January 20, 2011

***BY ELECTRONIC DELIVERY***

**Louis Jacques, MD**
Director, Coverage and Analysis Group
Centers for Medicare & Medicaid Services
Mail Stop S3-02-01
7500 Security Blvd.
Baltimore, MD 21244

**Re: CED Public Solicitation**

Dear Dr. Jacques:

The Biotechnology Industry Organization (BIO) is pleased to submit the following response to the Centers for Medicare and Medicaid Services' (CMS) public solicitation for comments on Coverage with Evidence Development (CED).[1] BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products.

As the representative of an industry that is devoted to improving health care through the discovery of new therapies, BIO shares CMS's desire to "accelerate Medicare beneficiaries' access to innovative items and services and use evidence to identify the setting(s) in which a patient population is more likely to see the greatest benefit from an item or service."[2] Our members invest billions of dollars each year in clinical research to develop and disseminate evidence to help guide the effective use of their therapies. This investment continues long after the Food and Drug Administration's (FDA's) stringent approval requirements for each of our therapies are met. We also support Medicare policies, such as the Clinical Trial Policy (CTP),[3] that encourage beneficiaries to participate in clinical research.

Before addressing the three specific topics CMS identified for public comment, we believe it is important to address coverage for drugs and biologicals more broadly. First, in the request for comments on CED, CMS states, "many new technologies are developed with insufficient attention to addressing the needs of the Medicare beneficiary population."[4] Although this statement might be true for some technologies, it is seldom, if ever, true for drugs and biologicals used by the Medicare population. These therapies are subject to a rigorous FDA review process, and their approved prescribing information clearly describes the population for

[1] CED Public Solicitation, Nov. 7, 2011, http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=8&McdName=CED+Public+Solicitation&mcdtypename=Guidance+Documents&MCDIndexType=1&bc=AgAEAAAAAAAA&.
[2] Id.
[3] National Coverage Determination (NCD) Manual, § 310.1.
[4] CED Public Solicitation.

which each therapy is approved and the data supporting each indication. CMS should not second-guess the FDA's decisions by requiring additional post-approval studies of a drug or biological for its approved indications. CED is not appropriate for the FDA-approved uses of drugs and biologicals that are approved for use in the Medicare population, including the disabled and patients older than age 65. Moreover, the Social Security Act's definition of "drugs or biologicals" requires that each drug or biological be included or approved for inclusion in the United States Pharmacopoeia or be "approved by the pharmacy and drug therapeutics committee (or equivalent committee) of the medical staff of the hospital furnishing such drugs and biologicals for use in such hospital."[5] These requirements, combined with FDA approval, provide additional assurance that the therapy has been thoroughly reviewed by independent experts prior to coverage.

In addition, CED also should not be applied to drugs and biologicals that are used for "medically accepted indications," as defined by the statute, or pursuant to longstanding Medicare guidance. Under the statute, "medically accepted indications" of drugs or biologicals used in anti-cancer chemotherapeutic regimens include the FDA-approved uses as well as uses that are listed in certain compendia or are supported by peer-reviewed literature.[6] Medicare also has long granted its contractors authority to determine that unlabeled uses of other drugs are "medically accepted" based on "the major drug compendia, authoritative medical literature and/or accepted standards of medical practice."[7] By using authoritative compendia and medical literature to define "medically accepted indications," the statute and Medicare's guidance protect beneficiaries' timely access to drugs and biologicals while also ensuring that Medicare's coverage policies are truly evidence-based.

Furthermore, CMS should proactively remove any pre-existing broad national non-coverage exclusionary policies, which explicitly deny coverage for new agents not listed in the policy prior to any review by CMS. These exclusionary policies inappropriately apply immediate non-coverage decisions to any new FDA-approved technology. In effect, such policies constitute an affirmative position that the agent has failed to meet statutory criteria for medical necessity, even though the agent has undergone no review by CMS.

While BIO appreciates CMS' attempt to solicit stakeholders' input regarding the CED process and understands that CMS leadership is looking for comments on a new CED process, we urge CMS to carefully consider the important principles governing CED that were established in the 2006 guidance document. We were disappointed that CMS withdrew this guidance document from its website when it posted the solicitation for public comment. The principles of the 2006 document were developed after careful consideration of stakeholder comments and warrant further consideration throughout this process of updating CED. The eight principles governing the application of CED as articulated in the guidance document are:

1. National Coverage Determinations (NCDs) requiring CED will occur within the NCD processes, which is transparent and open to public comment.

[5] SSA § 1861(t)(1).
[6] SSA § 1861(t)(2)(B).
[7] Medicare Benefit Policy Manual, ch. 15, § 50.4.2.

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 the FDA's authority in assuring the safety, efficacy, and security of drugs, biological products, and devices.
7. CED will not assume the 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.[8]

BIO strongly supports these principles because they protect beneficiary access to appropriate care, encourage development of useful clinical evidence, and ensure that any applications of CED use the limited resources of CMS, providers, and manufacturers efficiently without unnecessary duplication of efforts. BIO continues to believe that CED should occur within the auspices of an NCD and therefore, only be implemented at the national level. By implementing CED at the national level, CMS can overcome a number of potential challenges related to small study sample sizes, limited agency resources and duplicative clinical trials. In particular, by stating that CED should be used infrequently and not to duplicate or replace the FDA's authority, these principles recognize that CED should be applied to drugs and biologicals only in rare circumstances because these therapies are subject to rigorous testing prior to approval.

We provide specific comments on each of the three topics requested by CMS below.

**1. Implementation of CED through the NCD or other avenues under Part A and Part B.**

In its request for comments in CED and in recent statements to the media and stakeholders,[9] CMS has expressed interest in expanding application of CED beyond the NCD process. BIO strongly supports the first principle published in the 2006 guidance: "NCDs requiring CED will occur within the NCD processes, which is transparent and open to public comment." Any application of CED must be developed in a clear and predictable manner, with opportunity for public comment, to ensure that CMS reaches an appropriate decision. This is critical because CMS and stakeholders requesting an NCD might not be aware of all of the relevant literature and soon-to-published evidence and might not have considered all of the risks and benefits of the proposed decision. In addition, we urge CMS to provide clear guidance as to how a product will graduate from CED after the appropriate amount of evidence has been collected. The NCD process protects against inappropriate coverage determinations, including unnecessary applications of CED, by making CMS's draft decisions public and allowing interested parties to comment on them.

[8] Guidance for the Public, Industry, and CMS Staff, National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development, July 12, 2006.
[9] See, e.g., Interview with Louis Jacques, Biocentury This Week, November 20, 2011, biocenturytv.com.

In addition, CMS officials have suggested that the CTP could be used to expand application of CED.[10] BIO supports efforts to expand beneficiaries' access to care in clinical trials, but it is unclear how the CTP could be used to expand CED. Although both policies serve to encourage collection of data on items and services provided to Medicare beneficiaries, the CTP and CED have starkly different approaches to coverage of the item or service under investigation. The CTP allows Medicare to cover the routine costs of qualifying clinical trials.[11] Under this policy, the investigational item or service is not covered unless it is otherwise covered by Medicare outside of the clinical trial.[12] In contrast, as currently defined by CMS, CED permits Medicare to cover the investigational item or service even if it would not be covered by Medicare outside the trial. In order to use the CTP to develop evidence on items and services that would not be covered by Medicare outside a clinical trial, the CTP NCD would need to be revised to provide payment for the investigational item or service. Any such change should be made through the NCD process, with ample opportunity for notice and comment.

Finally, BIO urges CMS to make any change to CED or CTP that occurs in response to, or as a result of, the current public notice, subject to an additional notice and comment period so that stakeholders have the opportunity to comment on specific changes being proposed.

**2. Potential impact of CED on the Medicare program and its beneficiaries.**

The principles established in the 2006 guidance document can help to ensure that CED does not restrict beneficiary access to appropriate care or impede innovation that could improve care under the Medicare program. In particular, these principles require that CED should be used to expand access to care, should be used rarely, and should not be used when other forms of coverage are justified by the available evidence. CMS should take care to ensure that these principles are followed in practice.

If these principles are not applied, CED would impose significant burdens on beneficiaries, healthcare providers, and manufacturers. Although beneficiaries should be encouraged to participate in clinical research, they should not be forced to participate in research under CED in order to receive care that Medicare should cover based on the available evidence. Moreover, if the study criteria under a CED policy are defined too narrowly, they risk denying access to care for many beneficiaries who have comorbidities or are otherwise unable to participate in trials due to distance from a provider who is participating in the study or their unwillingness to change providers.

In addition to presenting obstacles to care for beneficiaries, CED can impose substantial costs on providers and manufacturers. To date, the costs of performing studies required by CED policies, including maintenance of registries and collection of data, have fallen on providers and manufacturers. If CMS continues to use CED, we urge the agency to exercise caution and work with stakeholders to ensure that any application of CED is truly necessary and is implemented in the most economical manner possible. We also urge CMS to revise its payment policies to reimburse providers for the costs of performing the data collection activities required by CED.

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[10] Interview with Louis Jacques, Biocentury This Week, November 20, 2011, biocenturytv.com.
[11] NCD Manual, § 301.1.
[12] Id.

**3. Suggested approach to CED to maximize benefit to Medicare beneficiaries**

Finally, we believe that the benefit of CED to Medicare beneficiaries would be maximized by continuing to apply the principles established in the 2006 guidance document. In particular:

- CED should not be used when other forms of coverage are justified by the available evidence.
- CED should, in general, expand access to technologies and treatments for Medicare beneficiaries.
- CMS should use CED infrequently.
- CED should lead to the production of evidence complementary to existing medical evidence, and should not duplicate existing studies.
- CED should not duplicate or replace the FDA's authority in assuring the safety, efficacy, and security of drugs, biological products, and devices.

As explained above, under these principles, CED should rarely be applied to drugs and biologicals, especially for their FDA-approved indications.

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BIO appreciates the opportunity to comment on CED. We look forward to continuing to work with CMS to address this and other issues in the future. Please feel free to contact me at 202-962-9220 if you have any questions or need any additional information. Thank you for your attention to this very important matter.

Sincerely,

/s/

Laurel L. Todd
Managing Director
Reimbursement and Health Policy