forward, making it difficult for patients to access care that reflects the most up-to-date science. A representative cross-section of PMC's membership urges CMS to modify the criteria for full coverage to better reflect established patterns of reimbursement and adoption of diagnostic testing in clinical practice.

### **Requirements for Coverage with Evidence Development (CED)**

In 2013, PMC provided feedback to CMS on the agency's revision of CED guidance. At that time, PMC called on CMS to maintain the use of CED only in circumstances where it would expand access for Medicare beneficiaries. PMC was concerned that the 2013 guideline revision signaled CMS' intent to utilize CED more regularly for new technologies and services and that CED could be applied in a manner

that impedes access to care by restricting the ability of providers to make decisions in the best interest of individual patients.

The Coalition's comments to CMS on CED also recognized that experience was gained from prior CED efforts. We observed that collaboration among stakeholders during the early stages of defining CED study designs, research protocols, and coverage decision-making was essential to successful implementation of CED. PMC's contention that broad participation throughout the CED process was particularly important in relation to personalized medicine, where science and clinical practice rapidly evolve and external expertise on appropriate research questions and study designs would be necessary.

Section B of the decision memo details the criteria for diagnostic NGS-based laboratory tests that would be considered for coverage under CED. CED is proposed when NGS tests for advanced cancer are FDA-cleared or -approved but no companion diagnostic indications currently exist. These tests must be registered in the National Institutes of Health (NIH) Genetic Testing Registry, and patients and furnishing laboratories must participate in a prospective consecutive registry, answering questions designed to compare patient outcomes, patient clinical characteristics, and initial clinical validation of the tests.

CED is also proposed for NGS tests that are not FDA-cleared or -approved, but coverage would be limited to participants in National Cancer Institute (NCI) clinical trials. We understand that these tests would be required to be registered in the NIH Genetic Testing Registry; be part of a trial in the NCI Clinical Trial Network; adhere to CED standards of integrity; have a written analysis plan; and address the same questions in the criteria for FDA-cleared or -approved tests designed to compare patient outcomes, patient clinical characteristics, and initial clinical validation of the tests.

In keeping with PMC's earlier comments to CMS in 2013 on its CED guidance, we believe the proposed CED criteria detailed for NGS diagnostic laboratory tests in advanced cancer are too restrictive, exclude alternative methods for data collection, burden study participants, and limit patient access. We doubt this was CMS' intention and we call on you to convene patients, providers, product developers, laboratories and other stakeholders to develop consensus on solutions to major issues impacting the larger community. We specifically recommend discussion of the need for flexibility in meeting CED requirements through the use of alternative data sources, the level of evidence sufficient for successful completion of CED and transitioning to full coverage, and how CMS plans to treat a gap in coverage for tests that were reimbursed prior to the NCA but will subsequently be denied coverage until a CED study is approved and underway.

## **Recommendations and Conclusion**

In summary, PMC recognizes and appreciates CMS' work with the FDA to reduce the time between FDA approval and Medicare coverage of the F1CDx through the voluntary Parallel Review Program. We urge you to finalize the NCD for this test, but strongly urge revision of the decision memo as it pertains to other tests using NGS technology for cancer if they are to be included in the final NCD. When revising the decision memo, we respectfully ask that CMS:

1. Prioritize testing using NGS technologies that aid in clinical care across numerous cancer types and stages by continuing to allow tests that do not meet the criteria in Section A to receive coverage.
2. Modify the scope of coverage proposed in the decision memo to minimize the effect it will have on reimbursement for clinical testing services already employed in the care of patients with early and advanced stage cancer, as well as tests that will be developed in the future.
3. Convene patients, providers, product developers, laboratories and other stakeholders to develop consensus on solutions to major issues with the proposed CED requirements.

Thank you for considering our comments. PMC welcomes the opportunity to serve as a resource for you in continuing to shape this policy so that it more effectively achieves the goal we share with CMS of delivering appropriate, efficient, and accessible health care to patients. If you have any questions about the content of this letter, please contact me at 202-589-1769 or [cbens@personalizedmedicinecoalition.org](mailto:cbens@personalizedmedicinecoalition.org).

Sincerely yours,



Cynthia A. Bens  
Senior Vice President, Public Policy

CC: Joseph Chin, M.D., M.S.  
Deputy Director, Coverage and Analysis Group  
Centers for Medicare & Medicaid Services

JoAnna Baldwin, M.S.  
Senior Technical Advisor, Coverage and Analysis Group  
Centers for Medicare & Medicaid Services

James Rollins, M.D., Ph.D.  
Director, Division of Items and Devices  
Centers for Medicare & Medicaid Services

Lori Ashby, M.A.  
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Katherine B. Szarama, Ph.D.  
Lead Analyst  
Centers for Medicare & Medicaid Services

FW: e-DearColleague: Support the Future of Medical Treatment:  
Cosponsor H.R. 5062, the Advancing Access to Precision Medicine Act

Fox, Lizzy <Lizzy.Fox@mail.house.gov>

Tue 3/6/2018 2:18 PM

To: Fox, Lizzy <Lizzy.Fox@mail.house.gov>;

Cc: Fox, Lizzy <Lizzy.Fox@mail.house.gov>;

FYI

**From:** e-Dear Colleague

**Sent:** Tuesday, March 6, 2018 12:06 PM

**To:** Fox, Lizzy <Lizzy.Fox@mail.house.gov>

**Subject:** e-DearColleague: Support the Future of Medical Treatment: Cosponsor H.R. 5062, the Advancing Access to Precision Medicine Act

## **Support the Future of Medical Treatment: Cosponsor H.R. 5062, the Advancing Access to Precision Medicine Act**

Sending Office: Honorable Eric Swalwell

Sent By: [Lizzy.Fox@mail.house.gov](mailto:Lizzy.Fox@mail.house.gov)

Request for  
Cosponsor(s)

### **Support the Future of Medical Treatment:**

#### **Cosponsor the *Advancing Access to Precision Medicine Act (HR 5062)***

*Supported by the Personalized Medicine Coalition, EveryLife Foundation for Rare Diseases, Biocom, the Advanced Medical Technology Association, the American Association of Cancer Research, and the American Society of Breast Surgeons.*

Cosponsors (as of 3/6/2018): Shimkus\* (R-IL), Peters\* (D-CA), Paulsen\* (R-MN), Vargas\* (D-CA), Soto (D-FL), Thompson (R-PA), Gallego (D-AZ), Fitzpatrick (R-PA), Norton (D-DC), Slaughter (D-NY)

Dear Colleague:

We urge you to join us to help improve patient outcomes and access to genetic and genomic testing by cosponsoring H.R. 5062, the *Advancing Access to Precision Medicine Act*.

Innovation in genomics has presented new opportunities to diagnose and treat genetic disorders like cancer and most rare diseases, as well as predict one's predisposition to a disease. Genetic and genomic tests have the potential to further the emerging field of precision medicine and to cut health care costs by facilitating better diagnoses and the consideration of preventive measures.

However, certain barriers, including the lack of insurance coverage and inability to see relevant health professionals, impede access to genetic and genomic testing. While technologies could bring a healthier America, achievements in this field will be limited in the future unless patients have affordable access to such testing. With the enactment of the *21st Century Cures Act*, which streamlines the drug and medical device approval process of the Food and Drug Administration and advances the Precision Medicine Initiative and Cancer Moonshot, further dialogue and analysis is needed to ensure innovative technologies can be effectively utilized.

Our bill would address some of these problems by directing the Department of Health and Human Services to enter into an agreement with the National Academy of Medicine to develop recommendations on how the federal government may reduce barriers to the utilization of genetic and genomic testing. The bill would also allow states to apply for an exception to the federal medical assistance percentage rate (FMAP), thereby providing them with more money, to provide whole genome sequencing clinical services for certain children on Medicaid who have an unresolved disease that is suspected to have a genetic cause. The purpose is to provide data regarding whether such services help settle a child's diagnostic odyssey, improve clinical outcomes, and ultimately reduce program expenditures. We believe that these actions will help support the transformation of our health care system to better focus on the uniqueness of each and every patient in the future.

Please join us in supporting these steps to improve access to genetic and genomic testing. If you would like to cosponsor the *Advancing Access to Precision Medicine Act* or have questions, please contact Lizzy Fox in Rep. Swalwell's office at [Lizzy.Fox@mail.house.gov](mailto:Lizzy.Fox@mail.house.gov), Brian Looser in Rep. Shimkus' office at [Brian.Looser@mail.house.gov](mailto:Brian.Looser@mail.house.gov), Anaïs Borja in Rep. Peters' office at [Anais.Borja@mail.house.gov](mailto:Anais.Borja@mail.house.gov), Andy Franke in Rep. Paulsen's office at [Andy.Franke@mail.house.gov](mailto:Andy.Franke@mail.house.gov), or Tim Walsh in Rep. Vargas' office at [Tim.Walsh@mail.house.gov](mailto:Tim.Walsh@mail.house.gov).

Sincerely,

Eric Swalwell  
Member of Congress

John Shimkus  
Member of Congress

Scott Peters  
Member of Congress

Erik Paulsen  
Member of Congress

Juan Vargas  
Member of Congress

**Related Legislative Issues**

**Selected legislative information:** HealthCare

## Related Bill Information

**Bill Type:** H.R.

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**Fiscal Year 2019 Agriculture, Rural Development, Food and Drug Administration, &  
Related Agencies Appropriations Testimony**  
**Cynthia A. Bens**  
**Senior Vice President, Public Policy**  
**Personalized Medicine Coalition**

March 30, 2018

Chairman Hoeven, Ranking Member Merkley and distinguished members of the subcommittee, the Personalized Medicine Coalition (PMC) appreciates the opportunity to submit testimony on the U.S. Food and Drug Administration (FDA)'s fiscal year (FY) 2019 appropriations. PMC is a nonprofit education and advocacy organization comprised of more than 200 institutions across the health care spectrum. PMC recognizes the crucial role the FDA plays in promoting medical product innovation. As the subcommittee begins work on the FY 2019 Agriculture, Rural Development, FDA, & Related Agencies Appropriations bill, we ask that you increase the FDA's budget authority for medical product activities by \$473 million as proposed in the President's FY 2019 budget request.

PMC supports FDA Commissioner Scott Gottlieb's plans for utilizing additional FY 2019 funding<sup>1</sup> to expedite the development of new therapies for patients with unmet medical needs; to advance the use of real-world evidence; to foster the growth of digital health technologies; and to enhance research on rare diseases. We believe that investing in these initiatives and strengthening the FDA's workforce will facilitate patients' access to personalized medicine products.

Personalized medicine, also called precision or individualized medicine, is an evolving field in which physicians use diagnostic tests to identify specific biological markers, often genetic, that help determine which medical treatments and procedures will work best for each patient. By combining this information with an individual's medical records, circumstances, and values, personalized medicine allows doctors and patients to develop targeted treatment and prevention plans.<sup>2</sup> Personalized health care has the capacity to detect the onset of disease at its earliest stages, pre-empt the progression of disease, and, at the same time, increase the efficiency of the health care system by improving quality, accessibility, and affordability.<sup>3</sup>

**I.) The Role of the FDA in Personalized Medicine**

Personalized medicine is a rapidly growing field. A 2015 study found that companies nearly doubled their R & D investment in personalized medicines over five years and expect to increase their investment by an additional third over the next five years.<sup>4</sup> According to the same study, biopharmaceutical researchers also predict a 69 percent increase in the number of personalized medicines in development over the next five years.

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<sup>1</sup> <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm596554.htm>

<sup>2</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf>

<sup>3</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf>

<sup>4</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc-phrma-personalized-medicine-investment-21.pdf>

The number of personalized medicines approved by the FDA per year has increased from 5 percent of new drugs in 2005<sup>5</sup> to 33 percent in 2017.<sup>6</sup> For the past four years, personalized medicines have accounted for more than a quarter of new drugs approved by the FDA each year.<sup>7</sup>

The FDA is the gateway for personalized medicines entering the market. FDA's Center for Devices and Radiological Health (CDRH), Center for Drug Evaluation and Research (CDER), and Center for Biologics Evaluation and Research (CBER) all have individual responsibilities for evaluating medical products for their safety and efficacy. As a more personalized approach to treatment has grown, new types of drugs, tools, technologies, and therapies using genetic information have challenged existing regulatory frameworks. In 2017, for example, FDA set six regulatory precedents including: the record approval of 16 new personalized medicine drugs; the approval of the first three gene therapies, two of which were cancer immunotherapies; the first approval of a tissue-agnostic cancer therapy; the first authorization for marketing of health-related genetic tests directly to consumers; the first approval of a personalized medicine biosimilar; and the first joint approval and coverage decision between the FDA and the Centers for Medicare & Medicaid Services (CMS) for a next-generation sequencing test.<sup>8</sup> Robust funding is needed to help the FDA keep pace with rapid biomedical innovation and facilitate access to personalized medicine.

## **II.) Facilitating the Development of New Personalized Medicine Products**

By passing the *21<sup>st</sup> Century Cures Act (The Cures Act)*, Congress acknowledged the need for an additional focus on and funding for FDA. The *Cures Act* authorized FDA to help further modernize drug, biological, and device product development and review, and to create greater efficiencies and predictability in product development and review. The *Cures Act* also improved the FDA's ability to hire and retain scientific, technical, and professional experts in specialized areas. As preventive, diagnostic, therapeutic, and analytical methods become more complex, these experts will help FDA approve novel products based on high-quality evidence. The following areas, which received attention from Congress during consideration of the *Cures Act*, present opportunities across the FDA to bolster personalized medicine.

### **Expediting Product Development**

Congress called on the FDA to establish one or more inter-center institutes to help develop and implement processes for coordination of activities in major disease areas between the drug, biologics, and device centers. FDA established the Oncology Center of Excellence (OCE) in January of 2017 to create a unified policy approach and clinical review for all drugs, biologics, and devices used in medical oncology. OCE leverages the combined talents and skills of all FDA regulatory scientists and reviewers who work in medical oncology product review and serves as a single point of contact for external stakeholders for FDA's work in cancer. OCE helps expedite the development of oncology and hematology medical products and supports an integrated approach to the clinical evaluation of drugs, biologics, and devices for the treatment of cancer. In its first year, OCE was essential to FDA's approval of two cell-based gene therapies and three in

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<sup>5</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf>

<sup>6</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM at FDA 2017 Progress Report.pdf>

<sup>7</sup> [http://www.personalizedmedicinecoalition.org/Resources/Personalized\\_Medicine\\_at\\_FDA\\_An\\_Annual\\_Research\\_Report](http://www.personalizedmedicinecoalition.org/Resources/Personalized_Medicine_at_FDA_An_Annual_Research_Report)

<sup>8</sup> [http://www.personalizedmedicinecoalition.org/Resources/Personalized\\_Medicine\\_at\\_FDA\\_An\\_Annual\\_Research\\_Report](http://www.personalizedmedicinecoalition.org/Resources/Personalized_Medicine_at_FDA_An_Annual_Research_Report)

vitro diagnostic tests. If properly resourced, the Center of Excellence model is one that could be transformative in other disease areas with unmet need.

### **Enhancing Research on Rare Diseases**

Identifying the biological markers of rare diseases presents great opportunity for new treatments and cures. FDA's Orphan Products Grants Program recently provided \$17 million in funding to support 15 new clinical trials on products for rare diseases, and for the first time the program funded natural history studies, or studies looking at patient experiences and the progression of symptoms over time.<sup>9</sup> Two of these studies examine biological markers and could provide key information for product development about how rare diseases progress.<sup>10</sup> Additional resources would help the FDA develop clinical trial networks to create an understanding of the natural history and clinical outcomes of rare diseases, which FDA would leverage when promising medical products are identified for patients.<sup>11</sup>

### **Fostering Digital Health Technologies**

Data-capturing technological devices, or digital health technologies, can play a key role in the collection of real-world evidence. Currently, FDA is piloting pre-certification, or one-time premarket review, for lower-risk digital health technologies, similar to the FDA's new approach to oversight of direct-to-consumer genetic health risk tests.<sup>12</sup> FDA would use the additional funding to create a Center of Excellence on Digital Health that would build new capacity to evaluate and recognize third-party certifiers as well as support a cybersecurity unit.<sup>13</sup> These efforts to streamline and design regulatory pathways around specific technologies will facilitate patient access to the latest technologies. The foundation laid at the FDA for digital health will become increasingly important for personalized medicine as patients assume a larger role in managing their own health care and are more informed by their ability to access their genomic data.

### **Advancing the Use of Real-World Evidence**

The use of medical data collected outside of a clinical trial, or real-world evidence, presents significant opportunities to improve patient access to personalized medicine. Because real-world evidence has the potential to provide information on populations that are not always captured in clinical trials conducted in traditional settings, the *Cures Act* required FDA to evaluate the potential use of real-world evidence to support the approval of new indications for already approved drugs or to help support or satisfy post-approval study requirements. In addition to the real-world evidence work already underway to fulfill the *Cures Act* provisions for drugs, the National Evaluation System for health Technology Program, which is directed by CDRH in collaboration with medical device stakeholders, promises to drive down the time and cost of real-world data collection and analysis for medical devices.<sup>14</sup> Despite enthusiasm for real-world

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<sup>9</sup> <https://blogs.fda.gov/fdavoices/index.php/2018/02/taking-new-steps-to-meet-the-challenges-of-rare-diseases-fda-marks-the-11th-rare-disease-day>

<sup>10</sup> <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm579375.htm>

<sup>11</sup> <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm596554.htm>

<sup>12</sup> <https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM592693.pdf>

<sup>13</sup> <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm596554.htm>

<sup>14</sup> <https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM592693.pdf>

evidence and efforts to establish a framework and methodologies for applying real-world evidence in the regulatory context, additional funding is needed to support systems that enable the FDA to use real-world evidence for purposes beyond adverse event monitoring.

The *Cures Act* included more than 50 sections requiring FDA involvement.<sup>15</sup> For FY 2019, the *Cures Act* authorized \$70 million for the FDA through the Innovation Account. Appropriating these funds is important, but we contend that this amount of funding alone is insufficient to fully support the agency. Activities that fall outside the scope of the *Cures Act* include CDRH's plans to develop final and draft guidances on next-generation sequencing and the co-development of diagnostic tests with therapeutic products.<sup>16</sup> These efforts to reduce uncertainties surrounding regulatory oversight of diagnostic tests will help streamline the path to market for personalized medicine products which are invariably informed by a diagnostic test.

### **III.) Conclusion**

PMC appreciates the opportunity to highlight the FDA's importance to the success of personalized medicine. Additional budget authority appropriations for the FDA in FY 2019 will help the agency maintain a highly skilled workforce that charts an efficient path for advancing innovative medical product development. The subcommittee's support for a \$473 million increase in budget authority appropriations will bring us closer to a future where every patient benefits from an individualized approach to health care. PMC looks forward to working with you as you contemplate the appropriate levels of funding for the FDA in FY 2019 and we will gladly provide additional information on the programs described in our testimony upon request.

#### Contact Information:

Cynthia A. Bens  
Senior Vice President, Public Policy  
Personalized Medicine Coalition  
1710 Rhode Island Ave. NW, Suite 700  
Washington, DC 20036  
[cbens@personalizedmedicinecoalition.org](mailto:cbens@personalizedmedicinecoalition.org)  
(202) 589-1769

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<sup>15</sup><https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/ScienceBoardtotheFoodandDrugAdministration/UCM556618.pdf>

<sup>16</sup> <https://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm580172.htm>

## Talking Points: FY 2019 Appropriations for the NIH and FDA

### NIH Funding

- **The Personalized Medicine Coalition requests that the National Institutes of Health (NIH) receive an increase of at least \$2.2 billion above the final Fiscal Year (FY) 2018 funding level, totaling at least \$38.4 billion**, to maintain the level trajectory of budget increases for the NIH of \$2 billion each year; account for biomedical inflation; and ensure that the Innovation Accounts provided through the 21st Century Cures Act supplement the agency's base budget through dedicated funding to specific programs, as intended.
- Investments made in **biomedical research** are critical for finding cures and treatments for diseases that affect millions of Americans. The NIH conducts research that is too expensive and risky for the private sector to undertake alone, and this research has led to major achievements in the understanding of rare diseases and disorders, as well as historically prevalent diseases like Alzheimer's, cancer, and Parkinson's.
- The NIH's **Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs** invest millions into health and life science companies creating new therapies. This funding incentivizes industry to conduct high-risk research on potential new drugs and therapies.<sup>1</sup>
- In addition to improving the lives of millions, NIH funding supports over 400,000 non-federal scientists and technical personnel at 2,500 research universities and facilities nationwide. The work of these individuals drives the demand for medical supplies and research equipment. NIH funding ripples far beyond its headquarters in Bethesda, Maryland, to benefit **researchers, manufacturers and suppliers** in every state.
- From 2003 to 2015, the NIH lost more than 20 percent of its purchasing power. This created a hyper-competitive environment in which less than 20 percent of grant applications for highly meritorious research are funded, making it difficult to retain and recruit new- and mid-career biomedical researchers.<sup>2</sup> In order to groom the next generation of researchers, the NIH launched the **Next Generation Researchers Initiative**. Additional funding will help the NIH allocate portions of its base budget to this program, which intends to increase support for early- and mid-career researchers to \$1.1 billion over five years.<sup>3</sup>

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<sup>1</sup> See <https://ncats.nih.gov/smallbusiness/priorities>

<sup>2</sup> <https://www.nih.gov/about-nih/who-we-are/nih-director/testimony-implementation-21st-century-cures-act-progress-path-forward-medical-innovation>

<sup>3</sup> <https://www.nih.gov/about-nih/who-we-are/nih-director/fiscal-year-2018-budget-request>

- The **All of Us™ Research Program** will collect genetic and health information from one million volunteers for a decades-long research project. To ensure a dataset inclusive of all Americans, in the past year the *All of Us™* Research program awarded its first four community partner awards to organizations well-positioned to engage and enroll communities usually underrepresented in biomedical research, including seniors, Hispanics and Latinos, African Americans, and the LGBTQ community.<sup>4</sup> This program will create an invaluable biomedical data set informing the development of new personalized medicines.
- The **Cancer Moonshot** has given 142 awards, each of which help establish national and international collaborations, to transform the way cancer research is conducted, such as the Partnership for Accelerating Cancer Therapies (PACT), a five-year public-private collaboration between the NIH and 11 leading biopharmaceutical companies to identify, develop and validate standardized biological markers of cancer to advance new immunotherapy treatments.<sup>5</sup> By sharing resources and research, these collaborations will facilitate new discoveries that bring treatment to cancer patients.
- After decades of NIH-funded research in genetics, gene editing is now possible. However, in order to develop new therapies utilizing this technology and hone its methods, more research and tools are needed. In January 2018, the NIH launched the **Somatic Cell Genome Editing program** to research these technologies and educate the scientific community.<sup>6</sup>
- Through the **Accelerating Medicines Partnership**, a public-private partnership between the NIH, the U.S. Food and Drug Administration (FDA), 12 biopharmaceutical and life science companies, and 13 non-profit organizations, the NIH is leading an effort to change the current model for the development of new diagnostics and treatments. Industry and non-profit participants fund 26% of the program, and the collaboration promises to shorten timelines, cut costs, and increase the success rates of new personalized medicines.<sup>7</sup>

### FDA Funding

- **The Personalized Medicine Coalition supports the President’s proposed increases of \$473 million in budget authority for medical product activities at the FDA with a total funding of \$3.3 billion (exclusive of \$2.5 billion in user fees) to strengthen the FDA’s workforce and advance the availability of innovative drugs and medical devices. The**

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<sup>4</sup> <https://www.nih.gov/about-nih/who-we-are/nih-director/testimony-implementation-21st-century-cures-act-progress-path-forward-medical-innovation>

<sup>5</sup> <https://www.nih.gov/about-nih/who-we-are/nih-director/testimony-implementation-21st-century-cures-act-progress-path-forward-medical-innovation>

<sup>6</sup> <https://www.nih.gov/news-events/news-releases/nih-launch-genome-editing-research-program>

<sup>7</sup> <https://www.nih.gov/research-training/accelerating-medicines-partnership-amp>

items proposed include: improvements in drug and device manufacturing, advances in the use of real-world evidence in medical product development, and revisions to the regulatory framework for digital health technology.<sup>8</sup>

- Investments in FDA’s staffing needs come at a critical time for personalized medicine. More than 80 percent of FDA’s budget is dedicated to personnel needs. Additional funding will ensure the agency can secure and retain the highly trained **workforce** required to carry out its mandate and strategic priorities through 2020.
- Thanks in part to user-fee funding, the annual number of novel devices approved by FDA quadrupled from 2009 to 2017.<sup>9</sup> The number of personalized medicines approved by FDA each year has also increased from 5% in 2005 to 26% in 2016.<sup>10</sup> Additional funding will allow FDA to **improve therapies available to patients and lower medical costs** by facilitating the development of new therapies for unmet medical needs, advancing the use of real-world evidence, and fostering the growth of digital health technologies.
- The use of real-world evidence presents significant opportunities to improve patient access to personalized medicine. The **National Evaluation System for health Technology (NEST)**, a program directed by the FDA Center for Devices and Radiological Health (CDRH) in collaboration with medical device stakeholders, promises to drive down the time and cost of real-world data collection and analysis.<sup>11</sup> However, additional funding is needed to support new systems at FDA enabling the agency to use real-world evidence in deciding on expanded use indications, new clearances, and new approvals.
- Using real-world evidence sometimes requires data from digital health technologies. Currently, FDA is piloting pre-certification, or one-time premarket review, for lower-risk digital health technologies, similar to the FDA’s new approach to oversight of direct-to-consumer genetic health risk tests.<sup>12</sup> FDA would use the additional funding to create a **Center of Excellence on Digital Health** that would build new capacity to evaluate and recognize third-party certifiers as well as support a cybersecurity unit.<sup>13</sup> These efforts to streamline and design regulatory pathways around specific technologies will facilitate patient access to the latest technologies.

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<sup>8</sup> See <https://strengthenfda.org/2018/03/03/making-the-case-the-alliances-ask-for-fy-19/>

<sup>9</sup> <https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM592693.pdf>

<sup>10</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf>

<sup>11</sup> <https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM592693.pdf>

<sup>12</sup> <https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM592693.pdf>

<sup>13</sup> <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm596554.htm>

- In accordance with priorities established in the 21<sup>st</sup> Century Cures Act, FDA is working to strengthen its relationships with the patient community and incorporate their perspectives into product development. For example, as part of its 2020 strategic priorities, CDRH intends to establish at least 10 **collaborative communities**, forums of public and private sector members including patients, to solve regulatory issues for medical devices.<sup>14</sup>
- In the coming year, CDRH plans to develop final and draft guidances on several issues related to personalized medicine, including next-generation sequencing and the co-development of diagnostics with therapeutic products.<sup>15</sup> These efforts to reduce uncertainties surrounding regulatory oversight will **streamline the path to market** for personalized medicine products.

### The Basics of Personalized Medicine

- **Definition of personalized medicine:** Personalized medicine, also called precision or individualized medicine, is an evolving field in which physicians use diagnostic tests to identify specific biological markers, often genetic, that help determine which medical treatments and procedures will work best for each patient. By combining this information with an individual's medical records, circumstances, and values, personalized medicine allows doctors and patients to develop targeted treatment and prevention plans.<sup>16</sup>
- **Benefits of personalized medicine:** Personalized health care has the capacity to detect the onset of disease at its earliest stages, pre-empt the progression of disease, and, at the same time, increase the efficiency of the health care system by improving quality, accessibility, and affordability.<sup>17</sup>
- **The challenge:** Bringing personalized medicine to every patient will require the health care system to transform away from one-size-fits-all, trial-and-error medicine toward a new, targeted approach that utilizes patients' molecular information to inform health care decisions.<sup>18</sup>

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<https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM592693.pdf>

15 <https://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm580172.htm>

16 <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf>

17 <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf>

18 <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf>

## The Growth of Personalized Medicine in Statistics

- In 2003, the NIH announced the completion of the Human Genome Project. Now, for the past four years, personalized medicines have accounted for more than one of every four new drugs approved by the FDA.<sup>19</sup>
- In 2017, FDA set six regulatory precedents, including the approval of the first three gene therapies, two of which were cancer immunotherapies, the first approval of a tissue agnostic indication for cancer therapy, first authorization for marketing of health-related genetic tests directly to consumers, first approval of a personalized medicine biosimilar, and the first FDA/CMS joint approval and coverage decision for a next-generation sequencing test.<sup>20</sup>
- Biopharmaceutical companies nearly doubled their R&D investment in personalized medicines over five years, and expect to increase their investment by an additional 1/3 over the next five years.<sup>21</sup>
- Biopharmaceutical researchers predict a 69% increase in the number of personalized medicines in development over the next five years.<sup>22</sup>
- A survey of leading manufacturers of personalized medicine companies identified scientific discovery as the biggest challenge facing personalized medicine, followed closely by regulatory and reimbursement barriers.<sup>23</sup>
- The number of personalized medicines approved by the FDA per year has increased from 5% of new molecular entities in 2005<sup>24</sup> to 33% in 2017.<sup>25</sup>

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<sup>19</sup> [http://www.personalizedmedicinecoalition.org/Resources/Personalized\\_Medicine\\_at\\_FDA\\_An\\_Annual\\_Research\\_Report](http://www.personalizedmedicinecoalition.org/Resources/Personalized_Medicine_at_FDA_An_Annual_Research_Report)

<sup>20</sup> [http://www.personalizedmedicinecoalition.org/Resources/Personalized\\_Medicine\\_at\\_FDA\\_An\\_Annual\\_Research\\_Report](http://www.personalizedmedicinecoalition.org/Resources/Personalized_Medicine_at_FDA_An_Annual_Research_Report)

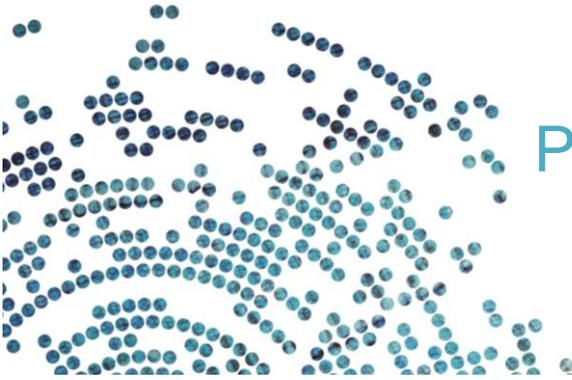
<sup>21</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc-phrma-personalized-medicine-investment-21.pdf>

<sup>22</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc-phrma-personalized-medicine-investment-21.pdf>

<sup>23</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc-phrma-personalized-medicine-investment-21.pdf>

<sup>24</sup> <http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf>

<sup>25</sup> [http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM\\_at\\_FDA\\_2017\\_Progress\\_Report.pdf](http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_2017_Progress_Report.pdf)



## Patient Advocacy Organization Working Group

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### OVERVIEW: PATIENT ENGAGEMENT AT PMC

As the health care system shifts from population-based to individualized care, decision-makers must develop patient-driven approaches and policies to ensure access to personalized medicine. Consequently, patient advocates and patient advocacy organizations are increasingly important partners for researchers, industry representatives and regulators advancing personalized medicine.

In order to integrate their point of view effectively into PMC's efforts to further personalized medicine, the Coalition is launching a Patient Advocacy Organization Working Group, which will inform PMC's policy strategy as well as develop shared messages and tools to empower individual patients to advocate for policies that bring personalized medicine closer to the patient.

### OBJECTIVES

As part of the group, which will be led by PMC's Senior Vice President, Public Policy, Cynthia A. Bens, participants will:

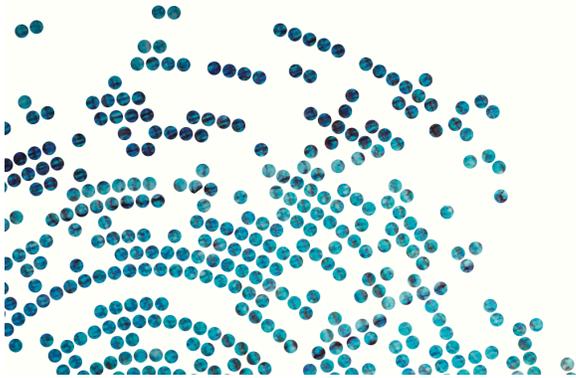
- Inform PMC's policy strategies and positions, including those related to research and development, regulatory oversight, reimbursement, and the delivery of personalized medicine in clinical settings
- Collaborate to align legislative priorities and leverage relationships with policymakers on topics such as appropriations
- Develop consistent, patient-centered messages that can be disseminated to their patient advocates and used in communications with policymakers
- Use PMC's policy updates to educate their members on personalized medicine issues
- Identify areas where PMC can grow its influence and membership
- Share information to foster partnerships with the Coalition and among working group members

### PARTICIPATION DETAILS

- The working group will convene via teleconference at least once per quarter, and as needed.
- Representatives from current PMC member organizations are invited to participate.
- The working group will complement the Coalition's other working groups convening health care providers and industry stakeholders on personalized medicine.

### CONTACT

To join or request more information, please contact David Davenport, Manager, Public Policy & Secretary to the Board at [ddavenport@personalizedmedicinecoalition.org](mailto:ddavenport@personalizedmedicinecoalition.org).



## Pharma and Diagnostics Working Group

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### OVERVIEW: INDUSTRY ENGAGEMENT AT PMC

Health care is in the midst of a shift from one-size-fits-all, trial-and-error medicine toward a new, targeted approach that utilizes patients' molecular characteristics to inform health care decisions. Completing this transformation will require solutions to nuanced regulatory and reimbursement challenges standing in the way of the rapid development and clinical adoption of more individualized care. Unfortunately, growing excitement for personalized medicine among patients, providers, and policymakers is tempered by increasing pressure to control costs across the U.S. health care system. To date, policy proposals aimed at reducing costs have failed to recognize personalized medicine's potential contributions to efficient, high-value care.

Policy conversations are beginning to focus more on designing the most effective care delivery models, developing appropriate measures of quality care, and identifying treatment outcomes that matter most to patients. In order to integrate these principles consistently into PMC's efforts to further personalized medicine, the Coalition is expanding its engagement with the Pharma and Diagnostics Working Group to inform PMC's policy strategy and advocacy activities related to research and development, regulatory oversight, reimbursement, payment reform, and health care quality.

### OBJECTIVES

As part of the group, which will be led by PMC's Senior Vice President, Public Policy, Cynthia A. Bens, and PMC's Senior Vice President, Science Policy, Daryl Pritchard, Ph.D., participants will:

- Formulate a comprehensive policy agenda that highlights policy challenges biopharmaceutical and diagnostic companies face in bringing personalized medicine interventions to patients
- Develop consistent messages based on this policy agenda that PMC can communicate to policymakers, patients, and the public
- Collaborate to align policy priorities among PMC members and leverage relationships with policymakers to advance legislation and regulations that promote the adoption of personalized medicine
- Identify areas where PMC can increase its influence and expand its membership
- Share information to foster partnerships among working group members

### PARTICIPATION DETAILS

- The working group will convene via teleconference at least once per quarter, and as needed
- Representatives from current PMC member organizations are invited to participate
- The working group will complement the Coalition's other working groups, which convene health care providers and patient advocacy organizations on personalized medicine

### CONTACT

To join or request more information, please contact David Davenport, Manager, Public Policy & Secretary to the Board at [ddavenport@personalizedmedicinecoalition.org](mailto:ddavenport@personalizedmedicinecoalition.org).

ANNUAL BURDEN ESTIMATES

Instrument	Number of respondents	Number of responses per respondent	Average burden hours per response	Total burden hours
Mandatory Grant Financial Report .....	900	4	5	18,000

*Estimated Total Annual Burden Hours:*

**Additional Information**

Copies of the proposed collection may be obtained by writing to the Administration for Children and Families, Office of Planning, Research and Evaluation, 330 C Street SW, Washington, DC 20201. Attention Reports Clearance Officer. All requests should be identified by the title of the information collection. Email address: [infocollection@acf.hhs.gov](mailto:infocollection@acf.hhs.gov).

**OMB Comment**

OMB is required to make a decision concerning the collection of information between 30 and 60 days after publication of this document in the **Federal Register**. Therefore, a comment is best assured of having its full effect if OMB receives it within 30 days of publication. Written comments and recommendations for the proposed information collection should be sent directly to the following: Office of Management and Budget, Paperwork Reduction Project, Email: [OIRA\\_SUBMISSION@OMB.EOP.GOV](mailto:OIRA_SUBMISSION@OMB.EOP.GOV). Attn: Desk Officer for the Administration for Children and Families.

**Robert Sargis,**  
*Reports Clearance Officer.*

[FR Doc. 2018-03976 Filed 2-26-18; 8:45 am]

**BILLING CODE P**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2017-N-3203]

**Wyeth Pharmaceuticals Inc. et al.; Withdrawal of Approval of 121 New Drug Applications and 161 Abbreviated New Drug Applications; Correction**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice; correction.

**SUMMARY:** The Food and Drug Administration (FDA) is correcting a notice that appeared in the **Federal Register** of June 21, 2017 (82 FR 28322). The document announced the withdrawal of approval of 121 new drug applications (NDAs) and 161

abbreviated new drug applications from multiple applicants, withdrawn as of July 21, 2017. The document indicated that FDA was withdrawing approval of NDA 204508, Clinolipid 20% (olive oil and soybean oil) USP, 16%/4%, after receiving a request from the NDA holder, Baxter Healthcare Corp. (Baxter), 32650 N Wilson Rd., Round Lake, IL 60073. Before the approval of NDA 204508 was withdrawn, Baxter informed FDA that it did not want the approval of this NDA withdrawn. Because Baxter timely requested that approval of this NDA not be withdrawn, the approval of NDA 204508 is still in effect.

**FOR FURTHER INFORMATION CONTACT:**

Florine Purdie, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6366, Silver Spring, MD 20993-0002, 301-796-3601.

**SUPPLEMENTARY INFORMATION:** In the **Federal Register** of Wednesday, June 21, 2017, appearing on page 28322 in FR Doc. 2017-12908, the following correction is made:

On page 28329, in table 1, the entry for NDA 204508 is removed.

Dated: February 21, 2018.

**Leslie Kux,**  
*Associate Commissioner for Policy.*

[FR Doc. 2018-03925 Filed 2-26-18; 8:45 am]

**BILLING CODE 4184-01-P**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

[Docket No. FDA-2018-N-0663]

**Tissue Agnostic Therapies in Oncology: Regulatory Considerations for Orphan Drug Designation; Public Workshop; Request for Comments**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice of public workshop; request for comments.

**SUMMARY:** The Food and Drug Administration (FDA or the Agency) is announcing the following public workshop entitled "Tissue Agnostic Therapies in Oncology: Regulatory

Considerations for Orphan Drug Designation." The purpose of the public workshop is to discuss factors FDA should consider when evaluating drugs for orphan designation that treat a tissue agnostic disease or condition in oncology, and additional factors related to orphan exclusivity FDA should consider when approving a product with a tissue agnostic indication.

**DATES:** The public workshop will be held on May 9, 2018, from 9 a.m. to 5 p.m. The public workshop may be extended or may end early depending on the level of public participation. Submit either electronic or written comments on this public workshop by June 8, 2018. See the **SUPPLEMENTARY INFORMATION** section for registration date and information.

**ADDRESSES:** The public workshop will be held at the FDA White Oak Campus, 10903 New Hampshire Ave., Building 31 Conference Center, the Great Room (Rm. 1503, Section A), Silver Spring, MD 20993-0002. Entrance for the public workshop participants (non-FDA employees) is through Building 1, where routine security check procedures will be performed. For parking and security information, please refer to <https://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>.

You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before June 8, 2018. The <https://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the end of June 8, 2018. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

*Electronic Submissions*

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are

solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

#### Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

*Instructions:* All submissions received must include the Docket No. FDA-2018-N-0663 for "Tissue Agnostic Therapies in Oncology: Regulatory Considerations for Orphan Drug Designation; Public Workshop; Request for Comments." Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- **Confidential Submissions**—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on

<https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

*Docket:* For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Nicole Wolanski, Office of Orphan Products Development, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 5210, Silver Spring, MD 20933, 301-796-6570, [OOPDOrphanEvents@fda.hhs.gov](mailto:OOPDOrphanEvents@fda.hhs.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. Background

The combination of government incentives, scientific advances, and the promise of commercial opportunity has fueled extraordinary investment in orphan drugs. Since the Orphan Drug Act was first passed in 1983, over 650 rare disease indications for drugs and biologics have been developed and approved for marketing. In fact, rare disease drug approvals have accounted for approximately 40 percent of the new molecular entities and therapeutic biologic products in the Center for Drug Evaluation and Research for the last several years.

Not only have we seen tremendous growth in the development of products for rare diseases, but the very landscape of rare disease product development is changing, with an increase in the development of targeted therapies, more interest in the development of biologics (including gene therapies), and tremendous growth in the oncology space. For example, in 2017 alone, FDA granted its first tissue agnostic approval (pembrolizumab for patients with unresectable or metastatic, microsatellite instability-high (MSI-H)

or mismatch repair deficient (dMMR) solid tumors) and first tissue agnostic orphan drug designations (larotrectinib and entrectinib, each for the treatment of solid tumors with NTRK-fusion proteins). FDA also approved the first cell-based gene therapy, KYMRIAH, for use in treating a rare pediatric cancer.

As advancements in genomics and precision medicine continue, FDA has been taking these new developments into account as it considers what constitutes a "disease or condition." For example, one question that has already arisen in oncology is whether a disease should be defined in a tissue/organ-specific or a tissue agnostic manner. Because the continued development of targeted therapies for molecularly defined groups has the potential to alter the landscape of orphan drug development, FDA is holding the public workshop to obtain input on the complex scientific and regulatory issues surrounding molecularly targeted drugs and biologics in oncology and the appropriate application of orphan drug incentives in that paradigm. This discussion will inform how the Agency can incorporate the latest science and drug development trends into the implementation of the Orphan Drug Act, all while continuing to reflect the goals intended by Congress.

##### II. Topics for Discussion at the Public Workshop

This public workshop will consist of both presentations and interactive panel discussions. The presentations will provide information to outline the goals of the workshop and help promote interactive discussions. Following the presentations, there will be a moderated discussion where speakers and additional panelists will be asked to provide their individual perspectives. The presentations and discussions will focus on several related topics. Topics will involve discussion of and seek input on factors FDA should consider when evaluating drugs for orphan designation that treat a tissue agnostic disease or condition in oncology and additional factors related to orphan exclusivity to consider when approving a product with a tissue agnostic indication. A detailed agenda will be posted on the following website in advance of the workshop: <https://www.fda.gov/NewsEvents/Meetings/ConferencesWorkshops/ucm592778.htm>.

##### III. Participating in the Public Workshop

*Registration:* To register for the public workshop, please visit the following website by April 25, 2018: <https://>

[www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm592778.htm](http://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm592778.htm). Please provide complete contact information for each attendee, including name, title, affiliation, address, email, and telephone.

Registration is free and based on space availability, with priority given to early registrants. Persons interested in attending this public workshop must register by April 25, 2018, 5 p.m. Eastern Time. Early registration is recommended because seating is limited; therefore, FDA may limit the number of participants from each organization. Registrants will receive confirmation when their registration has been received. If time and space permit, onsite registration on the day of the public workshop will be provided beginning an hour prior to the start of the meeting.

If you need special accommodations due to a disability, please contact Nicole Wolanski, at 301-796-6570, or [OOPDOrphanEvents@fda.hhs.gov](mailto:OOPDOrphanEvents@fda.hhs.gov) no later than April 25, 2018.

An agenda for the workshop and any other background materials will be made available 5 days before the workshop at <https://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm592778.htm>.

**Streaming Webcast of the Public Workshop:** For those unable to attend in person, FDA will provide a live webcast of the workshop. To register for the streaming webcast of the public workshop, please visit the following website by May 8, 2018: <https://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm592778.htm>.

If you have never attended a Connect Pro event before, test your connection at [https://collaboration.fda.gov/common/help/en/support/meeting\\_test.htm](https://collaboration.fda.gov/common/help/en/support/meeting_test.htm). To get a quick overview of the Connect Pro program, visit [https://www.adobe.com/go/connectpro\\_overview](https://www.adobe.com/go/connectpro_overview). FDA has verified the website addresses in this document, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

**Transcripts:** Please be advised that as soon as a transcript of the public workshop is available, it will be accessible at <https://www.regulations.gov>. It may be viewed at the Dockets Management Staff (see **ADDRESSES**). A link to the transcript will also be available on the internet at <https://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/ucm592778.htm>.

Dated: February 22, 2018.

**Leslie Kux,**

*Associate Commissioner for Policy.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Health Resources and Service Administration

#### Women's Preventive Services Guidelines

**AGENCY:** Health Resources and Services Administration (HRSA), Department of Health and Human Services (HHS).

**ACTION:** Notice.

**SUMMARY:** Applicable as of December 29, 2017, HRSA updated the HRSA-supported Women's Preventive Services Guidelines for purposes of health insurance coverage for preventive services that address health needs specific to women based on clinical recommendations from the Women's Preventive Services Initiative. This 2017 update adds two additional services—Screening for Diabetes Mellitus after Pregnancy and Screening for Urinary Incontinence—to the nine preventive services included in the 2016 update to the HRSA-supported Women's Preventive Services Guidelines. The nine services included in the 2016 update are as follows: Breast Cancer Screening for Average Risk Women, Breastfeeding Services and Supplies, Screening for Cervical Cancer, Contraception, Screening for Gestational Diabetes Mellitus, Screening for Human Immunodeficiency Virus Infection, Screening for Interpersonal and Domestic Violence, Counseling for Sexually Transmitted Infections, and Well-Woman Preventive Visits. This notice serves as an announcement of the decision to update the guidelines as listed below. Please see <https://www.hrsa.gov/womens-guidelines/index.html> for additional information.

**FOR FURTHER INFORMATION CONTACT:** Kimberly C. Sherman, Maternal and Child Health Bureau, HRSA at phone: (301) 443-0543; email: [wellwomancare@hrsa.gov](mailto:wellwomancare@hrsa.gov).

**SUPPLEMENTARY INFORMATION:** The complete set of updated 2017 HRSA-supported Women's Preventive Services Guidelines includes those that were accepted by the Acting HRSA Administrator on December 20, 2016, as well as two new services, Screening for Diabetes Mellitus After Pregnancy and Screening for Urinary Incontinence. For a complete listing and detailed

information about the December 20, 2016, updates, please see <https://www.federalregister.gov/documents/2016/12/27/2016-31129/Updating-the-hrsa-supported-womens-preventive-services-guidelines>. In addition, the December 20, 2016, updates, including information related to coverage of contraceptive services and exemption for objecting organizations from requirements related to the provision of contraceptive services, can be found at <https://www.hrsa.gov/womens-guidelines-2016/index.html>. Information regarding the two new services that were accepted by the HRSA Administrator on December 29, 2017, is set out below:

#### 1. Screening for Diabetes Mellitus After Pregnancy

The Women's Preventive Services Initiative recommends women with a history of gestational diabetes mellitus (GDM) who are not currently pregnant and who have not previously been diagnosed with type 2 diabetes mellitus should be screened for diabetes mellitus. Initial testing should ideally occur within the first year postpartum and can be conducted as early as 4–6 weeks postpartum.

Women with a negative initial postpartum screening test result should be rescreened at least every 3 years for a minimum of 10 years after pregnancy. For women with a positive postpartum screening test result, testing to confirm the diagnosis of diabetes is indicated regardless of the initial test (*e.g.*, oral glucose tolerance test, fasting plasma glucose, or hemoglobin A1c). Repeat testing is indicated in women who were screened with hemoglobin A1c in the first six months postpartum regardless of the result (see Implementation Considerations below).

#### 2. Screening for Urinary Incontinence

The Women's Preventive Services Initiative recommends screening women for urinary incontinence annually. Screening should ideally assess whether women experience urinary incontinence and whether it impacts their activities and quality of life. The Women's Preventive Services Initiative recommends referring women for further evaluation and treatment if indicated.

#### HRSA-Supported Women's Preventive Services Guidelines

The HRSA-supported Women's Preventive Services Guidelines were originally established in 2011 based on recommendations from an HHS commissioned study by the Institute of Medicine, now known as the National

**Character count:** 1999/2000

**Title:** Cost-effectiveness of multi-gene panel sequencing (MGPS) for advanced non-small cell lung cancer (aNSCLC) patients.

**Background:** MGPS, compared to single-marker genetic testing (SMGT), has the potential to identify more patients who could benefit from targeted therapies, but the impact on outcomes and total costs of care is uncertain. Our goal was to estimate the cost-effectiveness of MGPS vs SMGT in aNSCLC.

**Methods:** aNSCLC patients (stage IIIB or metastatic) diagnosed between 2011-2016 were identified from the Flatiron Health database, representing curated electronic health record-derived clinical information from >250 oncology practices nationwide. After stratifying patients in MGPS or SMGT cohorts, we analyzed the percentage of patients that receive targeted treatment; survival; and total costs of care. SMGT included *EGFR* and *ALK* testing; MGPS also allowed detection of *BRAF*, *RET*, *ROS1*, *HER2* and *MET* mutations. Cost data sources were the CMS Fee Schedule and 2017 ASP drug cost. We estimated the incremental cost-effectiveness ratio (ICER) and performed sensitivity analyses from a US payer perspective over a lifetime horizon, using a decision model.

**Results:** We identified 5688 aNSCLC patients receiving MGPS (n=875) or SMGT (n=4813), of which 22% tested positive for *EGFR* (18.5% MGPS, 17.3% SMGT) or *ALK* (3.59% MGPS, 3.78% SMGT). Among MGPS tested patients, an additional 8% were found to have *BRAF*, *RET*, *ROS1*, *HER2* or *MET* mutations. Of MGPS tested patients, 21% received targeted treatments vs 19% with SMGT. Observed survival was 1.14 life years (LYs) in SMGT vs 1.20 LYs in MGPS. Lifetime total costs were \$8,814 higher per patient for MGPS. The ICER of MGPS vs SMGT was \$148,478 per LY gained. If all patients with actionable mutations would receive targeted treatment in MGPS-guided care vs the proportion currently receiving targeted treatments under SMGT, the ICER would be \$110K/LY gained. Sensitivity analyses shows widely varying ICERs (\$139/LY to \$661,625/LY).

**Conclusion:** Based on data from a nationwide oncology patient database, MGPS has moderate cost-effectiveness compared to SMGT in aNSCLC patients. Efforts to increase the proportion of patients who receive targeted therapies would improve the cost-effectiveness of MGPS, assuming incremental costs and outcomes of targeted treatments remain unchanged.