The Biotechnology Industry Organization (BIO) appreciates this opportunity to testify at today's Medicare Coverage Advisory Committee meeting regarding proposed changes to CMS' current clinical trial policy. BIO looks forward to working with CMS to develop policies that promote access for all Medicare beneficiaries to potentially life saving clinical research.

BIO is the largest trade organization to serve and represent the biotechnology industry in the United States and around the globe. BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers, and related organizations in the United States. BIO is committed to ensuring beneficiary access to innovative biological therapies and our member companies' research continues to advance the understanding of disease pathology, therapeutic mechanisms of action, clinical effectiveness, and health-related quality of life. Consequently, we support CMS' efforts to clarify, strengthen and appropriately broaden its clinical trial coverage policy. BIO believes that Medicare beneficiaries must be allowed to participate in clinical research that furthers the knowledge about the quality of care that Medicare beneficiaries receive. BIO highlights five specific issues below for the Committee to consider when working with CMS on the clinical trials coverage policy.

1. Standards for Qualified Trials

CMS should permanently extend deemed status to IND-exempt trials

When CMS issued the NCD for clinical trials in 2000, the agency included a list of trials automatically "deemed" to be qualified as covered by Medicare. This list included trials conducted under an IND reviewed by FDA. CMS also included as "deemed," drug trials that are IND-exempt only until other qualifying criteria were developed. Criteria were not subsequently published for the IND-exempt trials, and thus IND-exempt trials have continued to operate as "deemed" under a temporary status.

BIO urges CMS to permanently extend deemed status to IND-exempt trials in the new clinical trial policy. This category of clinical trials is carefully regulated. FDA permits a clinical investigation of a drug product

lawfully marketed in the United States to be exempt from the IND process only if certain requirements are met.[1] This exemption is intended to apply primarily to researchers "who are beginning to explore new uses for marketed drugs (*i.e.* not pivotal studies) or who are using the drug as a research tool."[2] An IND-exempt investigation also is permitted only where safety is not an issue and the investigation is not being conducted to support a labeling change such as a new indication or a comparative safety claim.[3]

FDA expressly has encouraged use of this IND-exempt process for qualifying trials. For example, in 2004, FDA urged the oncology industry not to submit INDs for all clinical research for oncology products but instead to use the IND-exempt process where possible.[4] Clinical trials operating under the IND-exempt process have been influential in the post-approval development of many important therapies, and this is increasingly true as more companies seek to use the IND-exempt process, at FDA's urging. Permanently adding IND-exempt trials to the list of clinical trials "deemed" qualified for Medicare coverage will reduce uncertainty among patients and providers regarding Medicare coverage for routine medical costs.

BIO is concerned about CMS' suggestion that the new policy will attempt to "[c]larify the scientific and technical roles of federal agencies in overseeing IND Exempt trials."[5] We believe that the jurisdiction to regulate such trials clearly lies with FDA, and we do not believe that CMS' involvement in clarifying the scientific and technical roles of Federal agencies in overseeing these trials is a proper exercise of CMS' authority. As a payer for health services, CMS has the authority to examine whether an item or service meets criteria for coverage, and CMS may establish a list of clinical trials and other research studies that qualify for Medicare coverage of routine costs. CMS is not tasked with regulating or overseeing clinical trials, and we urge CMS not to assume the responsibilities of other agencies by seeking to participate in the oversight of clinical trials.

---

1 21 C.F.R. § 312.2(b); 52 Fed. Reg. 8798, 8801 (Mar. 19, 1987) (noting that "a study of a marketed drug involving an indication contained in the product's approved labeling would be subject to all relevant [IND] requirements" but would be "exempt from IND submission requirements if it met the conditions of § 312.2").
2 48 Fed.Reg. 26720, 26721 (June 9, 1983); *see also* 52 Fed.Reg. 8798, 8799-8800 (Mar. 19, 1987).
3 *Id.*
4 Food and Drug Administration, "Guidance for Industry, IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer," January 2004, available at www.fda.gov/cder/guidance/6036fnl.htm.
5 NCA Tracking Sheet for Clinical Trial Policy (CAG-00071R).

CMS should clarify that all Phase I studies (except for those conducted in healthy patients) and Phase II studies are eligible for coverage.

BIO believes that it is critical that CMS expand its coverage policy to include Phase I and Phase II studies. The current coverage requirement that clinical trials have therapeutic intent unfortunately leads to confusion and inconsistent coverage determinations by local Carrier Medical Directors. Specifically, it states that "any clinical trial receiving Medicare coverage of routine costs must . . . not be designed exclusively to test toxicity or disease pathology. It must have therapeutic intent." It further states that, to qualify for coverage, the "principal purpose" of the trial must be "to test whether the intervention potentially improves the participants' health outcomes." There have been conflicting interpretations regarding the meaning of these provisions. Coverage for Phase I studies is frequently denied and, under some restrictive interpretations of the NCD, coverage would be limited mainly to Phase III studies. These narrower restrictions limit access of Medicare beneficiaries to promising new investigational drugs in early stages of their development.

In revising the clinical trial policy, CMS should clarify that all Phase II studies as well as all Phase I studies, except for those conducted in healthy patients, are eligible for coverage. Although Phase I trials are frequently conducted in healthy volunteers to test dose ranges and pharmacokinetics, clinical trials in oncology are typically conducted in sick patients where evidence of response is frequently collected in addition to safety and pharmacokinetic data.6 Patients often enroll in Phase I trials when there is no standard of care treatment to combat their disease or the standard treatments have failed. Phase II studies are studies conducted to make preliminary determinations of efficacy and to collect additional data regarding safety. These trials can represent the last hope of therapeutic benefit for ill patients without other treatment options, and can help determine whether the development of a drug candidate should go forward. According to the American Society of Clinical Oncology, in recommending participation in a clinical trial "[i]t should not be relevant whether the scientific goals of the study are to determine toxicity and pharmacokinetics (Phase I) or to ascertain the response rate (Phase II) because the patient is receiving an appropriate treatment for his or her disease . . . . [in a Phase I

6 "Critical Role of Phase I Clinical Trials in Cancer Treatment," 15 Journal of Clinical Oncology 853, 854 (February 1997).

trial] there is a strong preclinical rationale for bringing the drug into the clinic with the expectation of positive clinical outcomes for some patients."[7]

Denying coverage for Phase I and Phase II clinical trials would be contrary to the intent and spirit of expanding access to potentially life saving clinical trials. Given their importance to patients and to the drug discovery process, Medicare should clarify that costs for all Phase II trials and all Phase I trials, except for those conducted in healthy patients, are covered.

2. CMS needs to clarify payment criteria for clinical costs in research studies

A clinical trial sponsor is not considered a primary payer

In developing this policy, BIO urges CMS to clarify that a clinical trial sponsor, study site, or investigator is not considered a primary payer when assuring a trial enrollee that they will not be responsible for uncovered out-of-pocket payments for medical services resulting from a trial-related illness or injury.

As you know, the Medicare statute requires payment for items and services that are reasonable and necessary for the treatment of illness or injury.[8] It is clear that medically necessary services provided to treat complications arising in the course of a clinical trial are intended to be covered by Medicare. Indeed, CMS regulations specifically authorize Medicare payment for complications arising from clinical trials involving the use of medical devices.[9] In addition, the current NCD itself calls for coverage by defining routine costs in qualifying clinical trials to include items and services for the treatment of complications.[10]

The Medicare Secondary Payer statute provides that Medicare payment is not available for items or services for which payment is available under a "primary plan."[11] "[P]rimary plan" is defined to include group

---

7 *Id.*
8 42 U.S.C. §§ 1395(d) (entitlement to have payment made for inpatient hospital services), 1395k(a)(1) (entitlement to have payment made for medical and other health services), 1395y(a)(1)(A) (exclusion for items that are not reasonable and necessary for treatment of illness or injury).
9 42 C.F.R. § 405.207(b). The regulation calls for payment even when the device itself is unapproved, making clear that coverage also is compelled where the device is an approved one.
10 Medicare Coverage, Clinical Trials, Final National Coverage Decision, *available at* http://www.cms.hhs.gov/coverage/8d2.asp.
11 42 U.S.C. § 1395y(b)(2)(A).

health plans, worker's compensation programs, automobile or liability insurance policy or plan (including a self-insured plan), and no fault insurance.12 Nothing in the Medicare Secondary Payer statute or its legislative history suggests that Congress intended to include clinical trial sponsors as primary payers where the sponsor offers in an informed consent document and related clinical trial agreement to make payment for *uncovered* expenses relating to illness or injury resulting from the trial. Such an interpretation runs contrary to Congressional intent as well as to the goal of encouraging the participation of Medicare beneficiaries in clinical trials. Accordingly, BIO urges that the clinical trial policy explicitly clarify that a promise by a clinical trial sponsor or study site to pay for uncovered trial-related illness or injury will not result in the sponsor being viewed as a "primary plan," or render the sponsor, site, or investigator a "primary payer," under the MSP provisions.

We also urge CMS to assure beneficiaries that they will not be denied coverage merely because they have volunteered to participate in a clinical trial. Beneficiaries should not be denied coverage for otherwise covered items or services because those items or services are provided through a clinical trial whose sponsor has agreed to cover those clinical care costs that are not normally (i.e., absent the trial) covered by the patient's insurance.

Medicare should cover trial related costs for Medicare beneficiaries regardless of whether the sponsor is paying for costs incurred by non-Medicare beneficiaries

Currently, CMS will not pay for clinical trial costs if they are for "items or services customarily provided by the research sponsors free of charge for any enrollee in the trial." Unfortunately, this policy confuses trial sponsors as they are not sure if CMS would deny access to Medicare beneficiaries to trials in which the sponsor covers certain services for non-Medicare beneficiaries. If the sponsor covers certain items or services for non-Medicare beneficiaries, CMS can decide not to cover these items and services for Medicare beneficiaries effectively denying them access to the trial.

---

12 *Id.* In the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), Congress amended the definition of "primary plan" to state that "[a]n entity that engages in a business, trade, or profession shall be deemed to have a self-insured plan if it carries its own risk (whether by a failure to obtain insurance, or otherwise) in whole or in part." Social Security Act § 1862(b)(2)(A).

Therefore, BIO urges CMS to clarify that CMS will cover trial-related costs regardless of whether the sponsor is paying for costs incurred by non-Medicare beneficiaries.

3. BIO opposes the removal the proposed self-certification process

BIO is concerned about CMS' intention to remove the self-certification process that never was implemented under the 2000 clinical trial NCD. We understand that an inter-agency panel met and developed criteria for the types of trials that should be covered under this process. We encourage the agency to release the panel's findings to the public and to propose an alternative qualifying process for those research studies that are not deemed to be qualifying clinical trials. This is necessary to ensure that Medicare beneficiaries have access to the full range of research studies being conducted and are able to participate in the studies that are most appropriate for their conditions.

4. CMS should establish data collection goals that minimize burdens to patients, providers, and clinical trial sponsors.

The data collection required by CMS, when in addition to any FDA-required data, adds to the costs of a clinical trial. We urge CMS to take every effort to minimize these costs. In determining whether additional data collection is necessary for Medicare covered trials, we urge CMS to carefully balance the value of the information gathered against the burden of collecting it, align any data collection requirements with FDA's clinical study requirements and with other research priorities to ensure that our research resources are used efficiently, and require that data collection continue only 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.

We also urge CMS to pay particular attention to the costs imposed on beneficiaries and providers. Beneficiaries' cost of care should not increase as the result of increased data collection requirements. If beneficiaries are forced to incur greater costs for receiving care in Medicare-covered clinical trials they will choose other, potentially less appropriate, care options. CMS also must minimize physicians' costs in operating clinical trials. Physicians who participate in clinical trials often donate considerable amounts of time and resources to evaluating patients' eligibility for trials, data collection, and drug administration services that frequently are not reimbursed by trial

sponsors. We also urge CMS to consider ways to compensate physicians more appropriately for the data collection activities they undertake, as well as services they provide relating to evaluating patient eligibility and drug administration.

5. <u>BIO supports increasing clinical trial participation</u>

BIO supports CMS' goal of encouraging more Medicare beneficiaries to participate in research studies, yet BIO is concerned that setting specific criteria requiring certain levels of Medicare enrollees in a clinical trial could have the effect of limiting beneficiary access to clinical trials. CMS has proposed developing criteria to assure that any Medicare covered clinical research study includes a representative sample of Medicare beneficiaries by demographic and clinical characteristics. While this could have the effect of making clinical trials more available to Medicare beneficiaries, many Medicare beneficiaries are ineligible for clinical trials due to age, co-morbidities, or complications. Others may choose not to participate if the trial would require 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. BIO urges CMS to develop a policy that recognizes the many impediments to enrolling Medicare beneficiaries in clinical trials. In order to ensure that Medicare coverage is available to those beneficiaries who do qualify for and choose to enroll in clinical trials, it is critical that CMS not impose stringent criteria that in fact hinder beneficiary participation in clinical trials.

BIO also encourages CMS to take additional steps to make Medicare beneficiaries more aware of ongoing clinical trials for which they may be eligible. BIO supports increased use of the NIH clinical trials registry as one means of educating Medicare beneficiaries about available clinical trials, and BIO urges CMS to consider other methods of more broadly disseminating this information as well.

<u>Conclusion</u>

We look forward to working with CMS to encourage increased Medicare beneficiary access to and participation in clinical trials. As this is an important policy for BIO and its members, we would be pleased to have the opportunity to discuss our comments with you in greater detail. Thank you for your attention to this very important matter.