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BY ELECTRONIC DELIVERY

Steve Phurrough, M.D.
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
Department of Health and Human Services
Mailstop: C1-12-28
7500 Security Blvd.
Baltimore, MD 21244

Re: Proposed Decision Memorandum for Medicare National Clinical Trial Policy (CAG-00071R)

Dear Dr. Phurrough:

The Biotechnology Industry Organization (BIO) appreciates this opportunity to comment on the Centers for Medicare and Medicaid Services' (CMS) Proposed Decision Memorandum for Medicare National Clinical Trial Policy (CAG-00071R) (hereinafter "Proposed CRP") as a reconsideration of its national coverage decision (NCD) on Medicare coverage of clinical trials. 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 members are involved in the research and development of healthcare, agricultural, industrial and environmental

biotechnology products. Our research initiatives advance the understanding of disease pathology and therapeutic mechanisms of action, clinical effectiveness, health-related quality of life, and health economic impacts of therapies in addition to clinical safety and efficacy.

BIO strongly supports evidence-based medicine and is committed to increasing the body of evidence available regarding diseases and their treatments. Our members invest millions of dollars each year on clinical studies, both before and after Food and Drug Administration (FDA) approval of their therapies, 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 practice of medicine and patient care. BIO also is committed to ensuring beneficiary access to innovative biological therapies. To that end, we support CMS' efforts to revise its NCD on Medicare coverage of clinical trials. We believe that a clarification of Medicare's coverage policy for clinical trials has the potential to strengthen the ability of biotechnology companies to develop and evaluate innovative therapies that will benefit Medicare beneficiaries.

As a general comment, BIO is concerned that the Proposed CRP diverges from the original intent of the agency's policy on Medicare coverage of clinical trials. In 2000, when the NCD on Medicare coverage of clinical trials first was developed, CMS (then the Health Care Financing Administration) recognized that beneficiaries should not be denied coverage of medically necessary care simply because that care was provided in the context of a clinical trial. The stated goals of the 2000 NCD were as follows: (1) to allow Medicare beneficiaries to participate in research studies, (2) to encourage research that adds to knowledge about therapies in the Medicare population and, by doing so, improve the quality of care that Medicare beneficiaries receive, and (3) to allow Medicare beneficiaries access to care that may have a health benefit, but for which unrestricted coverage is not yet available.[1]

BIO is concerned that the Proposed CRP not only moves away from these underlying goals, but that the Proposed CRP will in fact be in conflict with them. Specifically, we are concerned that CMS may be increasing the burdens on trial sponsors seeking Medicare coverage for reasonable and necessary care. In

[1] Proposed CRP at 4.

addition, although the Proposed CRP would greatly expand the scope of research studies subject to the requirements of the CRP, it also could create confusion about coverage of services that are currently covered, such as already-approved therapies, when provided in routine post-approval studies required by FDA. This confusion, and the potential bureaucratic burden it could impose on clinical researchers, could have a chilling effect on participation in clinical trials aimed at generating the very medical evidence CMS seeks.

BIO urges CMS to keep its underlying goals in mind when finalizing the CRP. The agency should clarify the requirements of the CRP in a manner that promotes Medicare beneficiary enrollment into clinical trials and assures them of coverage for their routine medical costs while enrolled in these clinical trials. Specifically, BIO requests that CMS include as "deemed" clinical trials exempt from the investigational new drug application (IND) process, at least until a separate centralized mechanism is established for approving these studies for inclusion. Second, BIO supports CMS' proposal to cover investigational clinical services in certain circumstances, and we seek additional clarification with regard to this proposal. Third, BIO believes that greater detail is needed in the implementation of certain of the Medicare-specific criteria in order to give beneficiaries, providers, and trial sponsors the certainty necessary to achieve the goals of the CRP. Fourth, BIO remains concerned that the CRP, and in particular those research studies that require Coverage with Evidence Development (CED), will impose additional data collection requirements on trial sponsors and asks CMS to consider ways to pay for some of the costs of those additional data requirements. Fifth, we urge CMS to address the Medicare Secondary Payer issues within the context of the CRP. Finally, BIO requests that CMS clarify the timeframe for implementation of the CRP and its applicability to research studies in various stages of development. These comments are discussed more fully below.

I. Coverage of IND-exempt Trials

In the Proposed CRP, CMS proposes to remove IND-exempt trials from the list of research studies "deemed" in compliance with the CRP, but does not provide another mechanism for these trials to be covered. BIO is extremely concerned about this proposal. We believe that failure to grant deemed status to IND-exempt studies will have the effect of limiting research studies in which Medicare beneficiaries are able to participate, particularly in areas of unmet need

such as oncology. BIO urges CMS to extend deemed status to IND-exempt research studies permanently. Alternatively, BIO urges CMS to include IND-exempt studies as "deemed" until a separate and centralized approval process can be established and implemented for these studies.

Exemption from the IND process 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 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 because these trials play an essential role in exploring innovative uses for approved therapies. 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] IND-exempt trials are a critical part of an established federal regulatory mechanism designed to expedite the approval of cancer therapies and encourage new uses of marketed products in cancer treatment. Outside the oncology setting, IND-exempt trials 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.

Designating IND-exempt trials as "deemed" qualified for Medicare coverage will reduce uncertainty among patients and providers regarding Medicare coverage for routine clinical services. While sponsors currently may seek coverage from local contractors, this process is inefficient and may result in varying coverage decisions, which poses challenges for research studies occurring in multiple sites. Failure to provide a clear centralized approval process for routine clinical services to be covered when part of an IND-exempt trial could render Medicare beneficiaries unable to obtain consistent coverage for therapies received

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[2] 48 Fed.Reg. 26720, 26721 (June 9, 1983); *see also* 52 Fed.Reg. 8798, 8799-8800 (Mar. 19, 1987). 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. 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").

[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.

during research studies that otherwise would be reimbursed outside the investigator-initiated trial. This will deter seniors from enrolling in potentially beneficial investigator-initiated studies and will deter publication of outcomes and data that could help improve the lives of Medicare beneficiaries. The inability of Medicare beneficiaries to participate in these critical research studies will undermine the fundamental goal of the CRP.

BIO appreciates CMS' acknowledgement that there is a "need to explore alternative processes for approving other types of studies such as IND exempt studies and studies of orphan drugs."[5] We support CMS' statement that it, along with the Agency for Healthcare Research and Quality (AHRQ), will seek public input in a discussion of various options. Nonetheless, BIO is concerned that this process may not be established in a timely manner. In issuing the NCD for clinical trials in 2000, CMS included as "deemed" IND-exempt trials only until other qualifying criteria could be developed. These criteria never were developed, and, as a result, IND-exempt trials have continued to operate as "deemed" under this temporary status. Failure to continue to deem IND-exempt trials, combined with delays in establishing a separate process for IND-exempt trials, will deny Medicare coverage to beneficiaries who could benefit from these clinical research studies. Leaving beneficiaries without access to coverage for these critical studies as well as without access to potential new therapies under study. It is imperative that CMS establish a clear and immediate avenue for centralized approval of IND-exempt trials. BIO urges CMS to undertake this effort expeditiously and to continue to cover IND-exempt studies under the CRP until such processes can be implemented. This is necessary to ensure that Medicare beneficiaries have access to the full range of research studies being conducted and that they are able to participate in the studies that are most appropriate for their conditions.

II. Coverage of Investigational Clinical Services

BIO supports CMS' proposal to cover investigational clinical services in Medicare-covered research studies both (1) where coverage for such services is a Medicare defined benefit, and (2) when the service is required as a condition of coverage pursuant to a NCD using CED. In order to achieve the CRP's goal of promoting Medicare beneficiary participation in clinical research, it is critical that a beneficiary be able to obtain coverage for the items and services that would be

[5] Proposed CRP at 24.

covered outside the context of a research study. In some research studies, the item or service being studied is not experimental and already has been determined to be reasonable and necessary for purposes of Medicare coverage. In these circumstances, Medicare should cover the investigational item or service within the context of a research study to the same extent as coverage otherwise is available to Medicare beneficiaries. BIO urges CMS to finalize this proposal and to clarify that coverage for the investigational item or service is available to beneficiaries participating in a research study in the same manner and to the same extent coverage is available to those beneficiaries not participating in the research study. BIO also urges CMS to include in the definition of investigational clinical services coverage for off-label indications for approved drugs and biologicals in Phase III studies.

In addition, BIO believes that CMS must not use the CRP to limit coverage for items and services currently covered by Medicare outside the context of a research study. Under Parts A and B, Medicare reimburses for drugs and biologicals in a range of settings. This includes coverage for on-label indications as well as off-label indications for cancer therapies when the indication is listed in an approved compendia and for medically accepted uses of other drugs and biologicals at the discretion of each Medicare contractor. We urge CMS to clarify that it does not intend the CRP to narrow that existing coverage or to require these covered uses to be part of CED or another study subject to CRP. Instead, Medicare coverage of approved therapies should not change depending on whether the therapy is part of a research study. Specifically, these therapies must continue to be covered consistent with existing reimbursement rules when provided as part of a research study that meets the requirements of the CRP.

BIO also supports coverage of the investigational item or service required as part of a NCD using CED. This will help to make CED a more feasible approach for trial sponsors, promote Medicare beneficiary enrollment into clinical trials, and increase the medical knowledge about therapies that have important implications for Medicare beneficiaries. Again, however, we are concerned that CMS not use the CRP to require otherwise covered therapies to be in a research study with CED in order for Medicare coverage to be available.

III. Implementation of the Medicare-Specific Criteria

As a general comment, BIO is concerned that many details regarding the implementation of this CRP are not clear. In particular, it is not apparent from the Proposed CRP how clinical trial sponsors or Medicare beneficiaries will know when a particular trial has met the criteria set forth in the CRP and thus the trial has been approved for coverage. This is particularly true with respect to the Medicare-specific criteria, and we believe more detailed guidance is needed with respect to the process for approving these criteria in order for trial sponsors to have certainty regarding Medicare coverage before enrolling beneficiaries in a clinical research study.

CMS proposes to clarify in the CRP that "CMS will use routine processes to ensure that the Medicare-specific standards and any standards required through the NCD process using CED are met."[6] We urge CMS to provide greater detail on how this approval process will work and to ensure that it is implemented in a manner that assures trial sponsors of certainty of Medicare coverage in advance of a research study and not retroactively. We understand that CMS may be considering a process by which it would review a random selection of research studies on a retrospective basis. We are extremely concerned that this approach would make both providers and beneficiaries reluctant to participate in research studies. These results would render the fundamental purpose of the CRP meaningless. If an approval process is established for Medicare-specific criteria, we encourage CMS to require submission of only the aspects of the protocol related to the Medicare-specific criteria rather than submission of the entire protocol.

Also with respect to the Medicare-specific criteria, BIO supports CMS' efforts to include certain Phase I trials in the CRP and requests certain clarifications of CMS' approach. Early phase trials are the building blocks for the development of approved therapies, and it is important to ensure that trial sponsors are not inappropriately burdened in the conduct of these studies in order to further the participation of Medicare beneficiaries. BIO also is concerned that some of the Medicare-specific criteria may not be appropriate for all research studies. BIO urges CMS to establish its standard regarding the consideration of certain subpopulations as well as the criteria related to the consideration of Medicare-specific issues in trial design in a manner that recognizes the wide range of research studies. We have discussed each of these comments in more detail below.

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[6] CRP at 24.

A. Coverage for Beneficiaries Participating in Phase I Research Studies

Under the Proposed CRP, one of the proposed Medicare-specific criteria is that the clinical research study not be designed to exclusively test toxicity or disease pathophysiology. The proposed criterion goes on to state that "[r]esearch studies, including some Phase I trials, whose protocols commit to measuring therapeutic outcomes as one of the objectives, may meet this standard only if the disease being studied is chronic, life threatening, or debilitating."

BIO believes it is critical that CMS expand its coverage policy to include expressly all Phase I studies except for those conducted in healthy volunteers/subjects, as well as include all Phase II studies. The current coverage requirement that clinical trials have therapeutic intent unfortunately leads to confusion and inconsistent coverage determinations. Under the existing NCD, coverage for Phase I studies frequently is denied and, under some narrow interpretations of the existing NCD, coverage is limited only to Phase III studies. BIO believes that this harms Medicare beneficiaries' access to promising new investigational drugs in the early stages of their development, particularly for diseases where there exists no current standard of care or where other treatment options have failed. Moreover, Phase I trials have an implicit therapeutic intent as part of research into the development of new therapeutic interventions, and it is only as a result of the conduct of these early phase trials that later phase studies are feasible. BIO supports CMS' proposal to expressly include certain Phase I trials under the CRP.

We suggest, however, that CMS revise the language to more closely mirror that proposed by the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) or AHRQ in finalizing this standard. Specifically, we are concerned that the statement that "[r]esearch studies, including some Phase I trials, whose protocols commit to measuring therapeutic outcomes as one of the objectives, may meet this standard only if the disease being studied is chronic, life threatening, or debilitating" can reasonably be construed to mean that all research studies, not just Phase I studies, may be covered only if the disease being studied is chronic, life threatening, or debilitating. We do not believe that CMS means to preclude Medicare coverage of any research study that does not meet this standard.

Instead, we suggest that CMS revise this criterion to state that "The research study must not be designed primarily to test toxicity or disease pathophysiology in healthy individuals. Phase I trials that have therapeutic intent as one of the objectives may meet this standard if the disease is chronic, life-threatening, or debilitating." This revised language would more clearly indicate what trials may not be covered under the CRP and would limit the restriction in coverage to those Phase I trials studying healthy volunteers/subjects.

B. Registration on Clinicaltrials.gov

BIO supports the concept of trial registration, particularly as a means for Medicare beneficiaries and others to learn about the research studies particularly relevant to their condition. We request that CMS provide study sponsors a reasonable way to comply with this requirement, such as specifying that posting on clinicaltrials.gov must occur within 30 days of a trial's approval by an institutional review board (IRB) or first patient visit. We ask that CMS work to make the website more user friendly for Medicare beneficiaries. In addition, CMS should provide links from Medicare.gov for beneficiaries interested in participating in trials and clarify that research study participation should not result in lack of coverage for routine care.

C. Participation of Medicare Beneficiaries in Research Studies

BIO supports CMS' goal of encouraging more Medicare beneficiaries to participate in research studies, and we believe that CMS' efforts to clarify Medicare coverage of clinical trials by developing a new CRP could have the effect of making clinical trials more available to Medicare beneficiaries. We appreciate CMS' efforts to develop guidelines regarding the representation of Medicare beneficiaries in Medicare-covered trials in a manner that reflects the challenges of enrolling Medicare beneficiaries and fosters the goal of increasing the participation of such patients. With respect to the Proposed CRP standard that the research protocol "must have explicitly discussed inclusion criteria and considered relevant subpopulations," however, BIO is concerned that this standard does not reflect the nature of the wide range of studies that will be subject to the CRP. BIO recognizes the importance of including relevant subpopulations where appropriate in clinical research. However, we are concerned that this standard, as proposed, will eliminate smaller studies from the CRP. Many trials covered under the current NCD involve only small numbers of patients. In a small trial, including

many Phase II studies, it may not be possible to assess results by certain subpopulations. This standard would have the effect of denying Medicare beneficiaries access to a wide range of small trials.

BIO also appreciates CMS' recognition that establishing stringent criteria regarding the enrollment of Medicare beneficiaries could have the effect of limiting beneficiary access to trials. This is critical in ensuring that Medicare coverage is available to those beneficiaries who do qualify for and choose to enroll in research studies. Many of the therapies in biotech companies' pipelines target conditions that primarily affect seniors, an important and growing population in need of new drug development for conditions common in later life. Member companies long have sought innovative therapies for Medicare's disabled population. It is critical that those Medicare beneficiaries who are able to qualify for a clinical trial be able to participate without concern that their care will not be covered. This, in turn, will better enable sponsors to include Medicare beneficiaries their research studies.

In sum, with respect to the Medicare-specific criteria, BIO urges CMS to design any approval process in a manner that provides sufficient detail and consistency so that trial sponsors, clinical researchers, or patients have a reasonable level of certainty regarding Medicare coverage when enrolling Medicare beneficiaries in a research study. We also urge CMS to clarify its proposed implementation of these Medicare-specific criteria in a manner that better recognizes the appropriate role of Medicare coverage in a research study as well as provides trials sponsors, researchers, and providers with adequate certainty regarding Medicare coverage during a research study.

IV. New Data Collection Requirements

We greatly appreciate CMS' efforts to clarify the interaction between CED and the CRP. Nonetheless, we continue to have some serious concerns regarding the potential application of CED to drugs and biological products. Most relevant to the CRP, we are concerned about the imposition of data collection requirements in addition to those required by FDA. We urge CMS to minimize additional data collection requirements and to set any data collection standards in a manner that can achieve its specific goals while imposing minimal burdens for patients, providers, and clinical trial sponsors. We also urge CMS to consider

covering the costs of additional data collection requirements imposed by a NCD with CED.

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 and 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. One option for appropriately compensating these costs would be to permit coverage of administrative costs specifically related to a NCD with CED. In the Proposed CRP, CMS has clarified that administrative services will not be covered by Medicare. Yet BIO urges CMS to consider covering certain administrative services when required by a NCD with CED, much like the Proposed CRP policy on covering investigational clinical services when those services are required pursuant to a NCD with CED. This would reduce the burden of collecting additional data, as is required by CED.

In determining whether additional data collection is necessary for Medicare-covered trials, we urge CMS to balance carefully 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 these data are justified by the potential value of the information to be collected. We believe it is critical that data collection needs be determined at the outset so that the study will produce the data needed to satisfy CMS' needs and to ensure that any coverage decisions relying in part on such data will be made in an efficient and timely manner. 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.

V. Medicare Secondary Payer Issues

In the Proposed CRP, CMS states that it will address Medicare Secondary Payer (MSP) issues separately from the Proposed CRP. Although BIO appreciates that a different office within CMS may have responsibility for MSP issues more broadly, we urge CMS to address these issues directly within the context of the CRP, and we reiterate our concerns here. It is critical to ensuring beneficiary participation in research studies that CMS clarify that when a clinical trial sponsor, study site, or investigator assures a study subject that he or she will not be responsible for out-of-pocket payments for medical services resulting from a trial-related illness or injury, that assurance will not turn the sponsor, site, or investigator into a primary payer, and render Medicare a secondary payer.

The Medicare statute requires payment for items and services that are reasonable and necessary for the treatment of illness or injury.[7] 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.[8] 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.[9]

The MSP statute provides that Medicare payment "may not be made…with respect to any item or service to the extent that payment has been made or can reasonably be expected to be made" under a "primary plan."[10] The statute defines "primary plan" to include (1) a group health plan or large group health plan and (2) a worker's compensation law or plan or automobile or liability insurance policy or plan (including a self-insured plan) or no fault insurance.[11] Nothing in the MSP statute or its legislative history suggests that Congress intended to expand the reach of the MSP provisions to preclude Medicare payment

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[7] 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).

[8] 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.

[9] Medicare Coverage, Clinical Trials, Final National Coverage Decision, *available at* http://www.cms.hhs.gov/coverage/8d2.asp.

[10] 42 U.S.C. § 1395y(b)(2)(A).

[11] *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).

for covered items and services when the sponsor of a clinical trial 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. In effect, such an interpretation of the MSP statute would turn clinical trial sponsors into primary health care insurers – a result surely not intended by Congress, and one that runs contrary to the policy of encouraging the participation of Medicare beneficiaries in clinical trials. Accordingly, BIO urges CMS to 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. CMS should assure beneficiaries that they will not be denied coverage merely because they have volunteered to participate in a clinical trial.

In addition, we ask that CMS clarify that neither the MSP statute, nor the exclusion from Medicare coverage for items or services for which a person has no legal obligation to pay,[12] operates to eliminate Medicare coverage for otherwise covered items where the sponsor has agreed to cover those clinical care costs that would not, in any event, have been recognized as an expense covered by insurance (e.g., the costs of care for uninsured trial participants). CMS should make clear that beneficiaries may not be denied coverage for otherwise covered items or services as a result of having volunteered to participate in a clinical trial whose sponsor has agreed to cover those clinical care costs that are not, for any particular patient, normally (i.e., absent the trial) covered by insurance.

VI. Implementation of the CRP

In implementing the CRP, BIO urges CMS to grandfather existing clinical trials, including any new trial sites for ongoing clinical trials. Where an ongoing clinical trial adds a new trial site, it is important that that new sites be able to operate under the same protocol as those sites that had studies underway prior to implementation of the CRP. At a minimum, the guidance on the timing of the CRP implementation and how it applies to different types of studies already underway is critical. Also, we urge CMS to provide clear guidance on exactly when the CRP will go into effect for new trials, taking into consideration research studies that already have been approved and are about to begin enrolling patients. It could be

[12] 42 U.S.C. § 1395y(a)(2).

extremely disruptive to these research studies to have to reconfigure protocols in order to comply with the CRP on the eve of enrolling patients.

VII. Conclusion

BIO appreciates this opportunity to comment on CMS' Proposed CRP. We hope that our recommendations are useful to the agency in developing a final CRP that establishes Medicare coverage of clinical trials in a predictable manner that ensures beneficiary access to innovative drugs and biologicals. Specifically, we urge CMS to:

- Expressly designate clinical trials exempt from the IND process as "deemed," at least until another centralized approval process for these research studies is established and implemented;
- Clarify that coverage of investigational services is available in a research study consistent with existing Medicare coverage of these items or services, as well as that the CRP does not intend to narrow existing Medicare coverage to require that already covered items or services must be part of a CRP research study in order to continue to maintain coverage;
- Include coverage of off-label indications for approved drugs and biologicals in Phase III studies in the definition of "investigational clinical services";
- Make clear how the CRP will be implemented in a manner that gives trial sponsors, providers, and Medicare beneficiaries sufficient certainty regarding coverage;
- Include Phase I studies in the CRP where the disease studied is chronic, life threatening, or debilitating;
- Ensure that standards regarding the inclusion of subpopulations can be applied in the context of a wide range of research studies, including smaller studies;
- Set any data collection standards in a manner that achieves CMS' specific goals without imposing undue burdens on patients, providers, and clinical trial sponsors;
- Explain that Medicare coverage of a clinical trial is not conditioned on the clinical trial sponsor serving as a primary payer for medical costs that may be associated with the trial; and
- Clarify how the implementation of the CRP will apply to research studies in various stages of development at the time the CRP becomes effective, and

grandfather trials and sites already underway as well as those studies about to begin.

We look forward to working with CMS to encourage increased Medicare beneficiary access to and participation in clinical trials. If you have any questions regarding our comments, please contact me at 202-312-9281. Thank you for your attention to this very important matter.

Respectfully submitted,

/s/

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