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BY ELECTRONIC DELIVERY

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Centers for Medicare & Medicaid Services
Department of Health and Human Services
Mailstop: C1-12-28
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Baltimore, MD 21244

Re: Draft Guidance for the Public, Industry, and CMS Staff: Factors CMS Considers in Making a Determination of Coverage with Evidence Development

Dear Dr. Phurrough:

The Biotechnology Industry Organization (BIO) appreciates this opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS) draft guidance document (Draft Guidance) regarding factors CMS considers in making a determination of coverage with evidence development (CED).1 BIO is the largest trade organization to serve and represent the biotechnology industry in the United States and around the world. BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers, and related organizations in the United States. BIO

1 Draft Guidance for the Public, Industry, and CMS Staff: Factors CMS Considers in Making a Determination of Coverage with Evidence Development, Apr. 7, 2003. (hereinafter "Draft Guidance").

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members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products.

The Draft Guidance on CED continues CMS' ongoing efforts to promote the expanded collection of evidence to help patients, physicians, and payers determine when a medical technology is appropriate for a specific patient. BIO strongly supports evidence-based medicine, and we are committed to increasing the body of evidence available regarding diseases and their treatments. Our members spend millions of dollars each year on clinical studies, both before and after Food and Drug Administration (FDA) approval of their products, to produce high-quality clinical evidence to support medical decision-making. We also support the dissemination of this evidence to further clinical knowledge and enhance and improve the clinical decision-making process.

Our commitment to developing evidence extends far beyond studies of a particular therapy. We support a rigorous evidence development process that encompasses all aspects of a disease from examining how it affects the body to studying the costs and benefits of therapies. Our research initiatives advance the understanding of disease pathology and therapeutic mechanisms of action, clinical effectiveness in naturalistic settings, health-related quality of life, and health economic impacts of therapies in addition to clinical safety and efficacy. The development and evaluation of therapies are parts of this broader process and must be considered in context.

Our members' existing evidence development process, combined with Medicare's current coverage policies, allows Medicare beneficiaries timely access to new therapies and encourages innovation. The Medicare statute and manuals give local carriers the flexibility and freedom to make timely, evidence-based coverage decisions, ensuring Medicare beneficiaries' access to drugs and biologicals for medically accepted uses. These policies also encourage innovation and continued research by giving patients a choice of new therapies as well as new uses of existing therapies. Moreover, these policies create a relatively stable and predicable reimbursement environment, which is critical for many of our smaller members who are dependent on private sector investment.

Unfortunately, the Draft Guidance is vague and confusing and conflicts with many of CMS' statements made during the Open Door Forum[2] and the agency's recent uses of CED. In addition to the questions posed by CMS in the Draft Guidance, our reading of the document raises many questions and concerns. Our comments address these concerns, as well as respond to CMS' questions. Although we recognize that CED could apply to other items and services, we limit our comments to the use of CED for drugs and biologicals only, not devices or procedures. We believe that distinguishing drugs and biologicals from devices and procedures in the Draft Guidance would allow CMS to describe its plans and data requirements with greater specificity, particularly given the different amounts and types of data required for their FDA approvals.

BIO is concerned that CED, as described in the Draft Guidance, could reduce access to innovative drugs and biologicals, harming patient care both now and in the future. CED, if not applied narrowly, could slow technology diffusion and innovation by limiting physicians' choice of therapies and freedom to use cutting-edge regimens. CED could deny many beneficiaries who do not meet clinical trials' criteria access to critical therapies. It also could create uncertainty about reimbursement for medical technologies and could interfere with private market research priorities, slowing the development of new life-saving therapies.

Accordingly, if CMS proceeds with CED, we urge the agency to:

- Add a "scope" section to the next draft that clearly states when CMS might apply CED and the effect of CED on local carriers' authority to make coverage decisions. We support the narrow scope that the agency has articulated publicly, whereby the application of CED must meet all of the criteria outlined below:

  - CED will be used only when it serves as an expansion of coverage;
  - CED will not be used for on-label use of drugs or biologicals;
  - CED will not be used where there are statutory provisions establishing the Congressionally-mandated evidence standard,

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2 Open Door Forum held May 9, 2005.

e.g., for off-label uses of drugs or biologicals used in anti-cancer chemotherapeutic regimens that are listed in the compendia, supported by peer-reviewed literature, or otherwise determined by a local contractor to be medically accepted;

- CED will not supplant carrier discretion, and carriers will continue to apply local coverage as they do today; and
- CED will be used only when requested by a trial sponsor to facilitate enrollment.

- Distinguish drugs and biologicals from devices approved through the 510(k) process, as CMS has done in the past, in recognition of the different amounts of data required for FDA approval.3 This also will allow the agency to be more specific in its descriptions in the CED guidance document.

- Ensure that both its efforts to define CED and to apply CED to specific technologies are open, transparent, and predictable by resolving inconsistencies between statements in the Draft Guidance and in other forums and involving all stakeholders in these key decision processes.

We urge CMS to issue a second draft of the guidance document, with an additional comment period, to address these concerns and allow stakeholders to provide comments on CMS' response, using the consultative and iterative process described by the agency in the Draft Guidance.4 In addition, we urge CMS to treat its recent application of CED to anti-cancer chemotherapy for colorectal cancer as a pilot project and to learn from it before applying a similar CED policy to other drugs and biologicals in the future. Only after a careful analysis verifying that coverage was indeed expanded and assurance that long-term patient access was maintained should CMS evaluate whether and how to apply CED again.

I. CMS' authority to implement CED is questionable.

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3 Health Care Financing Administration (HCFA), Medicare Program; Criteria and Procedures for Making Medical Services Coverage Decisions that Relate to Health Care Technology Proposed Rule, 54 Fed. Reg. 4302, 4306-07 (Jan. 30, 1989).

4 Draft Guidance, at 9.

At the outset, we are deeply concerned because CED is a major policy change, and we question whether it is a proper exercise of CMS' authority. We note that CMS is a payer for health services, not a public research institution. Using its authority as a payer, CMS may examine whether an item or service meets the criteria for coverage, but it cannot interfere with physicians' practice of medicine.5 Setting the nation's research agenda also is not within CMS' purview.

We are disturbed that CMS inappropriately may be assuming the roles responsibilities of other agencies, such as the FDA, the Agency for Healthcare Research and Quality (AHRQ), and the National Institutes of Health (NIH). Specifically, CMS appears to be interfering with the FDA's authority to mandate post-marketing studies of drugs and biologicals, the AHRQ's mission to sponsor and conduct research to develop evidence-based data on health care services, and the NIH's clinical research mission. For example, Congress approved Section 1013 of the Medicare Modernization Act (MMA), which authorized AHRQ to evaluate the "outcomes, comparative clinical effectiveness, and appropriateness of health care items and services" provided to Medicare beneficiaries. Recognizing the impact that HHS driven research may have, Congress expressly prohibited CMS from using data gathered through Section 1013 to withhold coverage of a prescription drug.6 CMS should not be permitted to circumvent this provision by undertaking activities specifically delegated by law to AHRQ through the application of CED.

We remind CMS that Medicare beneficiaries do not have the same ability to switch health plans as their private sector counterparts who can change plans if desired. If Medicare beneficiaries disagree with CMS' restrictions on the care they receive, they usually have no other option for health coverage and often have no alternate means to pay for the care they need. For these reasons, we urge CMS to ensure that coverage decisions do not restrict Medicare beneficiaries and physicians' ability to choose their most appropriate course of treatment.

As CMS notes in the Draft Guidance, the Medicare statute authorizes the agency to determine whether an item or service is "reasonable and necessary for

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5 SSA § 1801.
6 MMA § 1013(d).

the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."7 Throughout CMS' history, these determinations have been based upon the evidence available at the time of the coverage decision. The Draft Guidance does not explain adequately how this authority extends to CMS' efforts to develop more evidence about an item or service. Moreover, we are unaware of any legislative history supporting the use of the Medicare coverage process to promote evidence development. We will discuss these concerns in more detail in our comments on the forthcoming guidance document addressing the "reasonable and necessary" statutory language.

II. CMS must clearly describe the scope of CED.

In recent weeks, during its Open Door Forum and in meetings with stakeholders, CMS has attempted to clarify the scope of CED. CMS' descriptions of the items and services to which CED may apply and its effect on local carriers' coverage authority have provided some reassurance that CED may not harm beneficiary access to drugs and biologicals, but these details are not included in the Draft Guidance. Instead, the Draft Guidance fails to provide clear examples of when CED will be considered or used. For example, in the Draft Guidance, CMS states that it "does not anticipate a substantial number of new coverage decisions in the near future that apply the data collection requirement,"8. Similarly, during the May 9 Open Door Forum, CMS said that it would use CED infrequently and in narrow circumstances.

The Draft Guidance, however, lists broad circumstances in which CED will be considered and could encompass many uses of innovative therapies.9 Moreover, the agency's claims of narrow use of CED are belied by CMS' recent national coverage determination (NCD) on anti-cancer chemotherapy for colorectal cancer. CMS also says that it "intends to apply CED to issues with the greatest potential benefit for Medicare beneficiaries and the Medicare program."10 These conflicting and vague statements and actions provide very little guidance as to exactly when CMS plans to use CED. We ask CMS to

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7 SSA § 1862(a)(1)(A).
8 Draft Guidance, at 2.
9 Draft Guidance, at 9-10.
10 Draft Guidance, at 11.

provide a more detailed description in the next draft of the circumstances in which CED will be used.

Consistent with its public statements, and as previously stated, CMS should clarify in the next draft of this guidance document that all of the following criteria must be met to apply CED:

1. CED will be used very rarely in narrow circumstances;
2. CED only will be used to expand coverage;
3. CED will not be used for on-label use of drugs or biologicals;
4. CED will not be used where there are statutory provisions setting out the Congressionally-mandated evidence standard, e.g., for off-label uses of drugs or biologicals used in anti-cancer chemotherapeutic regimens that are listed in the compendia, supported by peer-reviewed literature, or otherwise determined to be medically appropriate;
5. CED will not supplant carrier discretion, and carriers will continue to apply local coverage as they do today; and
6. CED will be used only when requested by a trial sponsor to facilitate enrollment.

Limiting the use of CED to these circumstances would ensure that its application is predictable and consistent and used for the benefit of Medicare beneficiaries. For example, in the recent NCD on anti-cancer chemotherapy for colorectal cancer, CMS determined that it did not have sufficient evidence on certain off-label, non-compendia listed uses of four anti-cancer drugs and biologicals. The NCD mandated coverage for these uses in specific clinical trials, but also protected carriers' discretion to cover these uses outside the trials if determined to be medically necessary.[11] We urge CMS to state in the next draft of the guidance document that CED will be used only when all of these criteria are met. CMS also provides little insight into the extent to which it intends to consider cost and utilization in deciding whether to apply CED. While cost and utilizations may be appropriate parameters for CMS to take into account when it is deciding whether to undertake a national coverage decision or entertain the need for a CED, cost and utilization should not, in our view, be considerations when a particular CED is being designed. CMS should clarify the role of cost and utilization in the next draft of the guidance document.

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11 Medicare National Coverage Decision Manual (CMS Pub. 100-3), § 110.17.

To clarify statements in the Draft Guidance about the use of CED to assist CMS and its contractors in making coverage decisions,12 the agency should state explicitly that CED is to be applied as a national policy only and is not to be initiated by local contractors. In addition, CMS should clarify that CED will not apply to drugs and biologicals covered under Medicare Part D. BIO is very concerned that Part D plans will view or try to make the claim that drugs subject to a CED are experimental, and, therefore, not eligible for coverage under Part D. Such a consequence would be unfair and potentially financially devastating to a beneficiary. CMS must be clear about the relationship of CED to Part D and vigilantly monitor treatment denials by MA-PDPs and PDPs, which appear to be related to the inclusion of a drug in a CED trial.

Moreover, the agency should indicate that the agency will contact manufacturers prior to the opening of a NCD and the potential application of CED and involve them in an open and transparent dialogue as the issue is considered. 13 Adding these statements to the next draft would greatly clarify the scope of CED.

BIO is very concerned about the provision in the Draft Guidance that considers the use of CED in circumstances of treatments for rare diseases where CMS alleges that comprehensive evidence of effectiveness is "not always available or feasible to develop in a pre-marketing setting." BIO believes that this provision should be deleted from the final guidance document.

In the development of medicines for rare diseases, the patient population must be less than 200,000 and therefore there are a limited number of patients

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12 See Draft Guidance, at 5, 9 ("In general, CMS will consider requiring data collection as a condition of coverage when additional information is needed for *CMS and its contractors* to determine if an item or service is reasonable and necessary.") (emphasis added).

13 This issue is discussed in depth in our comments to the agency's first three draft guidances on NCDs. Letter from Jim Greenwood, President & CEO, BIO, to Coverage and Analysis Group, CMS, regarding comments on draft guidance entitled "(1) Factors CMS Considers in Opening a National Coverage Determination; (2) Factors CMS Considers in Referring Topics to the Medicare Coverage Advisory Committee; and (3) Factors CMS Considers in Commissioning an External Technology Assessment," May 6, 2005.

from which to draw to conduct clinical studies. The clinical studies required for approval usually have very specific inclusion and exclusion criteria and thus an even smaller number of patients are available for enrollment into clinical studies. Many rare diseases are slowly progressive and heterogeneous, and large studies of long duration are not feasible. Nevertheless, the standard for approval of orphan drugs and biologicals is the same as that applicable to drugs and biologicals intended for use in larger populations—substantial evidence of safety and effectiveness for the intended use. Given the challenges of collecting data in such small patient populations, it is important that CMS not try to require additional or different clinical studies to those already underway or committed to by the drug sponsor.

The FDA, and in many cases, experts through FDA Advisory Committees have already given extensive thought and consideration into what clinical data should be collected on an orphan product, its patient population and its use when approval is granted. In fact, any post-marketing study commitments have already been agreed upon by the FDA and drug sponsor at the time FDA approval is given. It would be inappropriate for these post-marketing commitment studies to be delayed in any way to accommodate additional data collection requests by CMS because sponsor are held to very strict timelines by the FDA for completing their commitments. For CMS to conduct its own completely separate analysis and develop a different set of requirements could delay patient access to these needed drugs for rare diseases. Additional requirements would also be expensive and duplicative for the small, biotechnology companies that frequently engage in research in rare diseases. Lastly, additional CMS requirements would be contrary to existing law and Congressional intent to incentivize drug sponsors to develop therapies for rare diseases with small market potential.

III. CED only must be used to expand access to care and must not interfere with the local coverage process.

We are concerned that CED will curtail access to drugs and biologicals currently available through the local coverage process. The local coverage process allows Medicare beneficiaries to have appropriate access to drugs and biologicals through an efficient, timely, and evidence-based decision-making process. As intended by Congress, this process allows beneficiaries to receive anti-cancer chemotherapy drugs and biologicals for off-label indications when

the use is supported in certain compendia or peer-reviewed literature, or when the contractor determines that the use is medically appropriate.[14] If these therapies are available only through clinical trials or other evidence gathering methods, many patients could be denied access to critical treatments.

As CMS must be aware, many Medicare beneficiaries are ineligible for clinical trials due to age, co-morbidities, or complications. Others beneficiaries may choose not to participate in a trial if it requires them to travel, change physicians, or experience other substantial inconvenience. This may be particularly true for patients in rural areas, minorities, and women, who traditionally have been under-represented in clinical trials. The local coverage process must remain intact to allow patients who do not qualify for clinical trials or who elect not to participate to receive appropriate therapies.

In the Draft Guidance, CMS says it does not "anticipate circumstances under which CED would represent a net reduction in coverage available under local coverage policies."[15] To ensure that CED does not harm access to care, we ask CMS to commit to specifying precisely which beneficiaries are having difficulty accessing the drug or biological to which CED is applied and how the application of CED is expected to increase patient access. We also urge CMS to provide clearer instructions to carriers that a NCD with CED does not affect their discretion to cover uses of these therapies outside the CED requirements. CMS then should monitor and report on access to care after a CED decision is implemented both to verify that access is expanded as expected and that patients continue to receive the care prescribed by their treating physician, regardless of their participation in the evidence development exercise. This analysis also should be performed for the applications of CED that the agency currently is implementing.

The patient access analysis should be part of a larger formal, comprehensive value of information analysis that CMS should be required to conduct whenever it proposes to apply CED. This analysis should be included in the draft decision memorandum to allow all interested stakeholders the opportunity to respond to it. Such treatment is consistent with the Regulatory

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14 SSA § 1861(t)(2); Medicare Benefit Policy Manual (CMS Pub. 100-02), ch. 15, § 50.4.5.

15 Draft Guidance, at 6.

Impact Analyses and Regulatory Flexibility Analyses prepared for major rules and rules impacting small entities. CMS would be required to clearly explain the potential costs, burdens, and expected benefits of CED before implementation. These requirements should be incorporated and described explicitly in the next draft of the Guidance Document.

IV. CMS should distinguish drugs and biologicals from devices and procedures in its guidance document on CED.

CMS should distinguish drugs and biologicals from devices and procedures in its next draft of the guidance document. In recognition of the FDA's rigorous drug approval process, CMS historically has treated coverage of drugs and biologicals differently than other items and services, particularly devices approved under Section 510(k) of the Federal Food, Drug, and Cosmetic Act. Indeed, in 1989, the agency said that its national policy is that drugs or biologicals approved for marketing by the FDA are safe and effective for on-label indications, but that FDA approval for marketing of a medical device does not necessarily lead to a favorable coverage recommendation, especially when the FDA approval is under Section 510(k).16 CMS should continue to acknowledge the different amounts and types of data required to approve these technologies by providing separate descriptions of its plans to use CED for drugs and biologicals versus devices. The agency also should separately describe the application of CED to procedures that do not require FDA approval.

V. CMS must clearly state its reasons for using CED.

CMS must clarify its reasons for using CED to allow us to comment more meaningfully on whether and how CED can be used to achieve these purposes. CMS' written statements in the Draft Guidance and its oral communications concerning the guidance (e.g., during the May 9, 2005 Open Door Forum) have caused confusion about why the agency plans to use CED. In the Draft Guidance, CMS states that the purpose of obtaining evidence is to

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16 54 Fed. Reg. 4302, 4306-07 (Jan. 30, 1989). See also, 52 Fed. Reg. 15560, 15561 (Apr. 29, 1987) ("Medicare coverage of drugs and biologicals is treated differently" than other item and services).

give the agency data to use in making payment determinations[17] and to provide useful information to doctors and patients for clinical decision-making.[18] CMS also says it will consider using CED when "additional information is needed for CMS and its contractors to determine if an item or service is reasonable and necessary."[19] During the May 9, 2005 Open Door Forum, however, agency staff said that the main purpose was to assist patients and physicians and acknowledged that the data gathered through CED might not be adequate for use in coverage decisions. CMS' examples of the two general circumstances in which CED may be used give more reasons for using CED: to ensure patient safety and to provide physicians with more information about a patient's course of treatment. As noted above, Congress explicitly directed that these objectives be met by AHRQ.

The various reasons for using CED have left us confused about exactly what type of policy CMS is proposing. The conflicting written and oral statements make it difficult to understand what policy the agency is advancing and thus to which points we should address our comments. We urge CMS to issue another draft that reconciles the Draft Guidance, the agency's recent use of CED, and the agency's verbal statements about CED.

VI. CMS must clarify the amount of evidence it needs before applying CED to an item or service.

Additionally, the Draft Guidance is not clear about the amount of evidence CMS needs about an item or service before deciding to use CED. During the Open Door Forum, you stated that CMS would use CED when the evidence is not complete to support full coverage and additional data would help CMS be confident about providing full coverage. The description provided during the Open Door Forum also does not correspond perfectly to the Draft Guidance's descriptions of the evidence required to reach any of the three possible coverage decisions.[20] It therefore is not clear when CMS would determine that enough evidence exists to apply CED instead of issuing a non-

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17 Draft Guidance, at 1.
18 Draft Guidance, at 5.
19 Draft Guidance, at 9.
20 Draft Guidance, at 3.

coverage determination or no national coverage determination. CMS should specify its evidence requirements in the next draft of the guidance document.

VII. CMS must work with stakeholders to ensure that a proposed evidence collection method will achieve its goals with minimal burdens on patients, providers, and manufacturers.

If CMS applies CED to an item or service, it must take care to ensure that its chosen research methods can achieve intended goals with minimal burdens on patients, providers, and manufacturers. We agree with CMS that:

- the value of the information gathered must be carefully balanced against the burden of collecting it;
- any CED requirements must be aligned with the FDA's clinical study requirements and with other research priorities to ensure that our research resources are used efficiently; and
- data collection only should continue as long as important questions remain and the effort and resources required to collect this data are justified by the potential value of the information to be collected.21

The Draft Guidance does not describe CMS' process for ensuring that these criteria are met. In particular, we are especially concerned about how CMS will determine what hypothesis will be examined, when sufficient evidence has been gathered, and when CED will be brought to a close. Unless the research question is clearly defined from the outset, we cannot be confident that the study will produce data to satisfy CMS' needs or that coverage decisions will be made in an efficient and timely manner. Robust clinical research starts by asking the correct research question. Clear articulation of the research question informs all other aspects of research, including study design, enrollment criteria, sampling methods, power calculations, ethical considerations, and analytical plan. The consequences of a poorly articulated research question are development of faulty or biased data, or engagement in data dredging exercises and its inherent risks of making spurious inferences.

To ensure that an application of CED achieves its goals(s) while minimally inconveniencing providers, patients and manufacturers, we urge

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21 Draft Guidance, at 5, 14.

CMS to consult stakeholders at each stage of the CED development process. For example, before beginning any evidence development process, CMS must work with stakeholders to assess the need for more evidence about a drug or biological, the value of the information to be collected, and the burdens on stakeholders of collecting it. With input from stakeholders, CMS must clearly articulate the specific research questions, goals, and limitations of the intended research design. As the evidence is gathered, CMS should consult with stakeholders about the data and its analysis. We support CMS' plan, described during the Open Door Forum, to release aggregate data to the public for additional analysis, but we emphasize that this is not a substitute for initial consensus about the trial's design and purpose.

In the Draft Guidance, CMS asks, "[H]ow should the costs of study design, data collection, analysis and other activities associated with these programs be fairly allocated to various stakeholders?"22 In addition to minimizing these costs as much as possible, we urge CMS to pay particular attention to the costs imposed on beneficiaries and providers. Beneficiaries' cost of care under CED should not be greater than under coverage without evidence development. If beneficiaries are forced to incur greater costs for receiving care in Medicare-covered clinical trials or other evidence development programs, they likely will choose other, potentially less appropriate, care options.

In addition to minimizing patient costs associated with CED, CMS also must minimize physicians' costs of CED. Physicians who participate in clinical trials often donate considerable amounts of time and resources to evaluate patients' eligibility for trials, data collection, and drug administration services that frequently are not reimbursed by trial sponsors. With Medicare's recent changes to reimbursement for drugs and drug administration and its pending reimbursement cuts for all physician services, many physicians are less able to afford to participate in clinical research. We recommend that CMS develop reimbursement codes and rates for non-routine services to make participation in research more financially feasible. We also recommend that CMS provide reimbursement for the routine costs of care, such as drug administration, in more clinical trials.

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22 Draft Guidance, at 15.

BIO also recommends that CMS encourage Medicare beneficiaries to participate in a wide range of clinical trials, rather than a select few identified by the agency. To increase beneficiaries' care options, BIO urges CMS to finalize its criteria for coverage of clinical trials under the 2000 NCD. Since September 2000, Medicare has covered the costs of routine services in qualifying clinical trials, including trials sponsored by the NIH and other federal agencies.23 CMS, however, has not yet finalized its criteria for covering other trials, such as those sponsored by industry or other groups. We recommend that CMS fully implement the 2000 NCD by finalizing these criteria so that Medicare beneficiaries will be able to participate in the clinical trials that are most appropriate for their conditions.

VIII. CMS must clarify the draft guidance document's description of the NCD process.

The Draft Guidance has caused confusion about the possible outcomes of the NCD process. First, we ask CMS to clarify that its statement that it "does not anticipate issuing additional decisions" without conditions does not mean that it plans to apply CED to every NCD.24 If the agency intends that every future coverage decision will be coupled with conditions such as patient diagnoses, positive test results, or other factors, CMS should explain this clearly in the revised guidance.

Second, in the Draft Guidance, CMS says the NCD process results in three broad types of coverage decisions: non-coverage, coverage with conditions, and coverage without conditions.25 The Draft Guidance omits a possible outcome to the NCD process, one that has been used recently in the draft Radioimmunotherapy for Non-Hodgkin's Lymphoma NCD.26 In cases for which there is inadequate evidence at this time for a change to coverage, CMS may leave the decision to cover the item or service to the carriers, using current manual instructions. CMS must state in the next draft that the NCD

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23 National Coverage Determinations Manual § 310.1.

24 Draft Guidance, at 4.

25 Draft Guidance, at 3.

26 Proposed Decision Memo for Radioimmunotherapy for Non-Hodgkin's Lymphoma (CAG-00163N), May 4, 2005, http://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?id=38.

process results in four, not three, types of coverage decisions: (1) non-coverage; (2) coverage; (3) coverage with evidence development; and (4) no national coverage decision, with coverage left to statutory mandate as well as the discretion of Medicare contractors. When the evidence is not adequate to justify a change in coverage policy and CED is not appropriate, the Draft Guidance should clarify that the result should be no national decision, not non-coverage.

IX. CMS must bring all stakeholders to the table to discuss CED and expanding support for clinical research.

BIO shares CMS' belief that the agency must work "consultatively and iteratively with external experts and stakeholders in developing the criteria and process for determining when to apply CED."[27] These discussions should bring all stakeholders together to discuss not only the use of CED for specific items and services, but also CED's effects on patients' access to innovative therapies, the broader clinical research system, and the drug and biological industries. CMS appears to view CED as a step toward a "systematic expansion of practical clinical research efforts to address the needs of health professionals and patients."[28]

The clinical research structure is far more complex than CMS may imagine, and it cannot be expanded successfully without the participation of all of its stakeholders, including patients, providers, researchers, manufacturers, and other government agencies. We believe that CMS' efforts to encourage more research must be pursued only through transparent processes and open dialogue with all interested parties. Furthermore, this dialogue must involve all stakeholders, so that CMS can benefit from a full discussion of individual concerns for all parties involved. We urge CMS to continue to consult with stakeholders on the development of its policies regarding CED and the expansion of clinical research. We also request that the agency make special efforts to provide opportunities, such as Open Door Forums, that allow all stakeholders to participate in the conversation at the same time.

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27 Draft Guidance, at 9.
28 Draft Guidance, at 4.

X. CMS must make certain that all human subject research conducted under CED meets all federal legal, ethical, and Health Insurance Portability and Accountability Act of 1996 (HIPAA) requirements.

On page 3, the Draft Guidance states the following: "The service is delivered in the context of specific data being collected. Coverage may be limited to providers who participate in and beneficiaries who are enrolled into a defined prospective data collection activity, when this data collection activity constitutes part of the evidence required to ensure the item or service provided to that patient is reasonable and necessary." The Draft Guidance should clarify that the prospective collection of outcomes evidence for coverage use, even by CMS, constitutes research with human subjects under the law and the Department's own regulations.[29] Accordingly, the basic principles of informed consent, including patient authorization for use and disclosure of health information, and institutional review board (IRB) review cannot be ignored. Medicare beneficiaries should not be compelled to participate in research as a condition of coverage without the protection that the regulations provide. Finally, CMS indicates that studies under CED often would involve de-identified data. It is not clear how this would be feasible because the de-identification standard under the HIPAA privacy rule is very stringent. We respectfully ask CMS to clarify these issues before moving forward with application of CED.

XI. Conclusion

BIO appreciates this opportunity to comment on the Draft Guidance document regarding the use of CED. We hope our recommendations help CMS to apply CED in a predictable manner that ensures beneficiary access to innovative drugs and biologicals. Specifically, we urge CMS to:

- clearly define the scope of CED;
- work with the Department, AHRQ and public stakeholders to ensure that CED is implemented consistent with Section 1013 of the MMA;
- use CED only to expand access to care and not interfere with the local coverage process that exists today;

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29 E.g., Federal Food, Drug, and Cosmetic Act §§ 505(i), 520(g), 21 U.S.C. §§ 355, 360j; 42 U.S.C. §§ 289, 289a-1; 21 C.F.R. Parts 50 and 56; 45 C.F.R. Part 46.

- distinguish drugs and biologicals from devices and procedures in its guidance document on CED;
- clarify that CED never will be used for on-label uses or off-label uses of drugs or biologicals used in anti-cancer chemotherapeutic regimens that are listed in a compendia, supported by peer-reviewed literature, or otherwise determined by a local contractor to be medically accepted indications;
- clearly state its reasons for using CED to allow us to comment meaningfully on the policy;
- clarify the amount of evidence it needs before applying CED to an item or service;
- work with stakeholders to ensure that a proposed evidence collection method will achieve its goals with minimal burdens on patients, providers, and manufacturers;
- clarify the draft guidance document's description of the NCD process;
- bring all stakeholders to the table to discuss CED and expanding support for clinical research; and
- ensure that all human subject research conducted under CED meets all federal legal, ethical, and HIPAA requirements.

We look forward to working with CMS to protect Medicare beneficiaries' access to innovative drugs and biologicals. If you have any questions regarding our comments, please contact Jayson Slotnik at 202-312-9273. Thank you for your attention to this very important matter.

Sincerely,

/s/

Jim Greenwood
President and CEO
Biotechnology Industry Organization