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BIOTECHNOLOGY
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September 26, 2008

Steve Phurrough, M.D.
Coverage and Analysis Group
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Mailstop: C1-13-18
7500 Security Blvd.
Baltimore, MD 21244

Re: Request for Comments regarding the July 30, 2008 CMS Posting of Potential National Coverage Decision Topics

Dear Dr. Phurrough:

The Biotechnology Industry Organization (BIO) appreciates this opportunity to comment on the Centers for Medicare and Medicaid Services' (CMS) Posting of Potential National Coverage Decision Topics (Potential NCD List). This publication is a subsequent step to CMS' April 11, 2006, issuance of the "Guidance for the Public, Industry, and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination" (NCD Guidance), which identified the factors considered by CMS in determining whether coverage of an item or service is reasonable and necessary for use by Medicare beneficiaries. The July 30 Potential NCD List includes CMS's first release of potential NCD topics, listing 20 such topics, and requests public comment on these topics.

BIO represents more than 1,200 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. Our healthcare industry members are devoted to discovering new treatments and cures for a wide range of diseases and providing patient access to these lifesaving therapies. Representing an industry that is devoted to discovering new cures and ensuring patient access to them, BIO strongly believes that the processes through which Medicare's coverage decisions regarding these therapies are made must be predictable, transparent, and open to the public. We commend CMS for its efforts

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to improve the NCD process to embody these qualities more fully. BIO previously commented on the need for transparency in the NCD process and we appreciate CMS' posting as a means of informing the public of these potential NCD topics. We offer the following comments to help CMS further create an open and transparent NCD process that will offer more opportunities for stakeholder interaction with the agency with regard to:

- Transparency and predictability within the NCD process;
- The inclusion of items in the NCD process based upon inappropriate factors;
- The appropriate use of the NCD process; and
- The process of identifying potential NCD topics.

These issues are discussed in detail below.

I. Transparency and Predictability Within the NCD Process

BIO has previously commented regarding the need for transparency and public input in the NCD process, and commends CMS for providing preliminary notice and opportunity for comment regarding the topics under consideration, as discussed in our comments to CMS "Draft Guidance for the Public, Industry and CMS Staff: Factors CMS Considers in Opening a National Coverage Determination" (March 9, 2005). We also have urged CMS to provide sufficient detail about each item or service under consideration and why it is being considered, as this information is necessary to help stakeholders understand CMS' interest in the particular item or service as well as the agency's approach to NCDs in general.

BIO finds that the Potential NCD List does not provide sufficient transparency regarding the topics selected because it does not identify the origin of the 20 topics chosen. We are interested in knowing whether the therapies were identified in the recent Medicare Evidence Development & Coverage Committee (MedCAC) meetings; whether the NCD process was requested by an external party for a particular NCD topic; whether it was the result of inquiries from providers, patients, or other stakeholders; or whether the request was initiated internally at the agency through a local carrier or by CMS national. While the Potential NCD List identifies seven circumstances, as outlined in the NCD Guidance that have prompted an NCD request for either a new item or service or an existing technology, CMS does not specify which circumstance connects to each proposed NCD topic. BIO urges CMS to specifically indicate how each item on the topic list was selected by mapping it back to one of these seven criteria. While there is a very brief (often only1-2 sentences) description of each proposed topic, CMS does not consistently state whether there is new evidence or what the clinical basis is for proposing a potential NCD. Further, there are no citations to publications, and there is no discussion or summary of evidence that CMS has reviewed in order to support each proposed NCD topic. Without such information, stakeholders cannot possibly be expected to formulate helpful

comments regarding CMS' concerns about a particular item or service. In addition, BIO urges CMS to review and respond to comments received regarding the Potential NCD List prior to initiating an NCD on a given item or service.

BIO also recommends that CMS specifically respond to the public comments received through the NCD process as it does in the formal rulemaking processes. In this way, stakeholders will have the opportunity to gain further insight into the CMS process, ultimately resulting in both a higher quality process and comments.

II. Concerns Regarding the Inclusion of Items in the NCD Process Based upon Inappropriate Factors

Within the information that CMS has provided for the proposed NCD topics, BIO has several specific concerns including the consideration of a therapy's cost in the NCD process, the timing of the NCD process as related to FDA approval, and off-label use. Each is discussed in turn.

A. Cost

For several listed items, CMS refers to "costs" in its description. For example, CMS states that "ESAs are a large cost in current ESRD treatment strategies". With regard to proton beam therapy for prostate cancer, CMS refers to the "very high upfront cost to build these facilities." As recognized by CMS, cost is not a proper consideration in the NCD process. The NCD Guidance states that ". . . the cost of a particular technology is not relevant in the determination of whether the technology improves health outcomes or should be covered for the Medicare population through an NCD." It is inappropriate for CMS to list these topics based upon cost, or to take action to pursue such NCDs. If the agency decides to change this policy, it should do so in a transparent manner by following the appropriate procedures, including a meaningful and open dialogue with stakeholders.

B. Listing of Items Prior to Initial FDA Approval

BIO notes that CMS has listed at least one item that was not yet approved for marketing by the Food and Drug Administration (FDA) at the time of its inclusion on the Potential NDC List. BIO fails to understand how CMS can consider initiating an NCD process prior to initial FDA approval of a product, and requests that CMS provide information as to what the basis for such inclusion could be. It is the role of FDA to review and evaluate safety and effectiveness data submitted for product approval and to reach a determination of whether that evidence supports marketing approval, what the appropriate patient population is, and what risks and warnings should be included in the product labeling. BIO urges CMS to acknowledge this role and to not substitute its own judgment for the role of FDA, or to initiate an NCD prematurely. It

is only after initial FDA approval of a product that CMS should consider the NCD process to determine whether that product is appropriate for the Medicare population.

By way of example, the Potential NCD List specifically identifies Thrombopoiesis stimulating agents, which were not yet approved for marketing by FDA at the time of their inclusion on the list, and states that "[l]ong term safety data are lacking." A statement that long-term safety data is lacking in a product that has not yet been approved seems preposterous. It is through the FDA process—and by means of post-marketing studies when required by FDA—that such data would emerge and be reviewed.

BIO does not believe that CMS should inject new elements into the coverage process that are not mentioned in the NCD Guidance. CMS is attempting to do this by requiring long term safety data or comparative trials (as briefly outlined in the proton beam therapy item) on new products in order for these products to receive Medicare coverage. This process could put Medicare beneficiaries years behind privately insured individuals in their ability to have access to new technologies. BIO does not believe that the Potential NCD List is an appropriate venue for CMS to announce new evidentiary requirements to support an NCD.

BIO recognizes that the regulatory pathway defined by FDA may or may not result in data applicable to the CMS population and addresses CMS' standards for "reasonable and necessary". The evidence process is incremental, beginning with safety and efficacy data to meet FDA requirements followed by the evolution of the evidence-base. BIO strongly recommends that CMS allow new products time on the market in order for the evidence-base to evolve and mature prior to considering the need for an NCD.

BIO does not believe it is the role of CMS to limit the diffusion of technology through NCDs. Instead, CMS should follow its own guidance document to use the NCD process to facilitate the diffusion of new technology. According to the agency's NCD Guidance, the agency may internally generate an NCD (i) if the new technology represents a substantial clinical advance and is likely to result in a significant health benefit if it diffuses more rapidly, and (ii) if more rapid diffusion of the technology is likely to have a significant programmatic impact on Medicare and on other Medicare-related public policies (e.g., reduction in health inequalities). BIO supports this use of the NCD process. However, in the Potential NCD List, we do not see the agency attempting to facilitate the diffusion of new technology. Rather, CMS appears to be doing the opposite by using the process to limit the diffusion of a new product. BIO believes that CMS' use of the NCD process to limit the diffusion of new technology in this manner could have serious negative implications for further innovation of life saving therapies which can lead to improved health outcomes for Medicare beneficiaries. BIO urges CMS to follow its own guidance document and utilize the NCD process to facilitate the diffusion of new technologies in the circumstances that CMS has identified.

Of additional concern regarding a policy allowing inclusion of pre-approval and other new and innovative therapies on the Proposed NCD List is the economic impact it may have on researchers and small companies, particularly with regard to access to capital to finance future research. CMS could be creating a significant barrier to market entry for novel therapies. Such a barrier may inadvertently and unduly influence the economics of product development, thereby distorting the financial markets that support the innovation of essential life-saving therapies. Certainly this is an unintended and inappropriate outcome for an agency whose mission is to administer an insurance program for the nation's most vulnerable populations. CMS must be mindful of the unintended consequences resulting from its actions in these rapidly changing, innovative areas.

C. Off-Label Use

BIO notes that CMS also refers to off-label use in regard to some of the proposed NCD topics. While these references are in the context of products that are not drugs or biologicals, BIO is concerned that the agency might raise off-label use issues in future listings of potential NCD topics. Given the unique aspects of coverage for off-label drugs and biologicals (e.g., the statutory directive in section 1861(t)(2) of the Social Security Act covering anticancer therapies), the Potential NCD List is not an appropriate venue for addressing off-label uses of drugs and biologicals.

Further, BIO urges CMS to proceed very cautiously in employing the NCD process in a manner that interferes with the role and judgment of physicians treating their patients. Physicians have the ability to make appropriate treatment decisions based upon the available medical literature and the unique circumstances of each patient. Patients respond differently to treatment interventions, based upon a variety of clinical factors, particularly in the case of innovative drug and biological therapies. Imposing coverage requirements that could limit the flexibility and professional judgment of physicians and fail to allow for patient differences is an inappropriate use of the NCD process and could lead to suboptimal health outcomes.

III. Appropriate use of the NCD Process

CMS recognizes in the Potential NCD List, as well as in the NCD Guidance, that inconsistent or conflicting local coverage decisions (LCDs) can lead to initiation of an NCD.

The local coverage process works well to ensure beneficiary access to appropriate drugs and biologicals. Its reliance on medical literature, clinical practice standards and compendia to determine when off-label uses of drugs and biologicals are medically accepted permits coverage to evolve with the standard of care. Medicare contractors' flexibility to adjust their coverage policies as the clinical evidence evolves, including the recognition of new therapeutic regimens

and the acknowledgment of safety concerns about existing treatments, helps to ensure that patients have timely access to the most appropriate therapies. The local coverage process also allows patients and physicians to request individualized coverage decisions. Because all patients are not identical, contractors' coverage policies also must have some variation to ensure access to needed therapies. We urge CMS to clarify its description of these circumstances to assure stakeholders that the NCD process will not supplant the local coverage process and its protections for access to care. The guidance document should clearly state that local coverage policies remain in effect during the NCD review process. CMS also should consult with stakeholders to determine when variation among local policies harms patient access to care.

IV. The Process of Identifying Potential NCD Topics

CMS indicated that it would announce potential NCD topics in the NCD Guidance of 2006, and released the first such listing in the Potential NCD list of July 30, 2008. BIO recommends that CMS provide greater information about the frequency with which the Potential NCD List will be published, and whether it is an iterative process. In addition, BIO would like CMS to outline its expectations regarding successive Potential NCD Lists and the basis upon which changes (or no changes) will be made.

Further, it appears that the Potential NCD List is, to some degree, an outgrowth of recent public meetings of the MedCAC, in its advisory role to CMS. These meetings included a Federal Evidentiary Priorities Workshop held by CMS on February 13, 2008, and a public CMS Evidentiary Priorities MedCAC meeting held on October 22, 2007, where panelists developed and rated a list of evidentiary priorities for CMS to consider in its efforts to improve the health of Medicare beneficiaries. As BIO stated in comments to CMS on April 2, 2008, we have concerns about both of these meetings. The February meeting was closed and thus did not benefit from public input. The October public meeting was wrought with confusion amongst the panelists and expert presenters regarding the type of research questions the MedCAC had been charged with developing, as well as the self-acknowledged limitations of panelists in providing guidance to CMS on research topics outside of their particular areas of expertise. BIO remains concerned regarding whether the MedCAC is an appropriate forum for meaningful dialogue and guidance to CMS on the relative importance of various clinical research topics. Given that this recent MedCAC process was flawed, BIO questions the inclusion of proposed NCD topics that resulted from these MedCAC meetings.

V. Conclusion

In conclusion, BIO supports CMS' efforts to make the national coverage process more transparent to the public. We believe the process has benefitted from increased transparency,

and will continue to do so. However, CMS must be mindful of its role in administering the Medicare program, and not overstep that authority into areas better addressed by other Federal agencies. Improved transparency and opportunity for public comment will help CMS to operate more efficiently and predictably.

We hope our suggestions will help CMS address these important issues in future iterations of the Potential NCD List. Please contact Laurel Todd at (202) 962-9220 if you have any questions regarding our comments. Thank you for your attention to this very important matter.

Respectfully Submitted,

/s/

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/s/

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