January 28, 2013

Louis Jacques, MD
Director, Coverage and Analysis Group
Office of Clinical Standards and Quality
Centers for Medicare & Medicaid Services
Mail Stop S3-02-01
7500 Security Boulevard
Baltimore, MD 21244

RE: Coverage with Evidence Development (CED) Draft Guidance Document

Dear Dr. Jacques:

The Advanced Medical Technology Association ("AdvaMed") appreciates this opportunity to comment on the Centers for Medicare & Medicaid Services’ ("CMS") draft guidance document on Coverage with Evidence Development ("CED") in the Context of Coverage Decisions.¹

AdvaMed’s member companies produce the life-saving and life-enhancing medical devices, diagnostic products and health information systems that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. AdvaMed members range from the largest to the smallest medical technology innovators and companies. Our members are impacted by the process CMS uses to determine whether an item or service meets the evidentiary standard to be found “reasonable and necessary,” and thus included in the Medicare benefit package.

The medical device industry has supported evidence-based coverage policy, and we appreciate the challenges faced by CMS in trying to improve the national coverage determination process. We also recognize that Medicare beneficiaries are unique and what is most appropriate for an “average” individual may not be the best option for all individuals. A coverage process that does not recognize these differences may result in more limited access to quality care for Medicare beneficiaries.

Medicare beneficiaries’ quality of care depends on access to the best treatments appropriate to their needs—including new treatments. Therefore, coverage with evidence development should promote patient access to advanced medical technologies, and should not discourage innovation. A coverage process that delays patient access to new technologies through excessive requirements, such as mandating the design of clinical trials or requiring burdensome data collection beyond what is necessary creates greater uncertainty regarding coverage and ultimately harms beneficiaries.

In the past, we have submitted a number of CED-related comments to CMS. In 2012, we offered comments on CMS’ open solicitation for CED comments, as well as on several proposed National Coverage Determinations (“NCD”) that either proposed or required CED and contained broader implications for the medical device industry beyond the item or service being considered for coverage in the particular NCD.

We have a number of concerns with the draft CED guidance document, as outlined in detail below. When CMS solicited comments on CED in November of 2011, the Agency’s stated intent was to revise the existing CED guidance with an eye toward “lessons learned” in order to improve the application of CED. We are primarily concerned that the revised, draft document does not further this goal, but rather creates more ambiguity than clarity regarding the application of CED.

Additionally, the draft CED guidance implies that the available evidence generated in order to achieve Food and Drug Administration (FDA) approval or clearance will rarely be sufficient for Medicare coverage, and coverage with evidence development will become the more common pathway to attaining Medicare coverage.

1. Additional Studies Will Frequently Be Required for Medicare Coverage

The draft CED guidance document presents four factors that serve as examples of when Medicare will consider applying CED:

- Relevance to health outcomes in the Medicare population
- Representativeness of available evidence
- Evolution and reevaluation of evidence base
- Generalizability of study results to typical settings

Two of these factors (the second and the fourth) relate to the generalizability of evidence. Based on these factors, which CMS considers illustrative of situations that would require the development of additional data, CMS seems to state that FDA-approval trials that did not include a population that reflected the demographic traits of Medicare enrollees (by age, sex, minority, and disability status) in the study would be grounds for CED – because the evidence is not
sufficient for Medicare coverage since the results of the study would not be considered to be
generalizable to the Medicare population. CMS also appears to state that FDA-approval trials
conducted in settings such as academic health centers with high quality care and research
capabilities that differ from the typical settings in which a Medicare beneficiary receives care
would also not be sufficient for coverage, and that CED would be required for coverage.

Medicare beneficiaries often are not eligible to participate in certain clinical trials based on their
age or the existence of comorbidities or other complicating factors. However, we do not believe
that these circumstances should automatically lead to a determination that the evidence is
insufficient to meet the reasonable and necessary standard for coverage following FDA approval
or clearance and that CED would be required. In the past, these types of trials have often been
adequate to make certain generalizations and to reach positive coverage determinations. CED
should continue to be used only in limited circumstances where the only alternative is non-
coverage.

2. Reinstatement of the Eight Principles Governing Application of CED from 2006
Guidance Document

CMS’ 2006 CED guidance document contained eight principles governing the application of
CED, which are conspicuously absent in the revised CED guidance document:

1. NCDs requiring CED will occur within the NCD process, which is transparent and open
to public comment.
2. CED will not be used when other forms of coverage are justified by the available
evidence.
3. CED will in general expand access to technologies and treatments for Medicare
beneficiaries.
4. CMS expects to use CED infrequently.
5. CED will lead to the production of evidence complementary to existing medical evidence.
6. CED will not duplicate or replace FDA’s authority in assuring the safety, efficacy and
security of drugs, biological products and devices.
7. CED will not assume NIH’s role in fostering, managing or prioritizing clinical trials.
8. Any application of CED will be consistent with Federal laws, regulations and patient
protections.

AdvaMed has supported these principles, particularly as they relate to the infrequent use of CED,
and then, only to expand access to technologies and treatments for Medicare beneficiaries. These
principles support Medicare’s stated goal of protecting beneficiary access to innovative items and
services. The removal of the principles adds to our concerns, expressed in detail throughout this
letter, regarding ambiguity and lack of clear guidance in the revised, draft CED guidance
document. We recommend that CMS restore these eight principles in a final, revised CED
guidance document.
3. **Use of CED to Evaluate the Clinical Effectiveness of Older, Established Technologies**

The draft CED guidance raises concerns regarding the evolution and reevaluation of the evidence base. We understand that changes in the body of evidence may occur over time and those changes may affect coverage decisions regarding currently covered technologies. However, if CMS reverses a coverage determination of a long-established FDA-approved technology and then invokes CED to gather evidence on a prospective basis, it thus results in non-coverage for existing patients who are receiving the treatment (item or service). Patients receiving the treatment, based on the clinical judgment of their physician, could suffer a hardship if denied access to the treatment. Medicare beneficiaries would be covered only if they lived in an area that allowed them to participate in a clinical trial, on a prospective basis. Such an approach is not in the best interest of beneficiaries for whom a physician has determined that the item or service is reasonable, necessary and clinically appropriate.

We continue to recommend that in those instances where CMS decides additional data collection is absolutely necessary to ensure continued coverage of an FDA-approved, currently covered technology, the Agency should continue to cover that technology for Medicare patients while the CED studies are conducted. CMS could consider providing incentives to participate in those clinical trials (such as reduced coinsurance, or the designation of participating sites as special centers.) This type of approach would allow CMS to continue to collect and evaluate clinical information regarding the use of the technology, without subjecting patients to loss of coverage, particularly when their physician(s) have determined the item or service to be clinically appropriate and clinically valuable.

4. **The Draft Guidance Creates More Ambiguity Than Clarity**

A. **Ending CED**

AdvaMed has often commented that the decision regarding when CED for the identified use of an item or service should end is one that should be discussed and agreed upon in advance by CMS and the study sponsors. CED-required data collection should have a well-defined endpoint established before the data collection begins, as determined by the specific protocol, and we recognize that flexibility will be important in this regard. While we believe this to be well understood, we had hoped that the CMS guidance document would discuss this process for determining in advance the duration of the data collection or the specific issues or questions CMS seeks to address through data collection, in order to create “stopping rules” for data collection, and to avoid burdensome and costly data collection without a clear end point.

We are also concerned by the discussion of the potential under CED for a gap to occur in coverage between the end of the study and the Agency’s review of the scientific results.
We urge CMS to ensure continuous coverage of an item or service after a study ends, to avoid disruption in coverage and continue to allow Medicare beneficiaries to benefit from important FDA-approved technologies and services until a new or revised coverage determination is issued.

B. The Role of the Agency for Healthcare Research and Quality (AHRQ)

The draft guidance document describes challenges of conducting CED, and points to a potential role for AHRQ to complement CED; however, there is little detail provided to clarify what exactly CMS anticipates AHRQ’s role to be, now or in the future. While the document seems to contemplate a role for AHRQ in facilitating CED by convening stakeholders to develop or design CED studies, or to provide financial support, more clarity is needed to better understand CMS’ thought process in including this section in the draft guidance document. CMS and AHRQ should clarify AHRQ’s specific role in coverage with evidence development.

C. Formal Evidentiary Criteria for CED

The draft guidance document touches on some of the discussion that took place at the May 16, 2012, meeting of the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) regarding the establishment of formal evidentiary criteria for CED. The guidance document does not make any specific recommendations regarding this topic, which we think is appropriate. Establishing criteria for invoking CED or to trigger an evidentiary review to determine whether CED should cease, continue or be modified is a process that should be undertaken on a product-specific basis and will vary depending on the unique nature of the technology or treatment that is the target of the CED.

CMS should continue to provide ample opportunities for public engagement on this topic. It is apparent that establishing an evidentiary threshold would be a difficult task, influenced by numerous factors and interactions. Flexibility in this area, rather than rigid standards, will be needed, as a single standard regarding evidentiary criteria would not be appropriate.

D. Medicare Administrative Contractors (MACs) and Coverage in Clinical Research

The draft guidance document summarizes the current Medicare Clinical Trial policy and the MACs’ current role in covering and paying claims related to beneficiary participation in clinical trials. While this is useful information, we recommend additional clarification that CED will only be used within the NCD process, and that CMS does not anticipate allowing Medicare contractors greater authority to carry out CED locally.
We recognized in previous comments the importance of protecting beneficiary access to new technologies and treatments, and noted that local coverage is often a pathway for beneficiary access in the absence of national coverage. However, we have strong concerns about any change in policy that would give local contractors greater authority to restrict or limit coverage through CED. In addition, we continue to have concerns about the potential for multiple, conflicting data collection requirements that might result from this action. This would be extremely burdensome and costly to manufacturers, and CMS should ensure that such circumstances are avoided.

5. Conducting and Evaluating CED

Finally, we would like to take the opportunity to restate our previous comments with respect to CED Implementation. We view CED as a collaborative exercise in which CMS (1) participates with stakeholders early on to identify data collection objectives, perhaps even prior to the issuance of an NCD, (2) considers study endpoints and the duration of data collection, and (3) is sensitive to funding constraints. In light of this, we believe that CED efforts should approach data collection in the following way:

- Engage a Full Range of Stakeholders in Determining CED Data Collection Objectives. A full range of interested parties — including manufacturers and other relevant experts, in collaboration with CMS — should be engaged to determine the clinical question to be addressed by the CED data collection exercise. This dialogue should take place early in the process, and include discussion of appropriate study endpoints, the number of patients required, and the duration of data collection after a practical consideration of the costs associated with this effort. In addition, CMS and this stakeholder group should agree to a clear data analysis, access and dissemination plan.

We do not believe it would be necessary or appropriate to convene a meeting of the MEDCAC in every instance in which CMS is considering CED; however, we do believe that each CED data collection exercise is unique and CMS should engage with relevant experts, including industry clinicians and technical experts, in order to have robust participation in the discussion.

- Require the Collection of Only the “Minimum Necessary” Data. Data collection is costly for providers and other stakeholders. Therefore, CMS guidance documents should clearly support the collection of only the “minimum necessary” data to answer the specific clinical questions that the study will address. Data collection should occur only to resolve explicit and well-defined, clinical research questions bearing on an ultimate coverage determination. To the extent possible, data collection should not place an additional burden on the parties involved.
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- **Address the Matter of Ending CED-Required Data Collection Efforts.** Under the previous CED guidance document, CMS stated that when the “length of time for data collection is not specified [in an NCD], CMS will evaluate the data on an ongoing basis to determine when the requirements of the NCD have been met and data collection is no longer necessary.”\(^2\) We disagreed with this approach, and instead commented that CED-required data collection should have a well-defined endpoint established before the data collection begins, in order to avoid unnecessarily burdensome and costly data collection.

6. **Study Design and Outcomes**

Some studies or patient populations present unique challenges to the conduct of randomized trials, and other study designs may be more appropriate to achieve the desired result. We note that the revised CED guidance document does not address the study designs that can be used for CED studies (e.g., randomized controlled trials, observational studies) except in the context of closing the coverage gap between when a CED study ends and the evaluation of that study. Nor does the draft guidance document discuss expectations with respect to clinical outcomes. As CMS works to finalize the guidance document, the Agency should consider including a discussion of evidentiary expectations, noting that while randomized controlled trials represent one type of evidence that would be acceptable, other study designs may be also be acceptable and appropriate to generate evidence that addresses the clinical questions bearing on a coverage determination. In our view, there is a role for observational studies, the use of powerful, “real-life” data sets, and other data collection measures in the CED process, particularly for the evaluation of diagnostic technologies.

With respect to clinical outcomes, CMS should consider discussing in its guidance document both intermediate outcomes associated with a procedure (e.g., 30-90 days) and longer-term outcomes (beyond 90 days), as well as quality of life and functional status, which are important considerations beyond mortality.

Finally, and perhaps most importantly, AdvaMed believes that proof of superiority should not be the goal when comparing a new technology against an existing one. For example, similar outcomes with a less invasive approach that promotes safety and quality should be taken into consideration in reaching a coverage determination.

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In summary, we had anticipated that the revised draft CED guidance document would provide greater clarity and guidance regarding the CED-related issues of concern to the medical device

industry, but since significant ambiguity remains, we urge CMS to revise and reissue a more detailed draft guidance document for comment. We seek to continue the dialogue with CMS on CED and to provide comments on behalf of the industry, particularly on issues affecting patient access to innovative technologies.

We appreciate the opportunity to share our views on this important matter, and we would be pleased to answer any questions regarding these comments or to meet with you on this matter at a time that would be mutually convenient. Please contact me at (202) 434-7219 or cbranham@AdvaMed.org if we can be of further assistance.

Sincerely,

Chandra N. Branham, JD
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AdvaMed