PMC PERSONALIZED MEDICINE COALITION

PMC Policy Committee Meeting
Thursday, April 27, 2017, 12:00 p.m. ET

Business Meeting: Discussion Packet

Contents:

1. PMC Resolution for Increased Funding of Biomedical Research at the National Institutes of Health for FY 2017 and FY 2018

2. PMC comment letter (draft) to Representatives Bucshon and DeGette on the discussion draft of the Diagnostic Accuracy and Innovation Act (DAIA)

3. Copy of Discussion Draft: "A bill to provide for a study by the National Academy of Medicine on the use of genetic testing to improve health care"

4. Copy of H.R. 1313: "Preserving Employee Wellness Programs Act"

5. PMC analysis of H.R. 1313: "Lawmakers Weigh Merits of Allowing Wellness Programs to Require Genetic Data from Participants" in *Personalized Medicine in Brief*

6. PMC Legislative Update

7. PMC's comment letter to the Institute for Clinical and Economic Review (ICER) on ICER's proposed updates to its value assessment framework (submitted April 3, 2017)

PMC PERSONALIZED MEDICINE COALITION

Resolution for Increased Funding of Biomedical Research at the National Institutes of Health for FY 2017 and FY 2018

Whereas consistent and sufficient funding of biomedical research provides a foundation for innovation in personalized medicine, thereby reducing the burden of disease and improving the lives of millions of Americans (such as the National Institutes of Health's *All of Us*℠ Research Program— a public effort to build a national, large-scale research enterprise with one million or more volunteers to extend personalized medicine to all diseases); and

Whereas only consistent and sufficient funding for the National Institutes of Health will lead to breakthroughs for personalized medicine;

The Personalized Medicine Coalition calls on Congress:

- to pass a spending bill in 2017 that includes the funding outlined in the 21st Century Cures Act for the National Institutes of Health (NIH),

- to increase FY 2017 NIH funding by at least $2 billion, that is in addition to the funding outlined in the 21st Century Cures Act, and

- to increase FY 2018 NIH funding by an additional $2 billion, that is in addition to the funding outlined in the 21st Century Cures Act.

PMC
PERSONALIZED MEDICINE COALITION

April XX, 2017

The Honorable Larry Bucshon
1005 Longworth House Office Building
Washington, D.C. 20515

The Honorable Diana DeGette
2111 Rayburn House Office Building
Washington, D.C. 20515

Sent via email: Jeffrey.Lucas@mail.house.gov; Polly.Webster@mail.house.gov

Re: The Diagnostic Accuracy and Innovation Act

Dear Representatives Bucshon and DeGette:

On behalf of the Personalized Medicine Coalition (PMC), which represents innovators, scientists, patients, providers, and payers, to promote the understanding and adoption of personalized medicine concepts, services, and products for the benefit of patients and the health care system, I am writing to share PMC's thoughts on the recently released discussion draft of The Diagnostic Accuracy and Innovation Act (DAIA).

PMC defines personalized medicine as an emerging 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 and other clinical information, personalized medicine allows doctors and patients to develop targeted prevention and treatment plans. The goal is to provide the right treatment in the right dose to the right patient at the right time.

Our interest in the discussion draft of the DAIA pertains to how it can support this emerging field. We seek to ensure that the field can move forward in enhancing patient care and improving the quality, safety, accuracy, and effectiveness of treatments, with the acknowledgement that innovation and access should be balanced with patient safety.

Many of PMC's members will present their own responses to this discussion draft and will actively advocate for those positions. To support the work of our member organizations, we therefore note the following disclaimer: nothing in these comments is intended to impact adversely in any way the ability of individual PMC members, alone or in combination, to pursue separate comments. Additionally, PMC does not hold a position on whether laboratory-developed tests (LDTs) should be regulated by the Food and Drug Administration (FDA) or by the Clinical Laboratory Improvement Amendments (CLIA) program at the Centers for Medicare & Medicaid Services (CMS). PMC's comments are focused exclusively on personalized medicine issues and are designed to communicate areas of consensus with regard to LDTs, which may be applicable to in vitro clinical tests (IVCTs) as described in the discussion draft.

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Last year, PMC moderated a series of discussions on potential legislative solutions with representatives from much of the diagnostics community, including but not limited to those with an interest in personalized medicine. Six consensus principles emerged from these conversations, and we review them in the context of the draft legislation below. PMC is committed to working with you and the relevant stakeholders on finding additional areas of consensus.

1. **Protect Public Health Labs.**

   Public health labs should be protected by any regulatory paradigm, which means that sentinel, infectious disease, and public health labs must be able to design, deploy, and use rapidly developed diagnostics to address critical public health needs.

   DAIA clearly indicates that FDA review requirements will not apply to tests intended to be used solely for public health surveillance. We appreciate the inclusion of this language and urge you to retain it in any future versions of the legislation.

2. **Allow flexibility and efficiency when managing modifications.**

   As diagnostic device developers have long argued, the way test modifications are managed by a regulatory system should be flexible and efficient to allow diagnostic tests to evolve with the clinical science that underpins them.

   The draft legislation would give FDA the flexibility to approve products with associated processes for allowing certain modifications to take place without additional premarket review, as was proposed in FDA's recently released whitepaper on LDT regulation. PMC believes this is an important feature of the framework so that improvements can be made without delaying access and increasing regulatory costs.

3. **Mitigate regulatory burdens for government and industry.**

   To reduce burdens on government and industry, regulatory agencies should recognize when certain safeguards are already in place. These mitigation strategies can help regulatory bodies keep pace with the rapidly evolving science of personalized medicine diagnostic testing.

   The draft legislation attempts to clearly delineate between FDA and CLIA associated activities. However, the requirements associated with adverse event reporting to both FDA and CLIA may be duplicative and we encourage you to explore how the two reporting systems can be harmonized or unified to prevent unnecessary administrative burdens and confusion about what types of information should be reported to whom.

4. **Design a grandfathering provision for tests already on the market along with a risk classification system for novel tests.**

   Tech firm NextGxDx estimates that there are more than 60,000 personalized medicine diagnostics offered by about 300 labs, with another eight to 10 coming to market each business day. To manage such an enormous workload, a regulatory agency must design a grandfathering system that will allow most tests to remain on the market unless there is a compelling reason to remove them.

The draft legislation would grandfather all LDTs, but require that a certain set of high-risk tests submit data to FDA within five years of the bill's enactment. PMC believes this approach lessens the burdens on FDA and laboratories significantly, while also seeking to protect patients by reviewing information associated with tests that could cause a patient serious or irreversible harm, prolonged disability, or death. In addition, the draft legislation would prevent duplication of state activities for grandfathered tests by exempting tests that have already been reviewed by the New York State Department of Health.

Likewise, it is critical that a consistent and transparent risk classification system be described before enactment of new legislation governing the oversight of IVCTs. PMC suggests that the DAIA mandate that FDA, in concordance with CMS, develop and publish a risk classification system subject to public review before a new risk-based regulatory oversight framework goes into effect. We believe that appropriate detail is needed. For example, FDA should clearly describe what elements of a diagnostic test contribute to high, moderate, or low risk classification. FDA should also outline a process by which it will adapt risk classification for IVCTs that are related to submissions for further indications of approved tests and for modifications that may be made to various types of tests during their life cycles.

It is also critical that the DAIA clearly outlines a risk classification structure before the date of effect because compliance is predicated on a test's risk classification. Laboratories should not have to guess which tests will be classified into which risk pool. Knowing in advance which tests are likely to be classified into each risk pool will allow laboratories to prepare for and comply with new regulations, rather than leaving them to react to risk assessments during the implementation process.

5. **Ensure regulatory burdens reflect testing volumes.**

Regulatory burden must reflect testing volume. For example, diagnostics designed for rare and unmet needs should be given careful and different consideration to ensure that tests are developed for micro-markets.

PMC appreciates that the draft legislation designs a special pathway for tests that fill unmet needs, and provides carve-outs for custom IVCTs and tests for rare diseases. However, the definition of a test for rare diseases might not be sufficient, such as to exempt newborn screening programs. PMC urges you to consider exemption language to cover these situations. In addition, the definition of custom IVCT may lead to confusion as laboratories develop LDTs in the future. The definition specifies that the LDT must be designed to treat a unique pathology or physiological condition for which no other in vitro clinical test is available in the United States. However, it is unclear how laboratories should be expected to know whether other custom IVCTs exist of this sort. Furthermore, it is unclear how laboratories should act if another LDT is approved that is similar to other custom IVCTs and what type of timeline they would be expected to meet once their LDT no longer meets the narrow definition. We recommend working with stakeholders to find a reasonable solution to this issue.

6. **Accept valid scientific evidence for regulatory purposes — even if that evidence does not include data from a randomized controlled trial.**

Personalized medicine challenges how health care products and services are conceived, developed, regulated, covered, paid for, and used by physicians. Evidentiary requirements for regulatory review must also evolve. The community agrees that regarding diagnostics, valid scientific evidence should be acceptable for regulatory review, even when that evidence does not include data from randomized controlled trials.

The draft legislation outlines various types of evidence to demonstrate analytical and clinical validity, including peer-reviewed literature, clinical guidelines, case studies or histories, consensus standards, reference standards, etc. We urge you retain this language in any future version of the legislation.

PMC appreciates the opportunity to provide comments now and in the future as you continue to work toward the appropriate balance between regulation, innovation, and access to personalized medicine diagnostic tests. We look forward to working with you on revisions. If you have any questions about the content of this letter, please contact me at eabrahams@personalizedmedicinecoalition.org or 202-787-5907.

Sincerely yours,

Edward Abrahams

Edward Abrahams
President

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115TH CONGRESS
1ST SESSION

H. R. _____

To provide for a study by the National Academy of Medicine on the use of genetic testing to improve health care, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

Mr. SWALWELL of California introduced the following bill; which was referred to the Committee on _____

A BILL

To provide for a study by the National Academy of Medicine on the use of genetic testing to improve health care, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "_____ Act of 2017".

SEC. 2. NATIONAL ACADEMY OF MEDICINE STUDY.

(a) IN GENERAL.—Not later than 60 days after the date of the enactment of this Act, the Secretary of Health and Human Services shall enter into an arrangement with

the National Academy of Medicine under which the Academy agrees to study—

(1) how genetic testing may improve preventative care measures and precision medicine initiatives;

(2) how the Federal Government may—

(A) encourage the expansion of health insurance coverage of genetic testing, including diagnostic, predictive, presymptomatic, and whole genome sequencing;

(B) support the development of evidence for the clinical utility of genetic tests; and

(C) strengthen related workforce training efforts, including increasing the number of genetic counselors;

(3) how genetic testing may improve the health outcomes for all populations in the United States, including—

(A) those with a rare disease; and

(B) infants and children in intensive care;

(4) how the utilization of genetic testing may reduce health care expenditures over time;

(5) how the current coverage determination framework under the Medicare and Medicaid programs may restrain the use of genetic tests that may improve clinical outcomes; and

(6) how the Centers for Medicare & Medicaid Services may make coverage determinations that better suit a precision medicine approach to treatment.

(b) REPORT.—The arrangement under subsection (a) shall provide for submission by the National Academy of Medicine to the Secretary of Health and Human Services and Congress, not later than 20 months after the date of enactment of this Act, of a report on the results of the study.

AMENDMENT IN THE NATURE OF A SUBSTITUTE TO H.R. 1313 OFFERED BY MR. BYRNE

Strike all after the enacting clause and insert the following:

SECTION 1. SHORT TITLE.

This Act may be cited as the ''Preserving Employee Wellness Programs Act''.

SEC. 2. FINDINGS.

Congress finds that—

(1) Congress has a strong tradition of protecting and preserving employee workplace wellness programs, including programs that utilize a health risk assessment, biometric screening, or other resources to inform and empower employees in making healthier lifestyle choices;

(2) health promotion and prevention programs are a means to reduce the burden of chronic illness, improve health, and limit the growth of health care costs;

(3) in enacting the Patient Protection and Affordable Care Act (Public Law 111–148), Congress intended that employers would be permitted to im-

plement health promotion and prevention programs that provide incentives, rewards, rebates, surcharges, penalties, or other inducements related to wellness programs, including rewards of up to 50 percent off of insurance premiums for employees participating in programs designed to encourage healthier lifestyle choices; and

(4) Congress has struck an appropriate balance among employees, health care providers, and wellness plan sponsors to protect individual privacy and confidentiality in a wellness program which is designed to improve health outcomes.

SEC. 3. NONDISCRIMINATORY WORKPLACE WELLNESS PROGRAMS.

(a) UNIFORMITY ACROSS FEDERAL AGENCIES.—

(1) PROGRAMS OFFERED IN CONJUNCTION WITH AN EMPLOYER-SPONSORED HEALTH PLAN.—

(A) IN GENERAL.—Notwithstanding any other provision of law, a workplace wellness program and any program of health promotion or disease prevention offered by an employer in conjunction with an employer-sponsored health plan that complies with section 2705(j) of the Public Health Service Act (42 U.S.C. 300gg–4(j)) (and any regulations promulgated with re-

spect to such section by the Secretary of Labor, the Secretary of Health and Human Services, or the Secretary of the Treasury) shall be considered to be in compliance with the following provisions (to the extent such programs are subject to the Acts described in such provisions):

(i) the acceptable examinations and inquiries set forth in section 102(d)(4)(B) of the Americans with Disabilities Act of 1990 (42 U.S.C. 12112(d)(4)(B));

(ii) section 2705(d) of the Public Health Service Act (42 U.S.C. 300gg–4(d)); and

(iii) section 202(b)(2) of the Genetic Information Nondiscrimination Act of 2008 (42 U.S.C. 2000ff–1(b)(2)).

(B) SAFE HARBOR.—Notwithstanding any other provision of law, section 501(c)(2) of the Americans with Disabilities Act of 1990 (42 U.S.C. 12201(c)(2)) shall apply to any workplace wellness program or program of health promotion or disease prevention offered by an employer in conjunction with an employer-sponsored health plan.

(2) OTHER PROGRAMS OFFERING MORE FAVORABLE TREATMENT FOR ADVERSE HEALTH FACTORS.—Notwithstanding any other provision of law, a workplace wellness program and a program of health promotion or disease prevention offered by an employer that provides for more favorable treatment of individuals with adverse health factors as described in section 146.121(g) of title 45, Code of Federal Regulations (or any successor regulations) shall be considered to be in compliance with—

(A) the acceptable examinations and inquiries set forth in section 102(d)(4)(B) of the Americans with Disabilities Act of 1990 (42 U.S.C. 12112(d)(4)(B));

(B) section 2705(d) of the Public Health Service Act (42 U.S.C. 300gg–4(d)); and

(C) section 202(b)(2) of the Genetic Information Nondiscrimination Act of 2008 (42 U.S.C. 2000ff–1(b)(2)).

(3) PROGRAMS NOT OFFERED IN CONJUNCTION WITH AN EMPLOYER-SPONSORED HEALTH PLAN.—

(A) IN GENERAL.—Notwithstanding any other provision of law, a workplace wellness program and any program of health promotion or disease prevention offered by an employer

that are not offered in conjunction with an employer-sponsored health plan that is not described in section 2705(j) of the Public Health Service Act (42 U.S.C. 300gg–4(j)) that meet the requirement set forth in subparagraph (B) shall be considered to be in compliance with—

(i) the acceptable examinations and inquiries as set forth in section 102(d)(4)(B) of the Americans with Disabilities Act of 1990 (42 U.S.C. 12112(d)(4)(B));

(ii) section 2705(d) of the Public Health Service Act (42 U.S.C. 300gg–4(d)); and

(iii) section 202(b)(2) of the Genetic Information Nondiscrimination Act of 2008 (42 U.S.C. 2000ff–1(b)(2)).

(B) LIMITATION ON REWARDS.—The requirement referenced in subparagraph (A) is that any reward provided or offered by a program described in such subparagraph shall be less than or equal to the maximum reward amounts provided for by section 2705(j)(3)(A) of the Public Health Service Act (42 U.S.C. 300gg–4(j)(3)(A)), and any regulations promul-

gated with respect to such section by the Secretary of Labor, the Secretary of Health and Human Services, or the Secretary of the Treasury.

(b) COLLECTION OF INFORMATION.—Notwithstanding any other provision of law, the collection of information about the manifested disease or disorder of a family member shall not be considered an unlawful acquisition of genetic information with respect to another family member as part of a workplace wellness program described in subsection (a) offered by an employer (or in conjunction with an employer-sponsored health plan described in section 2705(j) of the Public Health Service Act (42 U.S.C. 300gg–4(j))) and shall not violate title I or title II of the Genetic Information Nondiscrimination Act of 2008 (Public Law 110–233). For purposes of the preceding sentence, the term ''family member''has the meaning given such term in section 201 of the Genetic Information Nondiscrimination Act (Public Law 110–233).

(c) RULE OF CONSTRUCTION.—Nothing in subsection (a)(1)(A) shall be construed to prevent an employer that is offering a wellness program to an employee from requiring such employee, within 45 days from the date the employee first has an opportunity to earn a reward, to request a reasonable alternative standard (or

waiver of the otherwise applicable standard). Nothing in subsection (a)(1)(A) shall be construed to prevent an employer from imposing a reasonable time period, based upon all the facts and circumstances, during which the employee must complete the reasonable alternative standard. Such a reasonable alternative standard (or waiver of the otherwise applicable standard) is provided for in section 2705(j)(3)(D) of the Public Health Service Act (42 U.S.C. 300 gg-4(j)(3)(D)) (and any regulations promulgated with respect to such section by the Secretary of Labor, the Secretary of Health and Human Services, or the Secretary of the Treasury).

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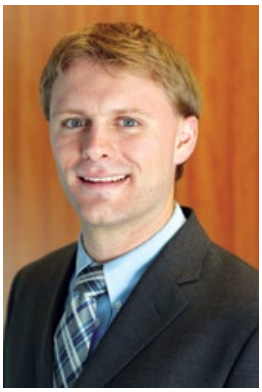
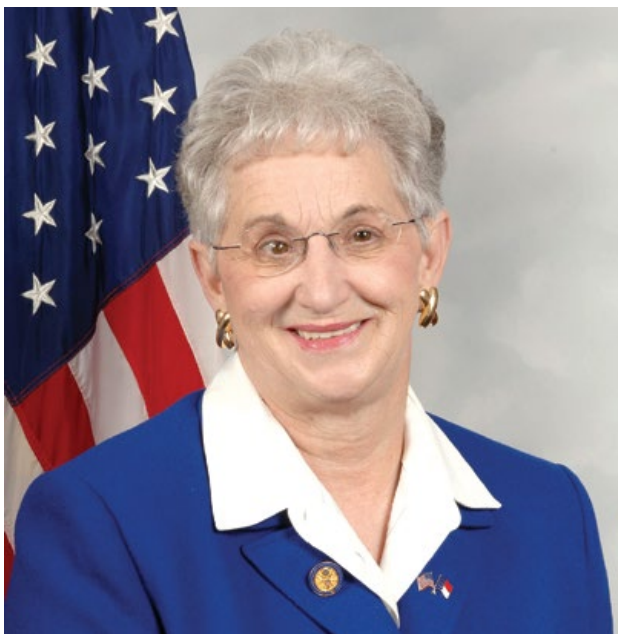
ISSUE BRIEF

Lawmakers Weigh Merits of Allowing Wellness Programs to Require Genetic Data From Participants



by Christopher Wells, PMC Communications Director

Passed in 2008, the Genetic Information Nondiscrimination Act (GINA), which provides a foundation for personalized medicine by assuring patients that sharing their genetic data cannot lead to discrimination, indicates that employers in the U.S. may "request, require or purchase" genetic information as part of employee wellness programs only if the employee provides "voluntary authorization." Nine years later, a House bill has ignited fierce debate about whether employers who require employees to provide genetic information to qualify for these programs, which are often associated with significant financial incentives, are violating the spirit of the law.



Rep. Virginia Foxx (R-NC) sponsored the Preserving Employee Wellness Programs Act (H.R. 1313) to "provide regulatory clarity so employers can have the certainty they need to continue offering their workers the option of participating in employee wellness programs." The Act has drawn criticism from genetic privacy advocates, who argue that the bill allows employers to coerce employees into sharing genetic information

Rep. Virginia Foxx (R-NC) sponsored the Preserving Employee Wellness Programs Act (H.R. 1313), which has passed through the U.S. House of Representatives' Committee on Education and the Workforce that she chairs, to "provide regulatory clarity so employers can have the certainty they need to continue offering their workers the option of participating in employee wellness programs." By explicitly stating that employers are permitted to require genetic information from employees who wish to participate in voluntary wellness programs, proponents say the bill would allow employers to facilitate personalized disease management plans for their employees without fearing that they are violating GINA's provisions. Genetic tests, they say, are comparable to other assessments already required from employees who volunteer to participate in the programs.

"Disease management programs, which are among the most successful wellness programs, often include diagnostic testing and screening for conditions or diseases," Foxx said in a statement posted on March 16, 2017. " … These types of tests and assessments—which only occur after an individual has voluntarily decided to participate in the program—help ensure the program effectively improves the health of those workers who choose to participate."

The law's critics, however, who include the Association for Molecular Pathology (AMP) and the American Society for Human Genetics (ASHG), see it differently. Pointing out that wellness programs offer financial incentives of as much as 30 percent of insurance premiums, they argue that requiring employees to provide genetic information in order to access those benefits coerces the provision of that information and conflicts with GINA's

> "People weigh this very carefully. They are reassured by the protections we tell them about, and they are frightened when protections are missing. This whole thing just adds uncertainty and fear."
>
> Robert C. Green, M.D., M.P.H., Geneticist, Brigham and Women's Hospital

effort to prevent employers from obtaining information that may be used for genetic discrimination. AMP and ASHG joined nearly 70 other organizations in signing a letter to oppose the bill.

"H.R.1313 would allow penalties up to a maximum averaging many thousands of dollars per year if employees decline to disclose information from genetic tests that they, their spouses, their children or their other family members have had, or if they do not reveal their families' medical histories," the letter reads. "Allowing penalties of this magnitude would clearly allow employers to coerce employees into revealing their private genetic information."

Researchers also point out that participants in genetic research are often unfamiliar with the nuances of GINA and are reassured by the law's nearly universal protections. Adding more caveats to GINA's protections, they say, could make it difficult for scientists to recruit participants in important new studies.

"People weigh this very carefully," said Robert C. Green, M.D., M.P.H., who regularly conducts personalized medicine studies in his role as a geneticist at Brigham and Women's Hospital. "They are reassured by the protections we tell them about, and they are frightened when protections are missing. This whole thing just adds uncertainty and fear."

Experts say Senate opposition to the bill, which legislators in the Committee on Education and the Workforce passed along party lines, will likely stifle its chances of becoming law.

PMC PERSONALIZED MEDICINE COALITION

Legislative Update
Personalized Medicine Coalition
115th Congress – 1st Session

Funding for Biomedical Research

2017 Appropriations: [Bill has not yet been released.]

President's 2018 Budget: America First: A Budget Blueprint to Make America Great Again (view budget)
On Department of Health and Human Services (excerpt): "The President's 2018 Budget requests $69.0 billion for HHS, a $15.1 billion or 17.9 percent decrease from the 2017 annualized CR level. This funding level excludes certain mandatory spending changes but includes additional funds for program integrity and implementing the 21st Century CURES Act" (page 21).
On National Institutes of Health (excerpt): "Reduces the National Institutes of Health's (NIH) spending relative to the 2017 annualized CR level by $5.8 billion to $25.9 billion. The Budget includes a major reorganization of NIH's Institutes and Centers to help focus resources on the highest priority research and training activities, including: eliminating the Fogarty International Center; consolidating the Agency for Healthcare Research and Quality within NIH; and other consolidations and structural changes across NIH organizations and activities. The Budget also reduces administrative costs and rebalance Federal contributions to research funding" (page 22).

Genetic Information Nondiscrimination Act (2008)

H.R. 1313: Preserving Employee Wellness Programs Act (view bill)
Sponsor: Rep. Virginia Foxx (R-NC-5); Co-Sponsors: 0 Democrats, 5 Republicans
Description: A bill to clarify rules relating to nondiscriminatory workplace wellness programs.
Summary: This bill exempts workplace wellness programs from: (1) limitations under the Americans with Disabilities Act of 1990 on medical examinations and inquiries of employees, (2) the prohibition on collecting genetic information in connection with issuing health insurance, and (3) limitations under the Genetic Information Nondiscrimination Act of 2008 on collecting the genetic information of employees or family members of employees. This exemption applies to workplace wellness programs that comply with limits on rewards for employees participating in the program.
Workplace wellness programs may provide for more favorable treatment of individuals with adverse health factors, such as a disability.
Collection of information about a disease or disorder of a family member as part of a workplace wellness program is not an unlawful acquisition of genetic information about another family member.
Status: March 8, 2017 – Ordered to be reported (amended) by the Yeas and Nays: 22 – 17 by the House Education and the Workforce Committee. On March 2, 2017 was deferred to the Committee on Education and the Workforce, in addition to the Committees on Energy and Commerce, and Ways and Means, for a period to be subsequently determined by the Speaker, in each case for consideration of such provisions as fall within the jurisdiction of the committee concerned. Introduced in House on March 2, 2017.

Diagnostic Regulation

Discussion Draft: [Diagnostic Accuracy and Innovation Act (DAIA)] (view draft)
Sponsors: Reps. Larry Bucshon (R-IN-8) and Diana DeGette (D-CO-1)

Description: A bill to establish a regulatory framework for in vitro clinical tests that advances innovation for patient benefit, protects patients, provides a predictable and timely path to market, ensures reasonable risk-based regulation, avoids duplicative regulation, advances precision medicine, and applies the same regulatory principles to the same activity regardless of entity type, and for other purposes.

Summary: "In vitro clinical tests (IVCTs) would have their own regulatory structure under the Food, Drug, and Cosmetic Act—separate and apart from traditional medical devices—that was developed with their unique attributes in mind from the outset. To eliminate duplicative regulation, the [DAIA] clearly establishes FDA jurisdiction over test development and manufacturing activities and maintains oversight of laboratory operations under the Centers for Medicare and Medicaid Services (CMS) pursuant to an updated Clinical Laboratory Improvement Amendments (CLIA) framework" (from Buschon's press release).

Status: March 20, 2017 – Discussion draft released by Representatives Buschon and DeGette, requesting feedback and comments on the discussion draft from stakeholders.

Research on the Use of Genetic Testing

Discussion Draft: [Untitled] (view bill)

Sponsor: Rep. Swalwell (D-CA-15)

Description: A bill to provide for a study by the National Academy of Medicine on the use of genetic testing to improve health care, and for other purposes.

Reimbursement & Coverage

S.794: Local Coverage Determination Clarification Act of 2017 (view bill)

Sponsor: Sen. Johnny Isakson (R-GA); Co-Sponsors: 2 Democrats, 1 Republican

Description: A bill to amend title XVIII of the Social Security Act in order to improve the process whereby Medicare administrative contractors issue local coverage determinations under the Medicare program, and for other purposes.

Status: March 30, 2017 – Introduced in Senate and referred to the Committee on Finance.

PMC
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April 3, 2017

ATTN: Steven D. Pearson, M.D., M.Sc.
President
Institute for Clinical and Economic Review
Two Liberty Square, Ninth Floor
Boston, MA 02109

by electronic delivery

Re: Proposed Updates to the Value Assessment Framework

Dear Dr. Pearson:

The Personalized Medicine Coalition (PMC) appreciates the opportunity to submit comments regarding the proposed updates to the Institute for Clinical and Economic Review (ICER)'s Value Assessment Framework outlined in the *Overview of the ICER Value Framework and Proposals for an Update for 2017 - 2018*.

Comprised of some 250 member institutions from every sector of the health care ecosystem, PMC, an education and advocacy organization representing patients, providers, payers, innovators, and scientists from around the world, promotes the understanding and adoption of personalized medicine concepts, services, and products to benefit patients and the health system.

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 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 prevention and treatment plans.

In responding to the overview, PMC is interested exclusively in the extent to which proposed updates to the Value Assessment Framework, herein called the Framework, reflect a consideration of the value of personalized medicine products, services, and concepts. Considerations related to personalized medicine can significantly impact the assessment of comparative clinical effectiveness and comparative value. Treatments that are targeted for use based on a patient's molecular characteristics and individual circumstances improve outcomes by allowing physicians to provide the most effective and safest treatment to each patient as early as possible. Doing so may in turn bring down costs by helping to avoid ineffective or harmful treatment options and reducing the downstream expenses associated with rapid disease progression and/or adverse events.

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To this end, PMC recommends that ICER recognize four overarching principles as it continues to consider concepts related to personalized medicine within the Framework:

1. Considerations related to personalized medicine can significantly impact comparative clinical effectiveness and value assessment
2. Diagnostic testing must be considered an integral part of the assessment of the value of treatment options where efficacy and/or safety information can be obtained
3. Methods for assessing value must consider emerging or evolving value elements over time
4. All stakeholders must continue to be engaged, and multiple perspectives must be integrated throughout the value assessment process in order to truly encompass and reflect value to the health care system

Statement of Neutrality

Many of PMC's members will present their own responses to ICER 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 updates to the value assessment Framework or related issues.

General Comments Regarding the Framework

We offer these comments about how the scope of the Framework may affect the field of personalized medicine in general.

The Population Perspective and Intended Uses

The Framework is intended to inform medical policies through a population-level perspective. ICER should not conflate, however, the impact of a therapy on patient health outcomes with the potential budget impact to any individual stakeholder or stakeholder group. We acknowledge ICER's statement that stakeholders focused on population-level decision-making, including payers and policymakers, are the intended audience of its value assessments. This does not discount or diminish, however, other key perspectives of value.

ICER should consider how assessing the value of different therapies to individual patients could facilitate improvements and efficiencies at the population level by getting the right medicine to a patient as early as possible. The final decision of which therapy, or combination of therapies, is most appropriate for a patient must (1) be left to the patient working with his or her provider, (2) involve consideration of the patient's clinical circumstances, and (3) involve consideration of a therapy's impact on a patient over the long term. Utilizing personalized medicine strategies, providers are able to identify individuals within larger populations that are more or less likely to respond to certain therapies. More precise treatments can reduce health care waste due to over- and/or under-treatment. Therefore, inclusion of these considerations should, on balance, lead to population-level efficacy, safety, and efficiency.

Appropriate Consideration of Diagnostic Tests

The Framework does not have a formal, consistent approach for the consideration of diagnostics intended to help guide treatment decisions where appropriate. Proposed changes to the Framework involve "evaluation of diagnostic tests and delivery system interventions by taking into account their unique nature or circumstances," but the Framework does not call on assessments to consider validation, utility, and economic impact of diagnostic tests. Guidelines for a consistent approach should consider (1) when diagnostics should/should not be included in assessment processes, (2) how (methodologically) diagnostics are included in the evidence review and economic evaluations, and (3) implications and standards for analyzing and reporting on patient subgroups.

Diagnostic testing in personalized medicine is a key step on the path to getting the right medicine to a patient as early as possible. It is imperative that the Framework considers testing an integral part of clinical decision-making by which efficacy and safety information of treatments can be obtained. The detection or measurement of biomarkers plays an important role in determining value across numerous clinical scenarios, many of which are subject to rapidly advancing scientific knowledge. The context of biomarkers within clinical scenarios must therefore be figured into the Framework's methodology. This is particularly important considering that ICER's updated Framework methods are set to be in place through 2019. Failure to explicitly address this important component of value at this time will undermine the usefulness and applicability of the Framework.

Process Updates Timeframe

The Framework's proposed updates will impact ICER evidence reports for the two-year period beginning in April 2017. Personalized medicine considerations will affect many, if not all, of ICER's value assessments going forward. ICER has already planned an assessment of, for example, ovarian cancer treatment, a disease state in which personalized medicine considerations will play a significant role.

The personalized medicine field is evolving too rapidly to accurately maintain a current assessment of treatment value with a two-year period between assessment reviews and updates. For example, shortly after ICER published its report on the value of non-small cell lung cancer treatments, technology advancements related to the use of biomarkers to help guide treatment decisions altered the value proposition for some treatments. For a value assessment Framework to remain useful over time, evidence reports need to be updated more routinely. ICER should provide criteria for when evidence reviews will be updated based on when new evidence, particularly on diagnostic stratification or other contextual factors, may come to light.

Comments Regarding Specific Update Proposals

Although ICER's proposed updates provide several incremental improvements toward consideration of personalized medicine practices and principles, further revision and refinement of the Framework is warranted to ensure the applicability and usefulness over the period in which the updated methodology will be implemented. Key areas are highlighted below.

Conceptual Structure of the ICER Framework

Inclusion of Evidence: Evidence review of clinical outcomes within the Framework is mostly limited to data accumulated for a product up to its market launch. This does not take into account emerging value factors and evidence after product launch. New and emerging technologies are disadvantaged in assessments where the Framework compares the value of established products vs. that of emerging products (e.g., pre-launch, new to market) since only early indicators of efficacy, safety, and value are acknowledged. A Framework that considers clinical outcomes continuously would likely provide a more informative assessment. The Framework should consistently employ methods to assess value at interim time points over a longer term using practice-based evidence wherever possible.

Framework Perspective: The proposed changes to the Framework's evaluation of "sustainable access to care" denote consideration of "long-term value" and "short-term affordability" for patients over discrete, predetermined time horizons. Instead, we recommend the Framework should examine a broad range of factors specific to each evidence review within the appropriate context to inform and support determination of high-value care. This may include short-term affordability and long-term value, but these factors alone are insufficient. Furthermore, the proposed change to evaluate sustainable access to high-value care falls short of a complete societal perspective of value. Elements such as systemic efficiency (i.e., getting the right treatment to a patient as early as possible), the contribution of innovation to further advancement of medicine, and the contribution of an innovation to an evolving care paradigm, etc., should be taken into consideration.

Comparative Clinical Effectiveness

We appreciate the steps ICER has taken to open the Framework to the inclusion of a broader range of data sources for assessments, extending beyond randomized clinical trials (RCTs) to include, for example, real-world evidence (RWE) and grey literature. The extent to which these can and will pragmatically be incorporated, however, is yet to be determined. RCTs have great value in determining clinical safety and efficacy of therapies, but value can differ when viewed through the lens of actual practice in the real-world situation. It is unclear how these data will be incorporated into ICER evaluations, models, and value metrics, but it is important that RWE carry an appropriate amount of weight in evaluations and that this is defined *a priori* in the Framework. Furthermore, conducting RCTs for some personalized medicines is not feasible because it would be impossible to develop a large enough cohort of patients with a rare genetic variant necessary to demonstrate clinical significance. In these cases, RWE is instrumental to the personalized medicine value assessment.

Incremental Cost-Effectiveness Analysis

ICER has proposed that it broaden its cost-effectiveness analyses, currently focused on cost per life year gained and cost per quality-adjusted life year (QALY), to permit consideration of alternate, or additional, cost-effectiveness and cost-utility measures, which may capture important disease-specific outcomes such as cost per consequence, when relevant. ICER has also proposed utilization of a range of incremental cost-effectiveness thresholds (section 4.6), which are determined based on the average weighting of 10 pre-specified elements of other benefits and contextual considerations voted on and ranked by an independent committee.

Despite the newly proposed approach to dynamically set thresholds determined by the elements of other benefits and contextual considerations, ICER's cost-effectiveness methods and thresholds do not adequately capture factors that are critical to demonstrating the value of personalized medicine, such as efficiency of treatment, avoidance of ineffective therapy, and reduction in adverse events. While the QALY's ability to provide a single measure of the "value" of a treatment makes it a commonly used metric for quantifying health benefits, patients do not receive treatments in isolation. Personalized medicine is a complex, multifaceted process with patients receiving care along a continuum — from diagnostic testing, clinician and genetic counselor consultation, disease management and monitoring, to medication therapy and hospitalization when necessary. The impact, value, and outcomes of each of these services rely on other steps within the continuum, as well as circumstances unique to each patient.

The consideration of services and treatments in silos does not recognize the complexity of individual patients, the reality of how personalized health care is delivered, or how these contribute to population health and well-being. Because health care is comprised of many, multifaceted interventions, a single measure cannot adequately capture true patient-centered value and the broad heterogeneity of clinically relevant characteristics and preferences across patients and diseases. PMC recommends disaggregating the single-value metric and considering a more comprehensive set of value elements that is inclusive and reflects personalized medicine services and concepts as well as individual patient circumstances.

Other Benefits or Disadvantages and Contextual Considerations

The Framework's proposed update document states that "Evaluations of long-term cost-effectiveness are made challenging because of the potential for evolution of devices/diagnostics and the attendant changes in cost, effectiveness, and the types of patients that will be treated." ICER answers this challenge by stating that the Framework will continue to incorporate specific unique approaches to evidence evaluation and use of diagnostic interventions as contextual considerations. While we appreciate that ICER recognizes the potential for these elements to impact value, and the potential for the evolution of treatment value due to devices/diagnostics, the consideration of "contextual considerations" falls short of adequately capturing the value factors that may be realized due to diagnostic tests. The 10 elements listed as contextual considerations do not encompass many value elements that may be relevant to diagnostic testing. For example, the list does not include determination of clinical trial eligibility or the opportunity to predict resistance to avoid ineffective treatment initially or make an informed change in treatment when patients fail to respond, all of which are critical elements of the evolving treatment landscape and help build evidence of value of novel drugs.

ICER proposes a visual analog scale to rate the importance of each of the 10 elements relative to one another [Section 4.2]. The independent public appraisal committee will rate these elements. It is not clear how elements will be weighted with consideration of the value, or how each impacts the overall value metric. The valuation will be unknown prior to the public meeting and unavailable for critical evaluation, comment, agreement/disagreement, or discourse in advance.

The proposed methodology of ranking the relative contribution to the overall long-term value of these contextual considerations, and other benefits and disadvantages, is subjective. Therefore, transparency on how ICER will ensure calibration across appraisal committees (i.e., Northeast CEPAC, Midwest CEPAC, California CTAF) to ensure consistency within and across committees is warranted. Moreover, the approach risks applying false weight and a false sense of precision and accuracy to these subjective value elements. Furthermore, the subjective relative ranking scale proposed by ICER may unfairly undervalue innovative personalized medicines, as it may be particularly problematic for newer treatments and therapies where evidence of societal and contextual benefits may be lacking. PMC strongly advocates that ICER devise a method to formally account for these elements explicitly in the Framework to assure that specific value elements are appropriately considered in evaluations and that they account for emerging evidence.

Report Development and Stakeholder Engagement

PMC commends ICER on efforts to further engage stakeholders on policy development, both in recent value assessment reports and in the proposed revisions to the Framework. Consideration of perspectives of all personalized medicine community stakeholders, especially patients, is critical to getting the right treatment to each patient as early in their care as possible. However, we respectfully note room for greater engagement that can more completely integrate patients and other critical stakeholders into the value assessment process.

Although patients and clinical experts will be permitted to attend and answer questions during appraisal committee meetings, they are still not voting members. This significantly undermines their voice in the process as the voting results are documented and reported in the final evidence report. Also, there is virtually no engagement with these stakeholders prior to formal meetings. Although efforts have been made to develop a patient engagement guide for participation and to partner with advocacy groups to conduct broad-based patient surveys to inform recent evaluations, participation remains largely ad hoc, and there is limited formal engagement in the process. In order to truly encompass and reflect clinical real-world experience and value to patients, these stakeholders' perspectives must be integrated throughout the process.

While we appreciate that the timelines for responding to proposed process updates have been increased, it is unclear if the extended comment period will apply to comments regarding assessment reports. PMC and its members can support ICER by providing in-depth, technical insights on the subject matter of ICER's evaluations. As a coalition, any insights we offer must represent the interests of a range of disciplines, and balance the perspectives and needs of our many members. Meanwhile, the field of personalized medicine is moving at an incredibly rapid pace. In this context, it is impractical for many stakeholders, particularly coalitions like PMC, to fully react to and respond to ICER's complex and lengthy reports in a short period of time. The length of open comment periods should reflect the importance, length, and complexity of the items to which the community is responding.

Furthermore, ICER does not seem to allow an adequate amount of time for their own review and reaction to stakeholder comments, particularly given the concurrent ongoing evaluations at any one time. PMC reiterates its recommendation that all comments submitted to ICER and their disposition should be publicly available. ICER should give its rationale for issues that it has chosen not to incorporate or address. Longer timelines for ICER's review and consideration of stakeholder input, and unlimited length requirements related to stakeholder feedback, will allow for greater community acceptance of assessments.

Economic Model Transparency

While ICER provides open comment periods for proposed Framework updates and value assessment reports, it does not make the economic models on which the comparative value is determined available for peer review or review by stakeholders. PMC believes that ICER should make the economic models it relies upon available so that anyone in the public can validate ICER's methods, data sources, and assumptions.

Conclusions/Recommendations

Personalized medicine has a profound impact on the comparative value of treatments, and now is the time for ICER to formally address, take into consideration, and clearly delineate the methods for integrating personalized medicine products, services, and concepts into the Framework as it impacts evaluations over the next two years. We hope this is the first step in public engagement on this topic, and we look forward to working with you to improve ICER's process so that the principles of personalized medicine, getting the right treatment to a patient as early in their care as possible, are incorporated into its work.

With these four overarching principles in mind, the Framework can better reflect and serve the needs of the health care community:

1. Considerations related to personalized medicine can significantly impact comparative clinical effectiveness and value assessment
2. Diagnostic testing must be considered an integral part of the assessment of the value of treatment options where efficacy and/or safety information can be obtained
3. Methods for assessing value must consider emerging or evolving value elements over time
4. All stakeholders must continue to be engaged, and multiple perspectives must be integrated throughout the value assessment process in order to truly encompass and reflect value to the health care system

PMC appreciates the opportunity to provide these comments. PMC and ICER are united by a shared goal of providing patients and health care providers with safe and effective technologies that will best serve the needs of patients and the health care system. If you have any questions about the content of this letter, please contact me at dpritchard@personalizedmedicinecoalition.org or (202) 787-5912. We look forward to further opportunities to provide feedback.

Sincerely yours,

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