PMC
PERSONALIZED
MEDICINE COALITION

February 23, 2015

The Honorable Lamar Alexander (R-TN)
Chairman
Senate Health, Education, Labor and Pensions Committee
455 Dirksen Senate Office Building
Washington, D.C. 20510

The Honorable Richard Burr (R-NC)
Member
Senate Health, Education, Labor and Pensions Committee
217 Russell Senate Office Building
Washington, D.C. 20510

Re: *Innovation for Healthier Americans: Identifying Opportunities for Meaningful Reform to Our Nation's Medical Product Discovery and Development*

Dear Senator Alexander and Senator Burr,

Thank you for engaging the community on the *Innovation for Healthier Americans* initiative. Your focus on improving public policies to promote the efficiency and effectiveness of medical product development is generating ideas that could greatly improve the quality of patient care in the United States.

The Personalized Medicine Coalition (PMC), representing innovators, scientists, patients, providers and payers, promotes the understanding and adoption of personalized medicine concepts, services and products to benefit patients and the health system. We thank the Committee for this opportunity to engage.

As you know, personalized medicine is an emerging field that uses diagnostic tools to identify specific biological markers, often genetic, that help determine which medical treatments and procedures will be 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 prevention and treatment plans, ultimately providing the right treatment to the right patient at the right time.

Our interest in the *Healthier Americans* initiative pertains to how personalized medicine can benefit the health care system by improving the quality, safety, accuracy and effectiveness of treatments. For example, in breast cancer, colorectal cancer and non-small cell lung cancer, diagnostic testing of tumor samples allows oncologists to target treatments to the particular biomarker(s) expressed by a given tumor. Testing improves the quality of the patient's care by providing information to help determine the most appropriate therapy for controlling the progression of the cancer. Furthermore, health care system spending can be reduced as considerable resources spent on ineffective treatments for a particular patient as well as the associated costs for visits to the doctor and the hospital are avoided. Newborn screening is another example of how personalized medicine benefits patients and the overall health system. Every newborn baby in the United States undergoes screening for genetic diseases that, if not detected within the first days of life, cause substantial morbidity and sometimes mortality. These tests save lives, reduce the costs of treating babies whose conditions would be undetected without screening and ultimately improve the overall health of the public.

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Scope, statements of neutrality and disclaimer

For personalized medicine to advance, PMC argues that policies should:

- incentivize the development of new, personalized approaches to care
- craft a predictable and flexible regulatory system that is responsive to new scientific discoveries and
- not disadvantage health care innovations through coverage and payment systems.

We are pleased that the Committee recognizes the importance of an appropriate regulatory structure to support personalized medicine. Since the white paper focuses primarily on regulatory issues, we will use this opportunity to restate some of our current concerns about that system.

As you know, last year, FDA signaled its intent to actively regulate laboratory developed tests (LDTs), a significant policy change for the field. PMC has analyzed the proposal and made suggestions to FDA. Many of those suggestions correspond to the questions posed in the white paper, and therefore, we highlight some of them below.

It should be noted that many of PMC's members will present their own responses to the Committee, and will actively advocate for those positions. To support the work of our member organizations, we therefore note the following disclaimer: nothing in this letter is intended to impact adversely in any way the ability of individual PMC members, alone or in combination, to pursue separate comments, litigation, or other remedies with respect to the responses to the Committee's questions or related issues.

PMC's response is focused exclusively on personalized medicine issues, including those related to molecular diagnostics, pharmacogenomic tests and targeted therapies, which are the hallmarks of personalized medicine.

We greatly appreciate the thoughtful and important questions that the Committee has raised, and at this time, we will only address the Committee's questions that are most applicable to personalized medicine. For clarity, we have restated the entire question for each of the questions we are addressing directly.

Does Congress need to re-examine the FDA's current decades-old standards in order to ensure that the agency is prepared to review the most cutting-edge medical products today and in the future? How do we ensure that the FDA is prepared to review the full range of medical products, including those that are the most novel, cutting-edge, and personalized for patients?

The FDA considers diagnostic tests medical devices, and therefore contends that these tests are regulated under the Federal Food, Drug and Cosmetic Act. Unfortunately, the current medical device regulatory framework does not appropriately address the unique challenges posed by diagnostic tests, which becomes even more important if FDA actively regulates personalized medicine LDTs.

For personalized medicine to advance, regulatory oversight must evolve. For example, novel diagnostic technologies, such as those that rely on next generation sequencing (NGS), hold great promise for advancing personalized medicine. NGS regulatory oversight represents a new frontier in regulatory processes. A single NGS test can identify multiple genetic variants. The results of the test could then lead to useful information about many different health conditions. Furthermore, while the NGS test itself might not change, the clinical application of the information provided by the test can change over time with additional knowledge about individual biomarkers and their clinical significance. Traditional methods of oversight for diagnostic tests that focus on the analytic and clinical performance of a single endpoint may be obsolete for these kinds of dynamic tools. In applying regulatory oversight, FDA must

seize the opportunity to provide meaningful yet flexible oversight of novel technical diagnostic platforms with dynamic clinical evaluative capabilities.

We are concerned that the current medical device statute, written in an earlier era, is too inflexible to allow FDA to adjust or modify the current standards for clearance or approval in order to encourage the development of personalized medicine tests or facilitate changes to them based on rapidly evolving clinical information. Innovation in the area of molecular diagnostics occurs at a much more rapid pace than for therapeutic products; thus, it is important that the regulatory framework allow for quick and efficient updates and improvements. To the extent that the FDA does not have the flexibility necessary to make this shift under current statutory authority, Congressional action might be necessary.

Given the advances in medical products, is it time to reassess whether separate centers are the right way to regulate medical products? Are there other ways of organizing the agency and regulatory pathways – based on disease areas, for example – that may be more efficient and effective?

For personalized medicine to move from bench to bedside, both the treatment and the diagnostic test used to target it must be cleared by separate centers within FDA. Most targeted treatments currently on the market are intended for the treatment of cancer. Reviewers of cancer drugs and diagnostic test kits developed to go with them are now very well coordinated; yet that coordination was informally developed over time. Because that coordination developed over time and through experience, not through formal rules, streamlined and predictable drug-diagnostic co-regulation does not often exist for targeted therapies in areas other than cancer. We suggest that FDA examine the efficiencies in the review of oncology drugs and diagnostics, and publish guidelines for co-regulation of other therapeutic areas. Such a step could improve the agency's efficiency in all therapeutic areas while working within its current structure.

How should the FDA rely on outside science when developing policy? How should FDA then communicate timely scientific and regulatory policy changes while still allowing for public comment and debate?

Very often in the field of personalized medicine, the medical progress in clinical research literature moves at a very fast pace. Those advances often benefit patients without FDA approval. FDA has signaled its intent to accept clinical literature when developing a regulatory framework for LDTs. We hope the agency continues to develop forward-thinking policies to incorporate the latest in clinical research into reviews, therefore continuing the path for personalized medicine to positively impact patient care. Where appropriate, FDA should rely upon data already in the clinical literature, and should not mandate new studies where adequate data already exist.

Regulatory policy changes should always be published as draft so that the public may comment on them. Only through an open process can unintended consequences be avoided.

Do the current legislative and regulatory policies regarding information sharing, communications, and labeling work?

In the field of personalized medicine, a great amount of fast-paced scientific information-sharing results in improvements in patient care. However, if current FDA medical device regulations are applied to LDTs, it is possible that patient care improvements could be slowed down significantly. Below, we explain two examples of why FDA medical device labeling does not necessarily fit LDTs, and make suggestions for how labeling issues for LDTs might be resolved.

Because the rules for device labeling conflict with Clinical Laboratory Improvement Amendments (CLIA) requirements for laboratory clinical consultation, and because LDTs are not marketed as physical

products in packages to which labels are readily affixed, FDA should provide a comprehensive explanation of how it would apply device-labeling requirements to LDTs. A laboratory should be permitted to fulfill any mandatory labeling requirements solely through its online directory of services. FDA should not require clinical laboratories to maintain labels or labeling in formats required for distributed/shipped products.

Current FDA device labeling regulations may also have negative consequences on the practice of medicine if applied to LDTs. Physician laboratory directors and laboratory medicine experts advise physicians on available tests, test results, and possible treatment decisions that follow testing as part of the practice of medicine and based on their medical training and expertise, upon which personalized medicine depends. Current device regulation may unintentionally impede physicians and laboratory medicine experts from effectively doing this aspect of their jobs.

Briefly, physicians and laboratory medicine experts routinely discuss options that may modify FDA-approved or cleared devices or the instructions for their use. When physicians and laboratory medicine experts are treated as manufacturers, such alternative uses cannot be discussed. When a test has been "labeled" for one use but is appropriate for another use, a manufacturer is, under almost all circumstances, prohibited from revealing that use, while physicians and laboratory medicine experts are still permitted to discuss and use them. We are concerned that the agency intends for such other uses to be treated as off-label until "labeling" requirements are met again based on the new intended use. Perhaps Congress could request that the FDA clarify the extent to which the agency intends for this prohibition to apply to physicians who, following developments in the scientific and clinical literature, identify alternative uses that could require changes to labels.

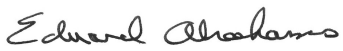
Conclusion

Thank you again for recognizing and tackling these important issues. PMC appreciates the opportunity to provide comments now and in the future as the Committee continues its work to identify the appropriate legislative balance between regulation, innovation and access to medical care.

We look forward to working with the Committee to develop legislation that will support personalized medicine innovations.

If you have any questions or require more information, please contact Amy M. Miller, Ph.D., by phone at 202-589-1769 or email at amiller@personalizedmedicinecoalition.org.

Sincerely yours,



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