August 24, 2026

VIA ELECTRONIC FILING - *http://www.regulations.gov*

Department of Health and Human Services, Office of Inspector General
Attention: OIG-2602-N

Re: Medicare and State Health Care Programs: Fraud and Abuse; Request for Information Regarding the Federal Anti-Kickback Statute and Beneficiary Inducements CMP (OIG-2602-N)

The Pharmaceutical Research and Manufacturers of America (PhRMA) and Biotechnology Industry Organization (BIO) appreciate the opportunity to respond to the request for information issued by the Office of Inspector General (OIG) seeking input on whether additions or modifications are needed to the safe harbor regulations under the federal Anti-Kickback Statute (AKS) or the exceptions to the beneficiary inducements civil monetary penalty provision (Beneficiary Inducements CMP) for remuneration provided to individuals in connection with their participation in clinical trials (the RFI).[1]

PhRMA and BIO applaud OIG for publishing the RFI as one of the key measures identified in the Operation TrialBlazer initiative announced by the Department of Health and Human Services (HHS) on June 22, 2026. PhRMA and BIO view the RFI and any subsequent proposed and final rulemaking as a critical piece to the success of Operation TrialBlazer and submit this response to support the Administration's efforts to "reduce unnecessary delays, increase participation in clinical research, strengthen domestic research capacity, and help ensure that the next generation of medical breakthroughs is developed in the United States."[2] For the reasons discussed below, PhRMA and BIO encourage OIG to create by regulation an AKS safe harbor and Beneficiary Inducements CMP exception (or clarification) to clearly protect certain remuneration to clinical trial patients. Modernizing participant-support policies can also strengthen the efficiency, quality, and competitiveness of the U.S. clinical research ecosystem by reducing avoidable barriers to clinical trial participation. PhRMA and BIO's comments seek to provide helpful background information and suggested guardrails to inform OIG's thinking as it moves towards a possible proposed rulemaking, which PhRMA and BIO strongly support.

I. About PhRMA and BIO

PhRMA represents the country's leading innovative biopharmaceutical research companies, which are focused on developing innovative medicines that transform lives and create a healthier world. Together, we are fighting for solutions to ensure patients can access and afford medicines that prevent, treat and cure disease. PhRMA member companies have

[1] 91 Fed. Reg. 37903 (Jun. 24, 2026).
[2] *HHS Launches Unprecedented Department-Wide Effort To Restore American Leadership in Clinical Trials*, U.S. Dep't of Health & Hum. Servs. (Jun. 22, 2026), https://www.hhs.gov/press-room/hhs-launches-clinical-trials-reform-initiative.html.

invested more than $900 billion in the search for new treatments and cures over the last decade, supporting nearly five million jobs in the United States.

BIO is the premier biotechnology advocacy organization representing biotech companies, industry leaders, and state biotech associations in the United States and more than 35 countries around the globe. BIO members range from biotech start-ups to some of the world's largest biopharmaceutical companies—all united by the same goal: to develop medical and scientific breakthroughs that prevent and fight disease, restore health, and improve patients' lives. BIO also organizes the BIO International Convention and a series of annual conferences that drive partnerships, investment, and progress within the sector. Learn more at bio.org.

PhRMA and BIO members have a longstanding commitment to sponsoring ethical and safe clinical research. Rigorous ethical standards—including informed consent, independent institutional review board (IRB) oversight, scientific integrity, and ongoing safety monitoring—help ensure that clinical research is conducted responsibly and transparently throughout the world, including in the U.S. By upholding these ethical principles, the biopharmaceutical research community fosters public trust, supports meaningful scientific progress, and helps deliver safe and effective medicines that improve and save lives for patients around the world. To that end, PhRMA members have adopted voluntary "Principles on Conduct of Clinical Trials & Communication of Clinical Trial Results"[3] and BIO has launched "BIO Clinical Trials: The Power of Participation" or ctpop.org, a resource that connects patients and families with scientifically sound resources on clinical trials.

II. U.S. Patients Face Serious Barriers to Clinical Trial Participation

Conducting clinical trials in the United States provides American patients early access to potential treatment options and generates data that help support approval for the U.S. market and evaluate treatments in the U.S. populations they are intended to serve. Indeed, U.S. patients most often express interest in participating in clinical trials to gain access to potential new treatment options for unmet medical need and expert medical care.[4]

Despite the critical role that clinical trials play in developing new therapies, participation in clinical research remains persistently low in the United States.[5] Studies consistently show that only a small percentage of eligible U.S. patients ultimately enroll in clinical trials, and inadequate enrollment is one of the primary reasons trials are delayed, extended, or terminated before completion.[6] And even if patients can enroll initially, participant attrition throughout all phases of a clinical trial is a significant challenge in clinical research. Dropout rates in Phase III clinical

[3] PhRMA, *Principles on Conduct of Clinical Trials*, (Oct. 2020) https://www.phrma.org/resources/phrma-principles-on-conduct-of-clinical-trials.
[4] Z. Feuer et al., *Non-oncology clinical trial engagement in a nationally representative sample: Identification of motivators and barriers*. 115 Contemp. Clinical Trials 106715 (2022), https://pmc.ncbi.nlm.nih.gov/articles/PMC11431411/.
[5] *See* Nat'l Cancer Inst., *HINTS Brief No. 48: Clinical Trial Participation Among U.S. Adults* (Health Info. Nat'l Trends Surv. 2022), https://hints.cancer.gov/docs/Briefs/HINTS_Brief_48.pdf.
[6] *See* B. Desai, *Recruitment and Retention of Participants in Clinical Trials: Critical Issues and Challenges*, 11 Persps. Clinical Rsch. 51 (2020); Walter Alexander, *The Uphill Path to Successful Clinical Trials: Keeping Patients Enrolled*, 38 P&T 225 (2013).

trials have been reported to exceed 30% in some studies,[7] for example. Such attrition causes gaps in study data, delays study completion, and can undermine the reliability and generalizability of trial results.[8]

As OIG acknowledges in the RFI,[9] many[10] U.S. patients who could benefit from participating in clinical trials face various medical and non-medical expenses and financial barriers that can discourage enrollment or ongoing participation in a clinical trial even if the study sponsor covers experimental and non-covered medical costs[11] and insurers cover standard of care costs.[12] Numerous studies confirm that both medical and non-medical out-of-pocket costs, including travel, food, lodging, expenses for caregivers traveling with the trial participant to support participation in the trial,[13] dependent care for the patient's household while the trial participant travels to the research site, and lost wages, constitute meaningful barriers to clinical trial participation and may discourage eligible patients from participating in screening for, enrolling in, or completing a trial.[14] These out-of-pocket expenses, financial burdens, and technology barriers include:

- **Cost-sharing obligations** associated with any standard of care items or services associated with the trial. OIG has acknowledged that out-of-pocket cost-sharing expenses may be cost prohibitive for many Medicare beneficiaries who otherwise would participate in a clinical trial.[15] Cost-sharing burdens are a medical expense that can range from high-deductible payments to 20% co-pays for standard of care items and services where the item or service is covered by insurance and not paid for by the sponsor of the study. Published studies corroborate OIG's concern. For

[7] *See* Walter Alexander, *The Uphill Path to Successful Clinical Trials: Keeping Patients Enrolled*, 38 P&T 225 (2013).
[8] *See* Roderick J. Little et al., *The Prevention and Treatment of Missing Data in Clinical Trials*, 367 New Eng. J. Med. 1355 (2012).
[9] "For some people, extra costs or burdens associated with trial participation may create a disincentive to enroll or stay enrolled in a clinical trial." 91 Fed. Reg. at 37903.
[10] Courtney P. Williams et al., *Influence of Cost-Related Considerations on Clinical Trial Participation: Results from the 2020 Health Information National Trends Survey (HINTS)*, 38 J. Gen. Intern. Med. 1200, 1200–06 (2023), https://pmc.ncbi.nlm.nih.gov/articles/PMC9713084/.
[11] For example, out-of-pocket expenses associated with non-covered genomic testing.
[12] *See, e.g.*, Giulia Bianconi et al., *Barriers and Facilitators to the Participation of Subjects in Clinical Trials: An Overview of Reviews*, 23 Contemp. Clinical Trials Commc'ns 100829 (2021); Amanda Crocker et al., *Transparency, Trust and Minimizing Burden to Increase Recruitment and Retention in Trials: A Systematic Review*, 134 J. Clinical Epidemiology 35 (2021); Erin Haynes et al., *Transportation, Childcare, Lodging, and Meals: Key for Participant Engagement and Inclusion of Historically Underrepresented Populations in the Healthy Brain and Child Development Birth Cohort*, J. Clinical & Translational Sci. (2025).
[13] For pediatric studies, two caregivers are often needed to support the patient.
[14] *See e.g.*, Off. of the Assistant Sec'y for Plan. & Evaluation, U.S. Dep't of Health & Hum. Servs., *Financial Stress Associated With Oncology Clinical Trial Participation: Issue Brief* (Jan. 16, 2025), https://www.ncbi.nlm.nih.gov/books/NBK611603/; Ryan D. Nipp et al., *Financial Burden of Cancer Clinical Trial Participation and the Impact of a Cancer Care Equity Program*, 21 Oncologist 467 (2016); Courtney P. Williams et al., *Financial Reimbursement for Clinical Trial Participation Costs: A Pilot Feasibility Study*, 10 JNCI Cancer Spectrum pkag048 (2026); Aleksandra E. Zgierska et al., *Transportation, Childcare, Lodging, and Meals: Key for Participant Engagement and Inclusion of Historically Underrepresented Populations in the Healthy Brain and Child Development Birth Cohort*, 8 J. Clinical & Translational Sci. e38 (2024).
[15] *See supra* n. 9.

example, in a recent survey of 650 cancer patients, nearly 50% of respondents reported that medical bills and other trial-related financial burdens caused financial hardship that contributed to significant challenges in participation in clinical trials.[16]

Even when a trial sponsor covers the investigational product and non-covered research costs, patients may experience different levels of financial burden depending on how routine care costs are covered in a trial. Coverage for standard-of-care items and services can vary based on plan design, network status, deductible exposure, coinsurance, copayments, billing practices, and state or program-specific requirements. A national framework should therefore avoid assuming that categorizing a service as standard of care makes participation financially neutral for all patients. Instead, a consistent approach should allow sponsors to use a uniform methodology across participants and sites that account for these differences and permits support for incremental, documented out-of-pocket costs where needed.

There can also be other non-covered / uninsured medical expenses that might create barriers to participation such as the need for fertility services for an eligible patient in preparation for participation in a clinical trial. Published studies identify high out-of-pocket costs as a significant barrier to patients' use of fertility-preservation services, particularly young adults.[17] While the Trump Administration announced major initiatives in May 2026 to expand access to fertility care, these initiatives do not address fertility preservation in the context of clinical trials, and this gap in support can create a significant barrier for patients of child-bearing age to participate in certain clinical trials.[18]

- **Other major financial burdens** associated with traveling to and from clinical trial appointments, including transportation costs for local or long-distance travel to research trial sites,[19] lodging, meals, incidental travel costs, caregiving and other family/household support (*e.g.*, grocery or other meal support), mental health support outside trial hours to support continued participation in the trial, and lost wages. In many cases, out-of-pocket expenses also carry significant logistical challenges for trial participants, not just financial barriers.

[16] Courtney P. Williams et al., *Understanding the financial cost of cancer clinical trial participation.* Cancer Medicine Open Access (2024), https://onlinelibrary.wiley.com/doi/epdf/10.1002/cam4.7185.
[17] C. Dorfman et al., *Impact of Financial Costs on Patients' Fertility Preservation Decisions: An Examination of Qualitative Data from Female Young Adults with Cancer and Oncology Providers*, 13(3) J. Adolescent Young Adult Oncology 502-13 (2024), https://pubmed.ncbi.nlm.nih.gov/38294823/.
[18] "President Trump Honors America's Moms with New Support for Families", The White House (May 11, 2026).
[19] Hala T. Borno et al., *At What Cost to Clinical Trial Enrollment? A Retrospective Study of Patient Travel Burden in Cancer Clinical Trials*, 23 Oncologist 1242, 1242–49 (2018), https://doi.org/10.1634/theoncologist.2017-0628; Shreya Badhrinarayanan, *The Challenge of Patient Enrollment in Clinical Trials*, Nat'l Cmty. Oncology Dispensing Ass'n (Oct. 14, 2025), https://ncoda.org/news/the-challenge-of-patient-enrollment-in-clinical-trials/.

- The Office of the Assistant Secretary for Planning and Evaluation (ASPE) has recognized that lost wages and expenditures for travel and lodging are among the most cited barriers for participation in clinical trials.[20]

- As the Agency for Healthcare Research and Quality (AHRQ) has reported, the problem is particularly acute for patient registries, where patients do not receive an interventional therapy at all and therefore the motivation to participate can be quite low absent adequate compensation.[21]

- In a study conducted by researchers from the University of Texas, nearly half of patients participating in an early-phase cancer clinical trial reported out-of-pocket spend of more than $1,000 per month to participate and resulting financial hardship.[22]

- A study of cancer survivors conducted by the American Cancer Society Cancer Action Network found that nearly 80% reported that subsidized transportation would increase their willingness to participate in a trial outside their local area.[23]

- A nationwide survey conducted by researchers at the University of Alabama Birmingham found that 1 in 4 respondents reported transportation, childcare, paid time off work, and other such payments to make the patient financially-whole would increase their willingness to participate in a trial.[24]

- **Technology and internet challenges** such as lack of access to smart technology[25] that could be used to efficiently participate in the trial (for example, to receive testing or clinical trial appointment reminders, report at-home results, or receive behavioral reinforcement that can encourage continued trial participation).

    - Researchers at the Mayo Clinic studying challenges in decentralized trials have found that roughly 20% of the U.S. population lacks broadband internet access or a smart phone, with elderly, rural, and other vulnerable

[20] Allison Kolbe & Trinidad Beleche, *Financial Stress Associated with Oncology Clinical Trial Participation*, Off. of the Assistant Sec'y for Planning & Evaluation, U.S. Dep't of Health & Hum. Servs. (Jan. 16, 2025), https://www.ncbi.nlm.nih.gov/books/NBK611603/.
[21] Richard E. Gliklich, Michelle B. Leavy & Nancy A. Dreyer eds., *Registries for Evaluating Patient Outcomes: A User's Guide, ch. 10, Recruiting and Retaining Participants in the Registry* (4th ed., Agency for Healthcare Rsch. & Quality 2020), https://www.ncbi.nlm.nih.gov/books/NBK562579/.
[22] Ryan W. Huey et al., *Patient-Reported Out-of-Pocket Costs and Financial Toxicity During Early-Phase Oncology Clinical Trials*, 26 Oncologist 588, 588–96 (2021), https://doi.org/10.1002/onco.13767.
[23] *Survivor Views: Telehealth and Clinical Trials (Survey Findings Summary)*, Am. Cancer Soc'y Cancer Action Network (Oct. 2021), https://www.fightcancer.org/sites/default/files/national_documents/survivorviews-telehealth-trials.pdf.
[24] Courtney P. Williams et al., *Financial Reimbursement for Clinical Trial Participation Costs: A Pilot Feasibility Study*, 10 JNCI Cancer Spectrum, no. 3, (2026), https://doi.org/10.1093/jncics/pkag048.
[25] Mobile Device Management (MDM) systems can lock device use to clinical trial apps.

patients particularly impacted.[26] Decentralized trials have the potential to reduce geographic and logistical barriers to participation, but they are dependent on consistent access to reliable technology. Limited broadband access, lack of compatible devices, and accessibility needs can make it more difficult for some patients to enroll in and remain engaged in decentralized studies. Where technology is necessary or appropriate for participation, support for devices, connectivity, and related tools should be viewed as participation-enabling support that facilitates enrollment and retention rather than as an inducement.

- Lack of access to technology also interferes significantly with enrollment and ongoing participation in trials at research sites. Mobile apps, text messages, and email reminders help participants manage appointments, communicate questions with study staff, access study requirements, and receive appointment reminders. For example, a separate Mayo Clinic study found approximately 77% clinical trial adherence over 12 months for patients who wore smart watches at least 70% of the time.[27]

These costs often present insurmountable barriers to eligible patients, particularly those from underserved communities, even when the investigational treatment is provided at no cost. This in turn can undermine efforts to strengthen domestic research capacity and provide clinical trial options to patients with unmet need.[28]

The form and timing of remuneration to clinical trial participants can also impact enrollment and retention.

- Expense reimbursement can pose a particular challenge for smaller reimbursable expenses, where participants often face challenges in collecting and submitting numerous low-dollar value receipts. For that reason, reasonable per diem pre-paid debit cards restricted to certain types of purchases such as public transportation, gas and mileage, parking, and meals purchased at the research site are more practical for trial participants than a lengthy wait for subsequent reimbursement.

- Travel and lodging may be paid for directly by a sponsor so that no expense is incurred by the patient.

[26] Noah Goodson et al., *Opportunities and Counterintuitive Challenges for Decentralized Clinical Trials to Broaden Participant Inclusion*, 5 npj Digit. Med. 58 (2022), https://doi.org/10.1038/s41746-022-00603-y.
[27] Angelina R. Wilton et al., *Participant-Centered Engagement for Sustained Adherence to Smartwatches: A 12-Month Prospective Decentralized Digital Health Study*, 18 Clin. & Transl. Sci. e70155 (2025), https://doi.org/10.1111/cts.70155.
[28] As a matter of practice, title for the devices typically remains with the sponsor and reasonable mechanisms would be established to collect such devices upon conclusion of the trial or the patient's withdrawal from the trial, whichever would occur sooner. Carrier plans would be paid for directly by the sponsor to the carrier to ease administration and consistent with title remaining with the sponsor.

- Stipends may be paid daily or weekly, or as a lump sum in connection with key milestones.[29]

- Technology may be shipped directly to the patient's home.

Vendors may be used to help execute any of the foregoing activities given the challenging logistics of many of these activities so long as such vendor arrangements meet the requirements of 42 C.F.R. § 1001.952(d)(1), the personal services and management contracts safe harbor. [30] Such controls are important for smooth trial participation and avoiding missed trial appointments or activities, and tools such as restricted use pre-paid debit cards with monitoring and travel vendors for transportation and lodging also help guard against the potential for misunderstanding by the patient regarding the scope of sponsor support.

These examples reflect that the form and timing of the remuneration must be flexible and suited to the trial and type of financial barrier in order to provide the practical support a patient may need to encourage enrollment and retention. Value caps should not be imposed because such caps would be unduly restrictive for certain trials and create a disincentive for those trials that create significant financial barriers for patients. Nor should limits be posed based on the phase of the trial.[31] IRB oversight of the nature and type of remuneration and informed consent—coupled with the U.S. Food and Drug Administration (FDA) regulations and our request for an AKS safe harbor and Beneficiary Inducements CMP exception as set forth below—will adequately safeguard against potential fraud and abuse around the nature, form, reasonableness, and timing of clinical trial remuneration.

The nature, form, reasonableness, and timing of such remuneration can vary from trial to trial, and a value cap could create a barrier to participation for some trials (*e.g.*, a larger stipend may be needed for rural patients who have to travel farther or longer to reach a trial site than a stipend for a patient who lives close to a trial site).[32] For that reason, we believe any value cap would be arbitrary and that a better approach to increase domestic research capacity is to establish a flexible standard that requires documentation of the nature, form, reasonableness, and timing of the remuneration under a specified plan submitted to the IRB.

In the alternative, if a fixed value cap is considered by OIG, PhRMA and BIO respectfully seek notice and comment to provide additional context to OIG as to why a fixed value cap would be unworkable. In lieu of such a proposal, we would urge OIG to consider guardrails for key concerns (*e.g.*, no requirements to forfeit payments in a manner that would penalize withdrawal from the trial) or a framework for pre-payment of known costs, reimbursement of certain expenses, and reasonable compensation based on a flexible documented payment methodology, among other categories.

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[29] "Trials may offer compensation as a single lump sum or in increments after certain milestones are completed." Allison Kolbe, *Use of Participant Compensation in U.S. Clinical Research Studies*, Off. of the Assistant Sec'y for Plan. & Evaluation, U.S. Dep't of Health & Hum. Servs. (July 2025), https://aspe.hhs.gov/sites/default/files/documents/2a53eba5b12d49257e5062fef1d60fd9/Compensation%20Issue%20Brief%20Final.pdf.

[30] 42 C.F.R. § 1001.952(d).

[31] As ASPE has recognized, "Differences [in compensation to patients] were [] modest between study phases, although early phase 1 trials offered compensation the most frequently." *See supra* n. 29.

[32] A. Bharucha, *Participation of rural patients in clinical trials at a multisite academic medical center*, 5 J. Clin. & Translational Sci. 190 (2021), https://pmc.ncbi.nlm.nih.gov/articles/PMC8596068/.

We note in prior favorable OIG advisory opinions, OIG has cited as a favorable factor caps on the enrollment of the number of patients in the trial. Many innovative clinical trial designs such as adaptive design and open registries may have no fixed enrollment cap. A hard cap on enrollment as a safe harbor condition could exclude the very innovative designs that are needed in order to increase research capability in the U.S. Enrollment flexibility is needed for any safe harbor in order for it to be workable for the various types of trial designs that sponsors might consider for domestic research activities.

Without appropriate support, all these categories of medical and non-medical costs can make clinical trial participation inaccessible or make it difficult for enrolled participants to remain in a trial. This in turn can negatively affect the clinical trial ecosystem and may limit the extent to which clinical trials reflect the patient population that will ultimately use a product if it is approved. Patients who participate in clinical trials are in search of medical options and scientific advancements, not financial enrichment. Sponsors likewise conduct clinical trials, regulated by FDA and overseen by IRBs, to develop medicines and obtain regulatory approval, not to improperly steer patients towards a particular therapy.

III. Existing Ethical and Legal Frameworks Do Not Fully Address Payments to U.S. Clinical Trial Participants

As one tool for addressing the burdens of clinical trial participation, FDA and the Office for Human Research Protections (OHRP) have recognized that "[p]aying research subjects in exchange for their participation is a common and, in general, acceptable practice," subject to important ethical and legal safeguards.[33] This principle has its roots in the broad ethical norms that apply to all clinical research and are set forth in internationally recognized documents, such as the Declaration of Helsinki and the Guideline for Good Clinical Practice of the International Conference on Harmonization.

A key principle in this context is that clinical trial investigators must obtain informed consent from participants only under circumstances that minimize the possibility of coercion or undue influence.[34] Accordingly, the amounts, methods, timing, and advertising of any remuneration provided to trial participants are subject to independent IRB oversight under applicable FDA regulations, the Common Rule, and other regulatory authorities.[35] Among other things, longstanding FDA guidance states that advertising for recruitment into clinical trials may state that subjects will be paid, but should not emphasize the payment or the amount to be paid,

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[33] U.S. Food & Drug Admin., *Payment and Reimbursement to Research Subjects* (Jan. 2018) *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/payment-and-reimbursement-research-subjects; *see also* OHRP, *Informed Consent FAQs*, *available at* https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html.

[34] *See* 21 C.F.R. § 50.20, 45 C.F.R. § 46.116(a)(2).

[35] *See, e.g.*, U.S. Food & Drug Admin., *Payment and Reimbursement to Research Subjects, Guidance for Institutional Review Boards and Clinical Investigators* (Jan. 2018) *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/payment-and-reimbursement-research-subjects; "Informed Consent: Guidance for IRBs, Clinical Investigators, and Sponsors" (Aug. 2023), *available at* https://www.fda.gov/media/88915/download; OHRP. *Informed Consent FAQs*; ICH Harmonised Guideline, *Guideline for Good Clinical Practice* E6(R3), at 9 (Jan. 2025), https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf.

by such means as larger or bold type.[36] Moreover, the same FDA guidance states advertising for clinical trial recruitment "should not promise 'free medical treatment,' when the intent is only to say subjects will not be charged for taking part in the investigation."[37]

IRBs are in the best position to assess all of these issues related to sponsor support for screening, enrollment, and ongoing participation in a clinical trial on a population- and trial-specific basis.[38] In other words, to the extent these forms of support are currently offered by clinical trial sponsors, they are subject to regulatory requirements and independent IRB review that provide checks and balances to protect patients.

And, within this framework, the HHS Secretary's Advisory Committee on Human Research Protections (SACHRP), has recognized that "[m]ost payments to participants do not pose concerns about undue influence and are often ethically important, assisting in recruitment and completion of trials, facilitating diverse participation, and acknowledging the value of participants' contributions to research."[39] This includes reimbursement for out-of-pocket costs incurred as a result of study participation (such as transportation, lodging, childcare, additional medical expenses, and meals outside the home), compensation for contribution of time and acceptance of research-related burdens and inconvenience, and small "appreciation" payments or gifts that are intended to thank participants for their contribution. SACHRP has recognized that the first two kinds of remuneration generally do not make research participation more attractive than alternatives, and that the last is unlikely to influence decisions about study participation, and therefore raises no concern about undue influence. Further, appreciation payments "may be particularly important when budgets do not allow full reimbursement or compensation, or when all participants are hospital inpatients for whom reimbursement and compensation are not pressing needs."

Over the years, OIG has addressed manufacturer sponsor clinical trial remuneration on a case-by-case basis in a limited number of favorable Advisory Opinions.[40] These Advisory Opinions have addressed manufacturer sponsor remuneration in the form of cost-sharing subsidies, but not other forms of manufacturer sponsor remuneration important to encourage enrollment and retention in clinical trials such as travel costs, caregiver expenses, dependent

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[36] U.S. Food & Drug Admin., *Recruiting Study Subjects, Guidance for Institutional Review Boards and Clinical Investigators* (Jan. 1998) *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recruiting-study-subjects.

[37] *Id.*

[38] *See, e.g.*, Council for International Organizations of Medical Sciences, *International Ethical Guidelines for Health-related Research Involving Humans* (2016) *available at* https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf ("Research ethics committees must evaluate monetary and other forms of compensation in light of the traditions and socio-economic context of the particular culture and population in order to determine whether the average participant expected to enroll in the study is likely to participate in the research against his or her better judgment because of the compensation offered. The appropriateness of compensation is likely better judged by local research ethics committees than by international ones.").

[39] "Attachment A – Addressing Ethical Concerns Offers of Payment to Research Participants," SACHRP Recommendations, *available at* https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-september-30-2019/index.html.

[40] OIG Advisory Opinion 26-05 (Mar. 16, 2026); OIG Advisory Opinion 23-11 (Dec. 27, 2023); OIG Advisory Opinion 22-05 (Mar. 16, 2022); OIG Advisory Opinion 21-17 (Nov. 1, 2021); and OIG Advisory Opinion 15-07 (Jun. 24, 2015).

care, lost wages, technology support, and more.[41] Further, as a technical matter, these favorable Advisory Opinions—while helpful guidance—provide legal protection only to the requesting manufacturer sponsor for only the specific arrangement and clinical trial described in the Advisory Opinion. Hence, for the last few years, PhRMA has suggested OIG adopt a clinical trial safe harbor via regulation to explicitly protect certain remuneration to Federal health care program beneficiaries participating in clinical trials.[42]

With the RFI, OIG now seeks feedback not only on cost-sharing subsidies as addressed in its prior Advisory Opinions, but also other forms of remuneration that can relieve the extra costs or burdens associated with trial participation, including but not limited to transportation expenses, childcare expenses, and stipends. PhRMA and BIO applaud OIG for openly recognizing in the RFI that the possible need for guidance extends far beyond cost-sharing to facilitate greater clinical trial participation by U.S. patients. The practical forms of remuneration identified in the RFI and other forms of remuneration tailored to facilitate clinical trial participation as we describe below are not intended to enrich or induce sick patients with undue incentives, but to provide pragmatic support and avoid financial loss for patients addressing unmet medical need and contributing to American science. For healthy volunteers, adequate clinical trial compensation approved by an IRB and consistent with FDA regulations is essential to ensuring robust participation by healthy Americans in early-stage research occurring in the United States.[43]

Thus, PhRMA and BIO's answer to OIG's question regarding whether more guidance is needed to explicitly protect remuneration to trial participants is a resounding yes, as sponsors are committed to AKS and Beneficiary Inducements CMP compliance and seek more regulatory certainty to support patients in enrollment and retention. For OIG's context, it has been reported that some sponsors "cite concerns about running afoul of federal restrictions on providing patients with what could be viewed as a financial incentive…despite clear guidance from the FDA and IRBs that such support is acceptable."[44] Without a clear AKS safe harbor and Beneficiary Inducements CMP exception from OIG, such concerns will persist among the sponsors who are otherwise in a position to support appropriate enrollment and retention efforts consistent with the goals of Operation TrialBlazer.

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[41] Likewise, existing OIG guidance addressing manufacturer-sponsored patient support for commercialized product also does not address the unique needs of patients participating in clinical trials for experimental uses of approved products and for unapproved products.

[42] PhRMA, Solicitation of Proposals for New and Modified Safe Harbors and Special Fraud Alerts (OIG-1125-N) (Feb. 9, 2026); PhRMA, Solicitation of Proposals for New and Modified Safe Harbors and Special Fraud Alerts (OIG-1124-N) (Jan. 27, 2025); PhRMA, Solicitation of Proposals for New and Modified Safe Harbors and Special Fraud Alerts (OIG-1123-N) (Feb. 2, 2024); and PhRMA, Solicitation of Proposals for New and Modified Safe Harbors and Special Fraud Alerts (OIG-1122-N) (Jan. 27, 2023).

[43] J. Fisher et al., *Phase I trial compensation: How much do healthy volunteers actually earn from clinical trial enrollment?*, 18(4) Clin. Trials 477-87 (2021), https://pubmed.ncbi.nlm.nih.gov/33938244/.

[44] Am. Cancer Soc'y Cancer Action Network, *ACS CAN Supports the Clinical Trial Modernization Act* (H.R. 3521 / S. 4440), https://www.fightcancer.org/sites/default/files/clinical_trial_modernization_act_factsheet_h.r.3521_s.4440_may2026_1.pdf.

IV. Regulatory Flexibility Would Encourage Enrollment and Retention While Posing Low Risk of Fraud and Abuse

We agree with OIG's reasoning in its favorable Advisory Opinions over the years permitting the subsidization of certain Federal health care program cost-sharing obligations for clinical trial participants. In those opinions, OIG identified the following safeguards supporting its conclusions that the arrangements posed low risk of fraud and abuse:

1. The remuneration was a reasonable means of promoting enrollment and retention of patients in the clinical trial.

2. The arrangement posed a low risk of steering or inappropriate utilization of items and services covered under a Federal health care program. In particular, OIG has recognized that (i) trial participants must satisfy enrollment criteria set forth in a study protocol and execute informed consent documents; and (ii) investigators and sites must comply with the study protocol and are subject to oversight by an IRB.

3. Any advertising of the remuneration would be subject to existing FDA requirements and guidance as well as IRB review.

4. Such remuneration would not present the risk of a problematic seeding arrangement because it would be limited remuneration provided during the study.

5. The studies complied with Medicare regulations where applicable (*e.g.*, 42 C.F.R. § 405.212).

Any safe harbor should not exclude cost-sharing subsidies from counting towards beneficiary true out-of-pocket expenses requirements.

Moreover, we believe the foregoing safeguards protect not only cost-sharing subsidies as were addressed in the OIG Advisory Opinions, but could also be used to explicitly protect important categories of non-medical expenses and other remuneration that can facilitate enrollment or retention in clinical trials with low risk of fraud and abuse under the AKS and Beneficiary Inducements CMP. These study-related non-medical expenses and other remuneration include the expenses listed above in Section II, limited to the time the patient is screened for and participating in the study. As with cost-sharing subsidies to clinical trial participants, any remuneration for non-covered medical expenses or for non-medical expenses must be appropriately tailored to the screening or trial activities, comply with applicable law and clinical trial standards, and undergo review by the IRB.

OIG should generally avoid drawing categorical distinctions based on the phase of development or sponsor type.[45] The relevant inquiry should be whether the study is bona fide clinical research involving an investigational product, an investigational use of an approved

[45] For example, healthy volunteers in early-stage research face unique considerations for compensation because they are exposed to research participation risks without any direct medical benefit. For these and other healthy volunteers, compensation considerations are commonly different compared to patients with unmet need. R. Walker et al., *Ethical Criteria for Improved Human Subject Protections in Phase I Healthy Volunteer Trials*, 44(5):2–21 Eth. Hum Res. (Sept. 2022), https://pmc.ncbi.nlm.nih.gov/articles/PMC9931499/.

product, or other scientifically valid evidence-generation activity subject to appropriate oversight, and whether the remuneration is reasonably related to reducing screening-related or trial participation-related burdens. A phase-specific or sponsor-specific limitation could leave comparable barriers unaddressed for many patients and could undermine representative enrollment across the clinical research ecosystem.

In light of the Administration's goals under Operation TrialBlazer, we encourage OIG to propose an AKS safe harbor by regulation to explicitly protect certain remuneration to patients participating in U.S. clinical trials. We believe an explicit AKS safe harbor will eliminate existing regulatory uncertainty that constrains various forms of appropriate remuneration, thereby giving sponsors confidence to provide appropriately structured remuneration with oversight from IRBs and consistent with all other applicable law and regulatory standards.[46] This in turn will support the Administration's goals of strengthening domestic research capacity and reducing delays in important clinical research taking place in the U.S.

The proposed safe harbor language below builds on the safeguards cited in OIG's recent Advisory Opinions and adds new safeguards to address the potential risk of problematic seeding arrangements, in which a sponsor offers subsidies to lock in future reimbursable utilization of an item or service.

An explicit safe harbor should also make clear that remuneration may be structured through reimbursement, direct vendor payment, advance payment mechanisms, restricted-use debit cards, or protocol-defined per diem or stipend amounts where itemization is impractical, provided the methodology is objective, documented in advance, and reasonably related to participation-related costs, time, inconvenience, or study burden. This flexibility is important because post hoc reimbursement alone can deter participation by patients who cannot afford to pay upfront costs.

ll) ***Remuneration to Support Patient Access to Clinical Trials.*** As used in section 1128B of the Act, "remuneration" does not include any direct or indirect payment or other support provided to beneficiaries to reduce the burden associated with participation in a clinical trial by the sponsor of such trial (or an agent on behalf of the sponsor), as long as the following standards are met:

(1) The trial and any coverage of items or services reimbursed by the Federal health care programs provided in the trial must be conducted consistent with all applicable coverage rules by any Federal health care programs providing coverage and reimbursement for beneficiaries participating in the trial as study subjects;

(2) The availability of any remuneration will be disclosed as required by law and the amounts, methods, timing, and advertising of any remuneration will be subject to review by the institutional review board (IRB) exercising oversight with respect to the trial;

[46] An explicit regulatory safe harbor is preferred to a Special Advisory Bulletin or FAQs because of the complexities of financial support needed in clinical trials and the corresponding need for notice-and-comment rulemaking for any explicit protection afforded to these activities.

(3) The remuneration is a reasonable means of reducing participation-related barriers and facilitating screening, enrollment, or retention of study subjects in the specific trial;

(4) The remuneration is available to all eligible study subjects regardless of insurance status;

(5) Participating Federal health care program beneficiaries must satisfy formal, objective, and predetermined enrollment criteria and execute an informed consent document;

(6) The remuneration should not be designed or implemented in a manner that promotes or locks in future utilization of a product, provider, or service outside the clinical trial; and

(7) Any reimbursement or advance payment of a patient's cost-sharing obligations will not be provided in excess of the patient's cost-sharing obligations under relevant Federal health care programs.

In connection with our proposal, we ask that you confirm that any safe harbor limitations apply only to Federal health care program beneficiaries not to commercially insured or uninsured patients.

In addition to the proposal above, we continue to believe a corresponding explicit Beneficiary Inducements CMP exception is needed and urge OIG to adopt such an exception or, at a minimum, clarify that the existing Beneficiary Inducements CMP access to care exception set forth in the definition of "remuneration" at 42 C.F.R. § 1003.110[47] applies more broadly to support provided directly or indirectly by clinical trial sponsors that reduces the burden of participating in a trial. Although the Beneficiary Inducements CMP does not apply directly to manufacturers, clinical trial sites are often providers subject to the Beneficiary Inducements CMP, such as hospitals or physician practices.[48] Clinical trial site providers may be asked to facilitate certain sponsor support (*e.g.*, distributing a meal coupon). Without an explicit new exception or clarification of the existing Beneficiary Inducements CMP access to care exception, providers may decline to participate in the trial or assist with providing the remuneration to patients out of concern that they are facilitating improper remuneration.

* * *

Developing new therapies is a long and complex process. U.S. clinical trials help generate the data needed for FDA approval and ensure that treatments are evaluated in the populations they will ultimately serve. Improved rates of enrollment and completion will help sponsors further support the Administration's critical efforts in Operation TrialBlazer. Explicitly protecting appropriate remuneration to U.S. patients represents a practical, patient-centered strategy that will reduce delays, strengthen domestic research capacity, expand patient access to innovative clinical trials, and support a more efficient, high-quality, and globally competitive U.S. clinical research ecosystem.

[47] See definition of "remuneration," subsection 6.
[48] 42 U.S.C. § 1320a-7a(a)(5).

PhRMA and BIO appreciate your consideration of these comments. Please feel free to contact us if there is any further information we can provide.

Respectfully submitted,

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