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1225 New York Avenue, NW, Suite 450
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January 28, 2013

VIA electronic delivery

Ms. Marilyn Tavenner
Acting Administrator
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Draft Guidance – Coverage with Evidence Development

Dear Ms. Tavenner,

On behalf of the Personalized Medicine Coalition (the “PMC”), we are pleased to submit comments on the Draft Guidance for the Public, Industry, and Centers for Medicare & Medicaid Services (“CMS”) Staff - Coverage with Evidence Development (“CED”) in the Context of Coverage Decisions (“the Draft Guidance”).

Personalized medicine is the tailoring of medical treatments to the individual characteristics of each patient, and the ability to classify individuals into subpopulations based on their susceptibility to a particular disease or their responses to a specific treatment. Personalized medicine therefore has the potential to optimize delivery and dosing of treatments so patients can receive the most benefit with the least amount of risk, cutting out the difficulties of the current trial-and-error process many patients endure to find the correct diagnosis and treatment for their condition. Clinicians rely on research to help them assess and understand a given patient’s disease and provide information to guide treatment decision-making. *Accordingly, PMC supports the agency’s efforts to improve access to new medical technologies through CED when additional information is necessary to answer specific clinical questions related to a Medicare coverage decision, with the caveat that application of CED should not negatively affect the ability of clinicians to provide the optimal treatment to each patient based on the patient’s individualized needs.*

Representing more than 225 academic, industry, patient, provider, and payer organizations, PMC is an education and advocacy organization that promotes the understanding and adoption of personalized medicine to benefit patients and the health care system. Given the mission of PMC and the desires of the

patient and provider communities we bring together, the Coalition has a keen interest in the agency's Draft Guidance and the application of CED. Specifically, this letter comments on the following:

- CMS should adopt the principles included in the 2006 CED guidance document.
- CMS should ensure that review of evidence and decisions about evidence development are clearly explained and transparent.
- CMS should clarify the role of the Agency for Healthcare Research and Quality ("AHRQ") in the application of CED.
- CMS should consider additional factors for CED.

These points are described more fully below:

I. CMS should adopt the principles included in the 2006 CED guidance document.

In its prior CED guidance, CMS included a list of eight principles to guide the application of CED. These principles provided a useful benchmark for all stakeholders and helped ensure that CED would be applied when appropriate and would not unnecessarily limit access to the optimal diagnostic and therapeutic items and services for patients. In the Draft Guidance, CMS does not provide these or any guiding principles, saying only that "some" of the 2006 principles are now moot. PMC strongly disagrees. We believe that these principles continue to be relevant and urge CMS to adopt them in the final CED guidance that it issues. PMC believes a number of the 2006 principles are particularly important to include in the final CED guidance, as discussed below.

A. CMS should consider alternative processes to foster collaboration in CED implementation.

PMC recognizes that CMS has gained valuable experience since the 2006 guidance document and recommends that CMS learn from prior CED efforts. Specifically, PMC believes that collaboration among stakeholders in the early stages of the CED process is essential to successful implementation. Stakeholder collaboration during the early stages of coverage decision-making and defining study designs and research protocols will provide valuable expertise to the CED process. CMS should consider establishing partnerships to allow innovators and other stakeholders to help advance the agency's goals for CED. PMC believes that broad participation of innovators and stakeholders throughout the process will help maximize the likelihood of successful CED implementation. PMC believes this type of partnership will be particularly important in relation to personalized medicine, where science and clinical practice are rapidly evolving and gaining external expertise and input on appropriate research questions and study designs will be essential.

B. CMS should use CED infrequently and only to expand access for Medicare beneficiaries.

In the 2006 guidance document, CMS indicated that it expected to use CED infrequently and in general to expand access to technologies and treatments for Medicare beneficiaries. PMC is concerned that CMS's intent to apply CED to older existing technologies and services, as well as to new ones, is evidence of an approach that departs substantially from these principles and indicates an interest in expanding the scope of CED in a manner that could impede access to care and restrict the ability of providers to make decisions in the best interest of the individual patient. PMC urges CMS to clarify that this is not the case by reaffirming all of the 2006 principles in the final CED guidance.

Further, the suggestion in the draft guidance that coverage for a product or service under CED could end during the interval between the end of the CED study and the completion of the agency's review of the study data is inconsistent with the notion that CED is intended to improve the quality of patient care and should be rejected. If the item or service covered under CED was covered before and during the study, coverage should not be terminated at the end of the study until that agency determines, after completion of its review of the study data, that the evidence does not support continued coverage. If CED is appropriately applied, such instances should be extremely rare.

C. CMS should not use CED when other forms of coverage are justified by the available evidence.

The two principles discussed above are related to another principle from the 2006 guidance document, that CED will not be used to determine coverage when it is justified by the other forms of evidence. PMC believes that, with regard to personalized medicine technologies, in most cases there will be no need for CED because of how these products and services are developed, approved and used.

Drugs and medical devices, for example, are reviewed and approved by the Food and Drug Administration (FDA) after a rigorous process based on supporting clinical validity data with a well-defined intended use in the patient population. Traditionally, CMS has found that the evidence necessary for FDA's determination that a product is safe and effective is adequate to determine that a procedure, test or therapy is reasonable and necessary. Diagnostic tests performed in the clinical laboratory are reviewed using well-accepted processes for determining the analytical and clinical validity of a test and are subject to ongoing review by accreditation bodies and through statute. They are often included in prevention, screening and treatment guidelines of specific conditions that are developed by physician specialty societies, AHRQ and the United States Preventive Services Task Force (USPSTF). CED should not be used to reconsider the existing processes described above, which are firmly established in medical practice.

D. Application of CED should not duplicate the efforts of other federal agencies and entities that review and conduct research.

The 2006 guidance document also included principles providing that CED would not duplicate or replace the FDA's authority in assuring the safety, efficacy, and security of drugs and would not assume the role of the National Institute of Health (NIH) in fostering, managing, or prioritizing clinical trials. Since the 2006 guidance was issued, the Patient-Centered Outcomes Research Institute (PCORI) has taken an active role in conducting research to provide information about the best available evidence to help patients and their health care providers make more informed decisions. CMS should ensure that its application of CED does not duplicate the efforts of any of these entities. This is necessary in order to make the best use of limited public and private resources available for research, to avoid redundancy, and to not impose overlapping and unnecessary burdens on patients and their caregivers.

E. CMS should apply CED only within the National Coverage Determination (NCD) process.

Finally, the 2006 guidance provided that CED would occur within the NCD process. CMS does not explicitly confirm this in the Draft Guidance, and statements included in its earlier solicitation for public comment on CED in fact included statements that suggested the agency intended to apply CED in other contexts. We are concerned that expanding CED to the local level could result in multiple or even conflicting data collection requirements, increasing burden and costs, as well as uncertainty regarding coverage and access to new technologies that are under a CED in one jurisdiction but not another. PMC urges CMS to adhere to this 2006 principle and to apply CED only within the NCD process. For CED to be effective and achieve its goal of producing evidence that will enable the agency to make informed coverage decisions, CMS will need to rely on input from knowledgeable stakeholders from all sectors, including industry, with regard to both review of the available literature, in design of the CED studies, and an appropriate timeline to produce the data the agency needs. The best way to accomplish this is to apply CED within the NCD process, which is well-known, transparent, and open to the public. Furthermore, it removes uncertainty regarding beneficiaries' access to a technology in one coverage area while it is being investigated in another.

II. CMS should ensure that review of evidence and decisions about evidence development are clearly explained and transparent.

In addition to applying CED through the NCD process, CMS should make extra efforts to ensure that the analyses of evidence and decisions about evidence development methods leading to the initiation or end of CED are clearly explained and transparent. PMC appreciates the Draft Guidance CMS has provided on the application of CED and its efforts to update the existing guidance to reflect the agency's experience with CED over the years. PMC believes that it is vitally important to the successful application of CED that the criteria CMS intends to use to analyze clinical data and evidence collection activities are clearly explained. The Draft Guidance takes steps in this direction by setting forth clearly when CMS expects CED to apply and its standards for scientific integrity. There is much more, however, that PMC believes CMS could do to ensure that stakeholders understand how the CED process will apply. For example,

CMS does not provide guidance on how it plans to determine the evidentiary criteria for a particular application of CED or what the criteria might be. We suggest that evidentiary criteria will not be the same for each CED and suggest that CMS work with stakeholders at the beginning of the CED process to ensure that there is appropriate flexibility and that a single standard is not used for every research question. The Draft Guidance also does not explain how CMS will review data generated from CED studies to make coverage determinations, which leaves many concerned that an item or service could be caught in a perpetual CED cycle. Filling in the gaps in the Draft Guidance to ensure that all stakeholders know exactly the process CMS intends to follow when applying CED will minimize the uncertainty that can hinder patient access to the most appropriate treatment.

Moreover, CMS should make the entire CED process transparent – from the decision to invoke CED, to the development of the study design, to the decision to end a study, and finally to the process for using the new evidence to make a coverage determination. We urge broad stakeholder engagement, including those from all sectors of personalized medicine. CMS discusses transparency in the Draft Guidance with regard to publication of the results of CED studies but by the time clinical literature is published, the opportunity for CMS to benefit from the knowledge and experience of stakeholders will have passed. The process must be transparent from the very beginning in order to ensure that CED is applied only for the most appropriate items and services, and in a manner that will not impede beneficiary access and will generate the data the agency needs to make coverage determinations.

III. CMS should clarify the role of AHRQ and the type of assistance it will provide.

CMS makes clear in the Draft Guidance that the sole basis for its authority to apply CED is the statutory authority to cover items and services that are reasonable and necessary to carry out research conducted pursuant to AHRQ’s authority under section 1142 of the Social Security Act. CMS describes the ways in which AHRQ’s authority and resources complement CMS’s interests in using CED, and CMS says that it believes that AHRQ’s role “will continue to develop.” Given that the statutory authority for CED is premised on research conducted or supported by AHRQ, PMC believes it is important for CMS to clarify the role of AHRQ in the application of CED. In particular, in light of the burdens of CED on all stakeholders, PMC hopes that CMS will provide more concrete guidance on the types of public/private partnerships AHRQ may establish to financially support CED studies. PMC also thinks it is important to ensure that AHRQ’s involvement in the CED process does not inhibit transparency, reduce opportunities for the involvement of knowledgeable stakeholders, or restrict access to non-government experts.

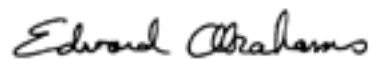
IV. CMS should consider additional factors for CED.

PMC requests that the draft guidance be altered to ensure that Medicare beneficiaries have access to life saving technologies and that physicians have the flexibility to practice medicine in the way that is most suitable for the individual patient. PMC has long advocated for research that improves the evidence-base on which medical decisions are made. We urge CMS to recognize that the evidence threshold to invoke CED should include factors such as patient preferences and quality of life measures among others. Personalized medicine is a fast-moving field. We learn more each day about how to focus treatments on those who will benefit, saving time, expense

and exposure for those who will not. We urge CMS to consider how to incorporate new evidence into CED decisions as new evidence may be published after a CED decision is made. Many personalized medicine technologies are new and evidence to support use of them may develop over time. We therefore ask that CMS allow all beneficiaries to have access to an item or service while it is under a CED. This will signal to patients and innovators that this policy is designed as intended: to improve patient care.

PMC appreciates the opportunity to provide comments on the Draft Guidance. If you have any questions about these comments, please contact Amy Miller at 202-589-1770, or via electronic mail to amiller@personalizedmedicinecoalition.org.

Sincerely yours,

A handwritten signature in cursive script that reads "Edward Abrahams".

Edward Abrahams, Ph.D.
President
Personalized Medicine Coalition