24 August 2026

The Honorable T. March Bell
Inspector General
Office of Inspector General
U.S. Department of Health & Human Services
330 Independence Avenue, SW
Washington, DC 20201

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), 91 Fed. Reg. 37902 (June 24, 2026)

Dear Inspector General Bell:

The American Cancer Society Cancer Action Network (ACS CAN) is joined in this letter by 128 other patient advocacy groups and professional societies in providing supporting comments to the request for information (RFI) issued by the U.S. Department of Health & Human Services (HHS), Office of Inspector General (OIG) regarding how arrangements that facilitate clinical trial participation fare under the federal health care program anti-kickback statute, 42 U.S.C. § 1320a-7b(b) (AKS) and beneficiary inducements civil monetary penalty law, 42 U.S.C. § 1320a-7a(a)(5) (Beneficiary Inducement CMP).[1]

For the last four years, ACS CAN and many of the undersigned organizations have supported the adoption of a new AKS safe harbor that, subject to a host of safeguards and limitations, would permit clinical trial sponsors to cover certain costs incurred by clinical trial participants without violating the AKS or Beneficiary Inducement CMP.[2] The comments below reflect continued support for the adoption of such a safe harbor.

1. ***Please explain whether offering Federal health care program enrollees remuneration facilitates clinical trial participation and the specific factors that make such remuneration either effective or ineffective at facilitating participation.***

We believe there is strong and widespread support for the proposition that offering prospective clinical trial participants certain types of remuneration—for example, offering to cover the costs of travel and lodging that a participant would not otherwise incur but for their participation in the clinical trial at issue—facilitates clinical trial participation. This, in turn, benefits patients, not only through facilitating the discovery and development of new treatments, but by allowing patients to participate in research and receive quality clinical care and monitoring. Trial participation has been shown to reduce inequities for rural, lower-income, and medically underserved patients, and to erase the generally poorer outcomes experienced by cancer patients in rural areas.[3] Broader participation means that trial populations better reflect the patients who will ultimately use approved treatments, which should improve the quality and usefulness of clinical evidence for patients, clinicians, payors, and regulators.[4]

Although clinical trials are, in the words of the administration, "the gold standard of clinical research and provide critical evidence for new treatments,"[5] clinical trial sponsors struggle to enroll patients.[6] Indeed, remarkably—and sadly—"an estimated 30% of clinical trials conducted between 2011 and 2021 were suspended or terminated after failing to reach [their] enrollment target."[7]

As the administration has observed, these failures often are the result of financial and logistical barriers—such as "distance to clinical trial sites, out-of-pocket medical expenses, missed work and lost wages, travel expenses, access to transportation, and childcare"—that "reduce opportunities to participate in trials for many Americans, particularly those living in remote or rural areas."[8]

In many cases, the costs incurred by patients to participate in a clinical trial can be significant. For example, ongoing analysis of crowdfunding campaigns related to cancer finds that individuals participating in or contemplating clinical trial participation state significantly higher financial needs than those not in trials. In a 2024 study, 29 percent of clinical trial participants needed $501–$1,000 per month to compensate for trial-related expenses, 16 percent needed between $1,001 and $2,000 per month, and 18 percent needed more than $2,000 per month.[9]

According to that same study, "travel-related expenses were the most frequently reported financial hardship stemming from cancer clinical trial participation," with almost 75 percent of participants "reporting financial burdens as a result of traveling to receive trial treatment."[10] This makes sense, as a recent study found that nearly 38% of the U.S. population over 35 years old must drive over 50 miles to participate in a clinical trial at an NCI-funded site, and almost 17% must travel 100 miles or more.[11]

Also not surprisingly, those living in remote or rural areas had "more than twice the risk of financial hardship compared to those traveling shorter distances"[12]; and this is exacerbated by the fact that patients "who have low incomes may be more likely to live in areas with less health care or clinical trial resources, and thus be required to travel farther distances to a site that offers cancer clinical trials."[13] For example, the 2024 study referenced above "found patients with lower incomes traveled a mean of 238 miles to participate in a clinical trial, compared to just 49 and 43 miles for those with middle and high incomes, respectively."[14] Not only is the risk of financial hardship higher in rural areas, but the risk of cancer itself is also higher. Rates of lung, cervical, and colorectal cancer are approximately 40%, 30%, and 20% higher, respectively, in rural areas when compared to urban areas.[15] See the Appendix for an analysis by ACS CAN of clinical trial availability within 20 or 100 miles of each state capitol building. The analysis determined the number of treatment trials for "cancer" and for "colorectal cancer" and found huge variations in availability, illustrating that, for many individuals, participation in a clinical trial would involve traveling significant distances. As an example, West Virginia is ranked second in the nation for cancer incidence, yet ranks 47th in clinical trial availability within 100 miles of the state capitol. By comparison, Kentucky ranks even higher in cancer incidence, but 20th in clinical trial availability within 100 miles of the capitol (see Appendix).

Under these circumstances, it is not surprising that a 2026 study found that 89 percent of cancer patients indicated they would be more likely to enroll in a cancer clinical trial if sponsors supported them financially.[16] Similarly, in a 2025 study, 86 percent of patients cited expenses as influencing their decision to participate in a clinical trial.[17] For its part, OIG has flagged this particular issue on multiple occasions over the past 25 years.[18]

In 2024, ACS CAN completed a collaboration with the HHS Assistant Secretary for Planning and Evaluation (ASPE) and Mathematica in which ACS CAN surveyed 112 current and recent cancer clinical trial participants about the cost and financial impact of trial participation.[19] Almost two-thirds of participants reported financial stress associated with their clinical trial participation. This stress was tied to (i) traveling to trial sites, (ii) challenges paying for food or rent, and (iii) using savings and incurring credit card debt to compensate for added costs.

Other evidence suggests that absent financial support, lower-income individuals are being disadvantaged in their ability to take part in clinical trials. In one study of cancer patients, individuals with household incomes under $50,000 were 32% less likely to participate in a clinical trial.[20] Another study found that when comparing individuals making less than $38,000 to those making over $63,000 with prostate, kidney, and bladder cancer, lower-income individuals are 36%, 47%, and 71% less likely, respectively, to enroll in clinical trials.[21]

There are many approaches to providing financial support that can help those who incur expenses due to enrollment in a clinical trial, ranging from reimbursement to prepayment to stipends; however, each can create different burdens and potential secondary issues related to substantiation and taxation. In a recent survey of nearly 1,000 cancer survivors, prepayment was the preferred method of support, with stipends the second most favored.[22]

Taken together, this evidence demonstrates that the financial and logistical burdens associated with clinical trial participation—particularly the added travel and cost burdens borne by rural and low-income patients—represent a substantial and well-documented barrier to enrollment, one that directly undermines the ability of clinical trials to reach their targets. Given the clear and consistent data showing that patients are significantly more likely to enroll when financial support is available, we urge that measures enabling sponsors to cover trial-related travel, lodging, and other out-of-pocket expenses are not merely beneficial but essential to improving clinical trial participation and, ultimately, advancing research for all Americans.

2. ***Please explain whether you view the Federal anti-kickback statute or the Beneficiary Inducements CMP as barriers to offering and providing appropriate remuneration to clinical trial participants and if so, why. In your answer, please describe any other identified barriers to offering and providing appropriate compensation/remuneration to clinical trial participants and how those barriers relate to any barriers created by the Federal anti-kickback statute and Beneficiary Inducements CMP.***

We believe the AKS and Beneficiary Inducement CMP materially deter clinical trial sponsors, sites, and their operational partners from offering remuneration that would be appropriate, equitable, and patient-protective in the clinical trial context. The AKS deals with "any remuneration" offered or paid to induce or reward the ordering or arranging for federally

reimbursable items or services, and the Beneficiary Inducement CMP separately addresses remuneration likely to influence a beneficiary's selection of a particular provider, practitioner, or supplier. Because the costs most relevant to trial access—transportation, lodging, parking, meals, childcare, dependent care, missed work, out-of-pocket medical costs, and modest stipends—are things of value, cautious sponsors and sites may decline to provide them, rather than risk the appearance of violating the statute, even where the purpose is only to remove a financial barrier to participation in scientifically and ethically reviewed research.[23]

This concern is not theoretical. OIG has acknowledged in this RFI that it has issued 10 favorable advisory opinions over the last two decades permitting the waiver or subsidization of certain Federal healthcare program cost-sharing obligations for clinical trial participants. This alone is clear evidence of a regulatory gap: OIG has repeatedly recognized that properly structured support can be low risk in particular clinical trial settings, yet sponsors and sites lack a generally applicable safe harbor or parallel CMP exception on which they can rely when designing patient-support programs at scale.[24]

The principal practical consequence is that the legal uncertainty compounds the very barriers that already prevent eligible patients from enrolling in and remaining in trials. The administration has identified distance to trial sites, out-of-pocket medical expenses, missed work and lost wages, travel expenses, access to transportation, and childcare as barriers that reduce opportunities to participate, particularly for patients in remote and rural areas. ACS CAN's own work with ASPE and Mathematica similarly found that current and recent cancer clinical trial participants experienced financial stress tied to travel, food and rent, savings depletion, and credit card debt. Where a sponsor is willing to offset or alleviate these burdens but uncertain whether the AKS or Beneficiary Inducement CMP permits it to do so, the fraud and abuse laws become an additional barrier to participation rather than merely a backstop against abusive arrangements.[25]

3. ***Please explain what categories of remuneration (including, for example, reimbursement for actual incurred expenses such as travel, lodging, parking, childcare, and meals; stipends; compensation for a participant's time; incentives to encourage enrolling in and completing the trial) and at what levels those categories of remuneration are useful to facilitate participation in clinical trials and why. Similarly, please explain what categories of remuneration are not useful to facilitate clinical trial participation. Please explain the extent to which such categories of remuneration already are offered to clinical trial participants. Please explain whether there are categories of remuneration that may be subject to heightened risks of fraud and abuse. To the extent that there is more uncertainty regarding how the Federal anti-kickback statute and Beneficiary Inducements CMP would apply to certain categories of remuneration, please explain.***

The most useful categories of remuneration are those that reimburse, pay directly, or reasonably estimate the actual, additional, incremental costs that a participant incurs because of trial participation. These include transportation, mileage, rideshare or shuttle services, airfare where long-distance travel is necessary, lodging, parking, meals while away from home, childcare, dependent care, caregiver travel where a caregiver is needed, and reasonable

technology or communication supports that allow a participant to comply with the clinical trial protocol. Medical coinsurance, copays, or deductibles also add financial burden even to those with insurance. Remuneration also includes modest, protocol-defined stipends calculated to approximate participant time, inconvenience, and recurring out-of-pocket burdens, provided that the amount, timing, and method of payment are reviewed in advance by the Institutional Review Board (IRB) and are not structured to pressure a participant to enroll, remain in, or complete a study against the participant's interests.[26]

The amount of support should be sufficient to remove the incremental financial burden created by the trial, rather than set at an artificially low nominal-value level that fails to address real-world costs. The available evidence shows that these costs can be substantial. In one 2024 study, 29 percent of trial participants needed $501–$1,000 per month to compensate for trial-related expenses, 16 percent needed $1,001–$2,000 per month, and 18 percent needed more than $2,000 per month;[27] other studies and reports similarly describe travel, lodging, parking, food, missed work, and childcare as recurring and material barriers. For that reason, we believe OIG should permit reasonable reimbursement of documented expenses and reasonable, pre-established stipends tied to visits, months, or other protocol-defined activities, so long as the protocol explains the methodology and the sponsor documents the payments made.[28]

By contrast, remuneration that is unrelated to the burdens of trial participation is not useful and should not be protected. Limits should be made consistent with FDA's guidance that reimbursement for reasonable travel and lodging does not raise undue-influence concerns, while other payments should be reviewed by the IRB for amount, method, and timing.[29]

No responses are provided for requests 4 and 5.

6. ***Please explain the role of an Institutional Review Board ("IRB") in reviewing the provision of remuneration to clinical trial participants and whether an IRB's review of the type, amount, and frequency of remuneration provided to clinical trial participants and the advertising of that remuneration is a meaningful safeguard against the harms resulting from fraud and abuse. If so, please specify the rationale and the standards the IRB should use.***

IRBs are highly motivated and competent to protect research subjects from fraud and abuse, including from inappropriate influence related to financial compensation. Neither the Common Rule nor the FDA regulations offer specific limitations on payment of research subjects, but both caution that IRBs should monitor proposed payments to ensure that they do not create "undue influence" or interfere with participant assessment of risks and benefits as they consider consenting to a trial.[30,31] IRBs therefore have both a regulatory responsibility as well as ethical reasons to evaluate offers of participant compensation. Due to a lack of detail in the regulatory guidance, however, IRBs have tended to err on the conservative side and limit payments to participants. This is in spite of a statement from the HHS Office of Human Research Protections (OHRP) that IRBs are "far more worried" about undue influence than OHRP;[32] similarly, FDA has stated that compensation of research participants is "common, and in general, acceptable."[33] Attempts to identify evidence of undue influence or coercion as a

result of participant compensation have failed to find an association, and there is evidence that low (or no) compensation is actually harmful to participants.[34] While IRBs have demonstrated an obligation and willingness to safeguard participants against harms resulting from fraud and abuse, further guidance to clarify appropriate, evidence-based standards and norms for participant compensation will allow IRBs to exercise their responsibilities in ways that protect participants while permitting fair compensation that affirms the value of trial participants, ultimately enhancing trial enrollment.

7. ***Please enumerate any safeguards that should be in place to ensure clinical trial participants who receive remuneration to participate in a clinical trial are not inappropriately steered to items or services offered by the individual or entity offering the remuneration outside the clinical trial.***

We believe the most important safeguard is a clear separation between remuneration that facilitates participation in a clinical trial and remuneration that steers a patient to items or services outside the trial. Protected support should not be conditioned on the participant's purchase, lease, order, prescription, receipt, or continued use of any item or service reimbursable by a Federal healthcare program outside the clinical trial. It should not require the participant to select, remain with, or switch to any particular provider, practitioner, supplier, pharmacy, treatment center, drug, device, or health plan after trial participation ends. It also should not be used to market non-trial items or services during transportation, lodging, enrollment, consent, or other patient-support interactions.[35]

A protected arrangement also should be grounded in a written, IRB-approved protocol that identifies the categories of support, the amount or calculation methodology, the timing and method of payment, any caps or other limitations, and the circumstances in which support is available. The sponsor should contemporaneously document the purpose, amount, date, and method of each payment or direct vendor payment and should make that documentation available to the Secretary upon request. These requirements would allow OIG to distinguish bona fide trial-enabling support from arrangements that use clinical research as a pretext for patient recruitment or product promotion.[36]

Additional safeguards should include objective and consistently applied eligibility criteria and availability of support without regard to insurance type except where necessary to comply with law. Participants should be told that accepting support will not affect their ability to change providers, withdraw from the study, decline other services, or make independent treatment decisions in consultation with their clinicians. These safeguards track OIG's long-standing concerns about patient steering, overutilization, patient choice, and program cost, while preserving the ability to remove access barriers that otherwise prevent eligible patients from participating in research.[37]

8. ***Please explain whether remuneration to clinical trial participants is provided during all stages of product development (e.g., phase 1–4 clinical trials) and whether different amounts or types of remuneration are necessary to promote participation in early-stage versus late-stage development. To the extent that there is more uncertainty regarding***

how the Federal anti-kickback statute and Beneficiary Inducements CMP would apply to certain stages of development, please explain. Describe what, if any, limitations would guard against the harms resulting from fraud and abuse in connection with different phases of clinical trials.

Financial needs of patients while in clinical trials are dependent on both personal factors (e.g., distance to trial site, need for childcare, lost wages, etc.) as well as trial-dependent factors (e.g., number and length of study visits). We are unaware of evidence that would suggest that trial phase independently impacts financial need and suggest that differential limits by phase not be implemented.

9. ***Please identify and explain if there are specific types or categories of clinical trials that should or should not pay remuneration to clinical trial participants due to that type's or category's relative risk of the harms resulting from fraud and abuse under the Federal anti-kickback statute and Beneficiary Inducements CMP. For example, please explain whether remuneration to clinical trial participants should only be protected under the Federal anti-kickback statute and Beneficiary Inducements CMP when provided to participants of government-sponsored clinical trials.***

Our primary experience is with cancer clinical trials, which we believe to be of generally low risk for fraud and abuse, especially given IRB review of any reimbursement programs associated with these trials regardless of the type of trial or the trial sponsor. A patient's need for financial support while participating in a clinical trial does not depend on sponsor type, and therefore we do not believe there should be restrictions based on sponsorship for the trials eligible to provide financial support to trial participants. Industry-sponsored trials in oncology outnumber NIH-sponsored trials by a ratio of nearly 10:1,[38] so not only would a safe harbor limited to only government-sponsored trials disadvantage patients in trials sponsored by other entities, it would also apply to only a small fraction of trials and, therefore, trial participants. Lastly, NIH-sponsored trials are chronically underfunded even without the provision of financial support to participants, and it is unfortunately less likely that government-sponsored trials would include funds in their budget to utilize the proposed safe harbor than industry-sponsored trials.

10. ***Please explain whether there should be advertising limitations relating to remuneration to clinical trial participants to protect the integrity of the clinical trial and guard against the harms resulting from fraud and abuse.***

We support advertising limitations that prevent remuneration from becoming a marketing tool, while still permitting clear and accurate information to be provided to patients, caregivers, investigators, and referring clinicians. The availability of trial-related reimbursement or support should be described in IRB-approved recruitment materials, the informed consent document, and patient-facing trial materials when necessary to allow patients to make an informed decision about participation. These materials should accurately describe the categories of support, the eligibility criteria, and any caps or limitations, but they should not present remuneration as a prize, rebate, or product promotion.[39]

In crafting a safe harbor, OIG could provide guidance that limits advertising that creates expectations of remuneration that would otherwise not be allowed within the structure of the safe harbor, while still allowing and encouraging IRB-approved neutral disclosure of the existence and terms of support in recruitment and consent materials.[40]

11. Please identify what, if any, additional or modified safe harbors to the Federal anti-kickback statute or exceptions to the definition of "remuneration" under the Beneficiary Inducements CMP may be necessary to protect remuneration to clinical trial participants and any arrangements necessary to offer and provide such remuneration. Please explain any key provisions that should be included in any additional or modified safe harbor or exception. Specifically, and to the extent that you did not do so in response to the questions above, please describe what conditions would be appropriate to include in a safe harbor or exception to protect against the harms resulting from fraud and abuse in the context of such arrangements, including what, if any, disclosures should be required by such safe harbors or exceptions. Additionally, please identify which criteria for modifying and establishing safe harbors under section 1128D(a)(2) of the Act (42 U.S.C. 1320a–7d(a)(2)), listed in section II.A above, would be impacted and how.

We believe OIG should adopt a new AKS safe harbor for reasonable trial-related support. A separate exception to the definition of "remuneration" under the Beneficiary Inducement CMP is unnecessary: by operation of section 1128A(i)(6)(B) of the Act (42 U.S.C. § 1320a-7a(i)(6)(B)), any payment practice that satisfies a safe harbor to the Federal anti-kickback statute is automatically excepted from the definition of "remuneration" for purposes of the Beneficiary Inducement CMP as well. A single, well-constructed AKS safe harbor, therefore, would protect clinical trial sponsors and their partners under both the AKS and the Beneficiary Inducement CMP without the need for a freestanding CMP exception.

The key conditions should be straightforward. The support should be provided pursuant to a written protocol reviewed and approved in advance by the responsible IRB. The protocol should identify each category of support; state whether support will be reimbursed to the participant, paid directly to a vendor, or provided through a flat stipend; specify the cap, period, visit, or activity covered; and describe the methodology used to calculate any stipend. The sponsor or its administrator should contemporaneously document each payment or direct vendor payment, should not bill or otherwise shift the support costs to Federal healthcare programs, and should make relevant records available to the Secretary upon request.[41]

Disclosures should be required in the informed consent process and in relevant patient-facing materials so that participants understand what support is available, who is providing or funding it, the limits on the support, and the fact that the support does not affect the participant's right to withdraw or make independent treatment decisions. Because satisfying these conditions would automatically extend protection under the Beneficiary Inducement CMP as well as the AKS, they should be sufficiently robust to justify that dual protection.[42]

These protections would advance the statutory criteria for modifying and establishing safe harbors. They would increase access to health care services and research opportunities,

increase the quality and generalizability of clinical evidence, improve the ability of facilities to serve medically underserved areas and medically underserved populations, and preserve patient freedom of choice by removing financial barriers without requiring the selection of any provider or product outside the trial. They should not increase overutilization or inappropriate Federal healthcare program costs because the protected remuneration would be limited to expenses incurred exclusively because of trial participation and would not reward providers or professionals for ordering items or services.[43]

12. Please explain, with specificity, why any existing safe harbors to the Federal anti-kickback statute or exceptions to the definition of "remuneration" under the Beneficiary Inducements CMP do not adequately protect the arrangements necessary to effectuate the provision of remuneration to clinical trial participants.

Existing safe harbors and CMP exceptions do not adequately protect the arrangements needed to provide clinical trial participants with the support described above. The local transportation safe harbor is useful by analogy, but it is not a clinical trial safe harbor. It is limited to transportation, does not address lodging, meals, childcare, dependent care, caregiver support, stipends, or other recurring trial burdens, excludes certain forms of transportation such as air transportation, and contains mileage and patient-status limitations that do not map well onto clinical trials that may require travel to specialized or NCI-funded sites. It therefore cannot provide comprehensive protection for the support needed to make trial participation feasible for patients who live far from a trial site.[44]

The patient engagement and support safe harbor and value-based safe harbors also are inadequate. Those protections are tied to value-based enterprises, value-based purposes, target patient populations, and other conditions that generally are not how clinical trials are designed, funded, or administered. In addition, important categories of entities involved in drug and device development may be excluded from certain value-based safe harbors or subject to limited pathways, and the patient engagement safe harbor is not a general authorization for cash or cash-equivalent trial support. Clinical trial sponsors should not have to restructure research support as a value-based enterprise merely to reimburse a participant for lodging, parking, childcare, or travel required by the protocol.[45]

The existing Beneficiary Inducement CMP exceptions likewise do not solve the AKS problem, and the deficiency cuts in both directions. The "promotes access to care" exception may be helpful for some items or services, and OIG has relied on that framework in favorable advisory opinions involving travel and lodging support for particular specialized treatments. But CMP protection does not itself create AKS protection, and arrangements that do not satisfy an AKS safe harbor remain subject to case-by-case analysis and potential AKS liability even where a CMP exception applies. This asymmetry follows from the structure of the statute: section 1128A(i)(6)(B) of the Act provides that satisfying an AKS safe harbor automatically confers protection under the Beneficiary Inducement CMP, but no parallel provision exists in the Federal AKS excepting a payment practice merely because it satisfies a CMP exception. Consequently, even a sponsor that structures its support to fit within an existing CMP exception

would remain exposed to AKS liability unless the arrangement also satisfies an AKS safe harbor or otherwise lacks the intent necessary for a violation.[46]

13. Please discuss any potential broader impacts or implications—and in particular, as they relate to the criteria set forth in section 1128D(a)(2) of the Act (e.g., an increase or decrease in access to health care services, an increase or decrease in costs to Federal health care programs)—that may result from the provision of remuneration to clinical trial participants, additional or modified safe harbors to the Federal anti-kickback statute, or exceptions to the definition of "remuneration" under the Beneficiary Inducements CMP. For instance, if remuneration would result in higher participation rates of federal health care program enrollees in clinical trials, could that lead to improved health care.

The broader implications of a properly tailored safe harbor that, by operation of law, would also extend protection under the Beneficiary Inducement CMP would be strongly positive. By reducing out-of-pocket and logistical burdens, OIG would make it easier for Federal health care program enrollees to participate in trials for which they are otherwise eligible. That would promote access to research opportunities and reduce inequities for rural, lower-income, and medically underserved patients. While cancer outcomes for individuals in rural areas are generally poorer than urban counterparts, participation in clinical trials has been found to erase these differences.[47] Reducing trial enrollment barriers also helps trials enroll populations that better reflect the patients who will ultimately use approved treatments. More representative trials, in turn, should improve the quality and usefulness of clinical evidence for patients, clinicians, payors, and regulators.[48]

We do not believe that reasonable cost support will cause the kind of overutilization or improper program cost increases that the AKS is designed to prevent. Patients with cancer or other life-threatening conditions, for example, typically require care whether or not they enroll in a trial, and Medicare and Medicaid coverage rules already address routine costs associated with qualifying clinical trials. Properly limited support would not pay physicians or other referral sources, would not reward ordering decisions, and would do no more than put the participant in the economic position the participant would have occupied absent the added burdens imposed by the trial. Any increase in utilization attributable to more eligible patients enrolling in appropriate trials should be understood as improved access to research, not inappropriate utilization of medically unnecessary care.[49]

There also are broader system benefits. Trials that fail to accrue sufficient participants waste research dollars, delay answers about promising interventions, and may leave underrepresented communities without evidence that adequately reflects their circumstances. Support that reduces travel, childcare, food, lodging, and lost-wage burdens can help preserve study integrity by improving enrollment and retention, while the safeguards described above protect patient freedom of choice, provider competition, and program integrity. For those reasons, we believe the safe harbor criteria point decisively toward protecting carefully limited trial-related support.[50]

14. Are there opportunities where OIG could clarify its position through guidance as opposed to regulation? For example, would a Special Advisory Bulletin, an FAQ response, or other guidance offer sufficient protection in some instances? If so, please elaborate.

OIG guidance would be helpful, but guidance should supplement rather than replace a new safe harbor. Because the AKS is a criminal statute and because the Beneficiary Inducement CMP carries independent administrative consequences, many sponsors and sites will remain reluctant to provide support based only on informal guidance. Advisory opinions are useful for specific requestors, but they do not create generally applicable protection for other sponsors, sites, or patient-support arrangements. A regulation is therefore necessary to create the certainty needed for equitable, scalable trial-support programs.[51]

The need for regulatory clarity is consistent with HHS's prior recognition, in the coordinated-care context, that the broad reach of the AKS and Beneficiary Inducement CMP can inhibit beneficial arrangements. It also is consistent with OIG's prior use of RFIs to identify whether new or modified safe harbors could foster beneficial arrangements while preserving program integrity.[52]

That said, OIG could use guidance to provide near-term clarity while rulemaking proceeds and to address lower-risk operational questions that do not require regulatory text. A Special Advisory Bulletin, FAQs, or other guidance could clarify that reimbursement for reasonable, documented travel, lodging, parking, meals, childcare, and caregiver expenses required by a clinical trial generally presents low fraud-and-abuse risk when reviewed by an IRB, disclosed in the informed consent process, documented by the sponsor, and not conditioned on use of items or services outside the trial. OIG also could clarify the difference between neutral disclosure of available support in recruitment and consent materials and impermissible advertising that uses remuneration as a marketing tool.[53]

Guidance also could summarize recurring safeguards from OIG's advisory opinions and rulemakings, including objective eligibility criteria, no cost shifting to Federal healthcare programs, no luxury or entertainment benefits, participant freedom to change providers or withdraw, and contemporaneous documentation. But the core protection for trial-related remuneration should be regulatory. The most durable approach is for OIG to issue guidance now and pursue rulemaking to codify a clear, administrable AKS safe harbor that, by operation of law, would also extend protection under the Beneficiary Inducement CMP for reasonable clinical trial participant support.[54]

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Thank you for the opportunity to comment on the Clinical Trials RFI. If you have any questions, please feel free to contact Mark Fleury, Policy Principal, ACS CAN, at mark.fleury@cancer.org, or Nishith Pandya, Director of Federal Advocacy, ACS CAN, at Nishith.pandya@cancer.org .

Signed,

American Cancer Society Cancer Action Network
1Day Sooner
Academy of Oncology Nurse & Patient Navigators
Academy of Physicians in Clinical Research

ADAP Advocacy Association
Adolescent and Young Adult Cancer Coalition
Alliance for Patient Access
Alliance for Women's Health & Prevention (AWHP)
American Association for Cancer Research (AACR)
American Association of Clinical Urology (AACU)
American Lung Association
American Society for Transplantation and Cellular Therapy
American Society of Hematology
American Society of Pediatric Hematology/Oncology
AnCan foundation
Anxiety and Depression Association of America
Association for Clinical Oncology (ASCO)
Association for the Accreditation of Human Research Protection Programs, Inc.
Association of American Cancer Institutes
Association of Black Cardiologists
Association of Northern California Oncologists
Association of Pediatric Hematology/Oncology Nurses (APHON)
Biomarker Collaborative
BlackDoctor
Brem Foundation to Defeat Breast Cancer
Cancer Active, Inc.
Cancer Support Community
Caregiver Action Network
Carolina BioOncolgy Institute & BioCytics Human Applications Lab
Cervivor, Inc.
Cheeky Charity
Children’s Brain Tumor Foundation
Coalition of Skin Diseases
Colon Cancer Coalition
Colorectal Cancer Alliance
Community Access National Network
Community Liver Alliance
Community Oncology Alliance (COA)
Connecticut Oncology Association
Crohn's & Colitis Foundation
Debbie’s Dream Foundation: Curing Stomach Cancer (DDF)
Depression and Bipolar Support Alliance (DBSA)
Derma Care Access Network
Digestive Disease National Coalition
Epilepsy Foundation of America
Esophageal Cancer Action Network (ECAN)
Exon 20 Group
Fight Colorectal Cancer
FORCE: Facing Our Risk of Cancer Empowered
Friends of Cancer Research
Gaucher Community Alliance
Gerontological Society of America
GI Cancers Alliance
Global Colon Cancer Association
GO2 for Lung Cancer
Haystack Project
Hope for Stomach Cancer
ICAN, International Cancer Advocacy Network
Illinois Medical Oncology Society (IMOS)
International Myeloma Foundation
Kidney Cancer Association
KidneyCAN
LESLIE'S WEEK a Stage 4 Breast Cancer Nonprofit
Livestrong
Living Beyond Breast Cancer
LUNGevity Foundation
Lupus and Allied Diseases Association, Inc.
Lupus Foundation of America
Lymphedema Advocacy Group
Maryland-DC Society of Clinical Oncology
Medical Oncology Association of Southern California (MOASC)
Melanoma Research Alliance
Melanoma Research Foundation
Men's Health Network
MET Crusaders
METAvivor
Multiple Myeloma Research Foundation
Myasthenia Gravis Association
National Alliance of State Prostate Cancer Coalitions
National Association of Hispanic Nurses
National Black Nurses Association
National Brain Tumor Society
National Cancer Registrars Association
National Coalition for Infant Health
National Comprehensive Cancer Network (NCCN)
National Health Council
National Hispanic Health Foundation
National Hispanic Medical Association
National Kidney Foundation
National Minority Quality Forum
National Patient Advocate Foundation
National Scleroderma Foundation
NCODA (Network for Collaborative Oncology Development and Advancement)
NMDP (formerly National Marrow Donor Program)
NRG1 Energizers
Ohio Hematology Oncology Society
Oklahoma Society of Clinical Oncology, Inc.
Oncology Nursing Society
Ovarian Cancer Research Alliance
Parkinson's Foundation

Patient Empowerment Network
PDL1 Amplifieds
Pennsylvania Prostate Cancer Coalition (PPCC)
PlusInc
Prevent Blindness
Prevent Cancer Foundation
Preventive Cardiovascular Nurses Association
Prostate Health Education Network
Rural Minds
Sharsheret | The Jewish Breast & Ovarian Cancer Community
Shercare
Society For Clinical Research Sites
Society of Utah Medical Oncologists (SUMO)
Stupid Cancer, Inc.
Susan G. Komen
The Headache and Migraine Policy Forum
The Prostate Cancer Clinical Trials Consortium
Tigerlily Foundation
Triage Cancer
Triple Negative Breast Cancer Foundation
Twisted Pink
Unite for HER
US Hereditary Angioedema Association
UsAgainstAlzheimer's
wAIHA Warriors
Women As One, Inc.
Young Survival Coalition
Your Prostate Cancer.help
ZERO Prostate Cancer

Appendix:

Cancer Incidence vs. Clinical Trial Availability by State

Capital, State	State rank by incidence rate (cases per 100,000)	State rank by clinical trial availability (100 mile radius of capitol)	Clinical trials available within 20 miles of capitol		Clinical trials available within 100 miles of capitol	
			All cancers	Colorectal	All cancers	Colorectal
Montgomery, AL	32nd	45th	8	0	100	13
Juneau, AK	31st	52nd	0	0	0	0
Phoenix, AZ	48th	28th	472	45	474	46
Little Rock, AR	17th	37th	140	3	163	3
Sacramento, CA	45th	12th	217	13	728	47
Denver, CO	49th	19th	548	55	580	55
Hartford, CT	8th	1st	114	4	1811	147
Dover, DE	21st	3rd	9	1	1388	121
Tallahassee, FL	22nd	50th	13	0	39	2
Atlanta, GA	10th	21st	497	32	553	38
Honolulu, HI	42nd	44th	107	3	107	3
Boise, ID	38th	42nd	119	4	119	4
Springfield, IL	20th	15th	115	3	637	53
Indianapolis, IN	37th	24th	256	19	534	39
Des Moines, IA	3rd	38th	139	5	162	5
Topeka, KS	23rd	31st	49	0	352	23
Frankfort, KY	1st	20th	0	0	576	42
Baton Rouge, LA	5th	34th	85	6	243	17
Augusta, ME	11th	43rd	18	2	109	2
Annapolis, MD	24th	4th	64	4	1380	120
Boston, MA	50th	9th	841	74	991	85
Lansing, MI	25th	11th	92	4	811	92
St. Paul, MN	4th	17th	328	20	612	44
Jackson, MS	16th	48th	65	1	83	5
Jefferson City, MO	13th	36th	30	1	173	13

Helena, MT	33rd	46th	16	1	94	3
Lincoln, NE	34th	32nd	64	4	325	23
Carson City, NV	46th	40th	20	1	137	7
Concord, NH	26th	8th	23	1	998	82
Trenton, NJ	6th	2nd	76	4	1689	140
Santa Fe, NM	51st	39th	16	1	157	8
Albany, NY	9th	35th	58	0	196	5
Raleigh, NC	12th	18th	54	3	609	42
Bismarck, ND	30th	49th	56	3	66	4
Columbus, OH	15th	13th	485	24	701	45
Oklahoma City, OK	19th	33rd	270	25	289	25
Salem, OR	43rd	27th	11	1	483	34
Harrisburg, PA	28th	6th	127	7	1200	92
Providence, RI	39th	7th	173	8	1119	94
Columbia, SC	35th	30th	39	0	369	16
Pierre, SD	14th	51st	18	2	18	2
Nashville, TN	27th	14th	649	79	658	79
Austin, TX	40th	22nd	227	23	549	72
Salt Lake City, UT	29th	29th	415	36	424	37
Montpelier, VT	18th	26th	23	1	501	38
Richmond, VA	41st	10th	239	11	885	83
Olympia, WA	36th	16th	59	2	618	47
Charleston, WV	2nd	47th	39	3	85	5
Madison, WI	7th	25th	236	18	526	37
Cheyenne, WY	44th	23rd	23	1	538	52
Washington, DC	47th	5th	822	82	1245	110
San Juan, PR	52nd	41st	128	13	134	13
All USA			**4501**	**321**	**27338**	**2214**

Methodology Note: Trial data was collected using Clinicaltrials.gov during June 2026. Search criteria used were Phase 1-3 Interventional within 20-miles and 100-miles from state/territory capitol building address. State level cancer incidence rankings are sourced from NCI/CDC State Cancer Profiles (latest single year).

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[1] Medicare and State Health Care Programs: Fraud and Abuse; Request for Information Regarding the Federal Anti-Kickback Statute and Beneficiary Inducements CMP, 91 Fed. Reg. 37902 (June 24, 2026), available at https://www.govinfo.gov/content/pkg/FR-2026-06-24/pdf/2026-12676.pdf.

[2] American Cancer Society Cancer Action Network, Comment letter on Solicitation of Proposals for New and Modified Safe Harbors and Special Fraud Alerts (Feb. 9, 2026), https://www.fightcancer.org/sites/default/files/acs_can_2026_safe_harbor_proposalfinal9feb.pdf.

[3] Unger JM, Moseley A, Symington B, Chavez-MacGregor M, Ramsey SD, Hershman DL. Geographic Distribution and Survival Outcomes for Rural Patients With Cancer Treated in Clinical Trials. *JAMA Netw Open.* 2018;1(4):e181235. doi:10.1001/jamanetworkopen.2018.1235.

[4] Clinical Trials RFI, 91 Fed. Reg. 37902 (June 24, 2026); U.S. Dep't of Health & Human Servs., ASPE, Empowering Patients to Participate in Clinical Trials (July 2025), at 1; Holly Fernandez Lynch et al., Fair Payment and Just Benefits to Enhance Diversity in Clinical Research, J. Med. Ethics (2021).

[5] U.S. Dep't of Health & Human Servs., Office of the Assistant Secretary for Planning & Evaluation (ASPE), Empowering Patients to Participate in Clinical Trials (July 2025) (July 2025 ASPE Brief), at 1.

[6] See, e.g., Shriver SP, Sahar L, Douangchai Wills V, Adams DV, Fleury ME, Assessing populations with access to National Cancer Institute–funded sites using local distance-based service areas, Clin. Transl. Sci. (2025) (finding large geographic gaps in proximity to NCI-funded research infrastructure—especially for rural and lower-income populations—implicating distance and access as core impediments to participation and accrual); Stout NL, Nikcevich D, Henderson TO, et al., Improving Rural Clinical Trial Enrollment: Recommendations from the Rural Health Working Group of the Alliance Clinical Trials Network, J. Clin. Oncol. 42:1722–1725 (2024) (identifying persistent enrollment challenges tied to travel burden, site location, staffing, and operational constraints in rural U.S. settings and proposing remedies to improve accrual); Williams RJ, Tse T, DiPiazza K, Zarin DA, Terminated Trials in the ClinicalTrials.gov Results Database: Evaluation of Availability of Primary Outcome Data and Reasons for Termination, PLoS ONE 10:e0127242 (2015) (finding "insufficient rate of accrual" a leading reason for termination of registered trials with posted results); Carlisle B, Kimmelman J, Ramsay T, MacKinnon N, Unsuccessful Trial Accrual and Human Subjects Protections: An Empirical Analysis of Recently Closed Trials, Clin. Trials 12:77–83 (2015) (documenting unsuccessful accrual as a recurrent cause of premature closure and identifying features associated with slow enrollment); and Lee C, Werner TL, Deal AM, et al., Clinical Trial Metrics: The Complexity of Conducting Clinical Trials in North American Cancer Centers, JCO Oncol. Pract. 17:e77–e93 (2021) (describing accrual and operational complexities at North American cancer centers that impede on-time target enrollment).

[7] July 2025 ASPE Brief, at 1.

[8] Id. See also Williams CP, Deng L, Caston NE, et al., Understanding the Financial Cost of Cancer Clinical Trial Participation, Cancer Med. 13(8):e7185 (2024) (in a U.S. survey, 47% of trial participants reported trial-related financial hardship, most commonly from travel; 13% of nonparticipants declined due to cost; over half reported reduced willingness to join future trials, with many needing $200–$1,000+/month to offset expenses); Williams CP, Reh N, Chen M, et al., Financial Barriers to Breast Cancer Clinical Trial Participation: A Qualitative Study in the Deep South, Support. Care Cancer 33:771 (2025) (patients who declined trials cited direct and indirect expenses—travel, lodging, parking, food, and missed work—as influential deterrents; confusion about insurance coverage and recurrent cost sharing also noted); U.S. Dep't of Health & Human Servs., ASPE, Empowering Patients to Participate in Clinical Trials (July 2025) (noting patients frequently cite cost and travel as major factors; highlighting missed work, childcare/dependent care, and out-of-pocket medical costs as barriers that hinder recruitment and retention); U.S. Dep't of Health & Human Servs., ASPE, Use of Participant Compensation in U.S. Clinical Research Studies (July 2025) (observing that financial impacts of participation—travel expenses, lost wages, and other out-of-pocket costs—are thought to reduce participation and discussing compensation as a strategy to offset burdens and improve recruitment/retention); Nipp RD, Powell E, Chabner B, Moy B, Recognizing the Financial Burden of Cancer Patients in Clinical Trials, Oncologist 20:572–575 (2015) (reporting substantial "indirect" burdens including travel and lodging—often hundreds of dollars per month—and urging noncoercive financial assistance to mitigate access barriers); Borno HT, Zhang L, Siegel A, Chang E, Ryan CJ, At What Cost to Clinical Trial Enrollment? A Retrospective Study of Patient Travel Burden in Cancer Clinical Trials, Oncologist 23:1242–1249 (2018) (documenting significant travel distances and burdens—greatest for some NIH-sponsored and phase I studies—underscoring indirect cost barriers to enrollment); and Williams CP, Geiger AM, Norton WE, de Moor JS, Senft Everson N, Influence of Cost-Related Considerations on Clinical Trial Participation: Results From the 2020 Health Information National Trends Survey (HINTS), J. Gen. Intern. Med. 38:1200–1206 (2023) (showing that travel, parking, lodging, and caregiving costs substantially influence willingness to participate and that reimbursement can mitigate burden).

[9] Williams CP, Deng L, Caston NE, et al., Understanding the Financial Cost of Cancer Clinical Trial Participation, Cancer Med. 13(8):e7185 (2024). See also Nipp RD, Powell E, Chabner B, Moy B, Recognizing the Financial Burden of Cancer Patients in Clinical Trials, Oncologist 20:572–575 (2015) (reporting average indirect, nonmedical costs of roughly $600 per month for trial participants); Huey RW, George GC, Phillips P, et al., Patient-Reported Out-of-Pocket Costs and Financial Toxicity During Early-Phase Oncology Clinical Trials, Oncologist 26:588–596 (2021) (finding that 48% of patients in early-phase oncology trials incurred ≥$1,000 per month out-of-pocket); Nipp RD, Lee H, Powell E, et al., Financial Burden of Cancer Clinical Trial Participation and the Impact of a Cancer Care Equity Program, Oncologist 21:467–474 (2016) (documenting

reimbursements that averaged approximately $185/month for in-state participants, $300/month for regional participants, and $900/month for those traveling from out of region to offset travel and lodging); U.S. Dep't of Health & Human Servs., Office of the Assistant Secretary for Planning & Evaluation, Empowering Patients to Participate in Clinical Trials (July 2025) (noting survey evidence that cancer trial participants commonly need about $200–$1,000 per month to offset trial-related expenses); and Williams CP, Reh N, Chen M, et al., Financial Barriers to Breast Cancer Clinical Trial Participation: A Qualitative Study in the Deep South, Support Care Cancer 33:771 (2025) (patients suggested compensation in the range of $50–$700 per month to cover travel, parking, lodging, food, and missed work).

[10] Williams CP, Deng L, Caston NE, et al., Understanding the Financial Cost of Cancer Clinical Trial Participation, Cancer Med. 13(8):e7185 (2024). See also Williams CP, Reh N, Chen M, et al., Financial Barriers to Breast Cancer Clinical Trial Participation: A Qualitative Study in the Deep South, Support Care Cancer 33:771 (2025) (patients who declined trials widely identified travel as the most common expense; average one-way distance ~33 miles with parking, gas, lodging, and food burdens frequently described); Borno HT, Zhang L, Siegel A, Chang E, Ryan CJ, At What Cost to Clinical Trial Enrollment? A Retrospective Study of Patient Travel Burden in Cancer Clinical Trials, Oncologist 23:1242–1249 (2018) (lower-income patients traveled a mean 238 miles to enroll vs. 49–43 miles for middle/high income; greatest travel burden observed in some NIH-sponsored and phase I studies); U.S. Dep't of Health & Human Servs., Office of the Assistant Secretary for Planning & Evaluation, Empowering Patients to Participate in Clinical Trials (July 2025) (patients "often cite cost and travel distance" as major factors; rural participants must travel farther, compounding recruitment/retention challenges; missed work and childcare frequently implicated); U.S. Dep't of Health & Human Servs., Office of the Assistant Secretary for Planning & Evaluation, Use of Participant Compensation in U.S. Clinical Research (July 2025) (notes that travel expenses, lost wages, and other out-of-pocket costs are thought to reduce participation and that compensation can offset these burdens); and Nipp RD, Powell E, Chabner B, Moy B, Recognizing the Financial Burden of Cancer Patients in Clinical Trials, Oncologist 20:572–575 (2015) (documents substantial indirect costs for trial participants—often hundreds of dollars per month—driven by travel and lodging).

[11] Shriver SP, Sahar L, Douangchai Wills VL, Adams DV, Fleury ME, Assessing populations with access to National Cancer Institute–funded sites using local distance-based service areas, Journal of Clinical and Translational Science 9:e218 (2025) (doi:10.1017/cts.2025.10148).

[12] Williams CP, Deng L, Caston NE, et al., Understanding the Financial Cost of Cancer Clinical Trial Participation, Cancer Med. 13(8):e7185 (2024). See also Shriver SP, Sahar L, Douangchai Wills VL, Adams DV, Fleury ME, Assessing Populations With Access to National Cancer Institute–Funded Sites Using Local Distance-Based Service Areas, Clin. Transl. Sci. (2025) (reporting that NCI-funded research sites cluster in urban centers, leaving rural and low-income populations with markedly longer travel—nearly 17% of U.S. adults over 35 would drive >100 miles to reach an NCI-funded site—and highlighting pronounced gaps in regions such as the South, Appalachia, the West, and the Great Plains); U.S. Dep't of Health & Human Servs., Office of the Assistant Secretary for Planning & Evaluation, Empowering Patients to Participate in Clinical Trials (July 2025) (noting that rural trial participants "often" must travel much greater distances, creating recruitment and retention challenges, and that travel-related time and costs compound burdens such as missed work and dependent care); Stout NL, Nikcevich D, Henderson TO, et al., Improving Rural Clinical Trial Enrollment: Recommendations From the Rural Health Working Group of the Alliance Clinical Trials Network, J. Clin. Oncol. 42:1722–1725 (2024) (describing persistent rural enrollment barriers tied to long travel distances to trial sites and limited local research infrastructure); Borno HT, Zhang L, Siegel A, Chang E, Ryan CJ, At What Cost to Clinical Trial Enrollment? A Retrospective Study of Patient Travel Burden in Cancer Clinical Trials, Oncologist 23:1242–1249 (2018) (documenting substantial travel distances to enroll in trials, with the greatest burdens in certain settings; lower-income patients traveled a mean 238 miles versus 49–43 miles for middle/high income, underscoring the disproportionate burden on patients living farther from major centers); Lee H, Bates AS, Callier S, et al., Analysis and Optimization of Equitable U.S. Cancer Clinical Trial Center Access by Travel Time, JAMA Oncol. 10:652–657 (2024) (demonstrating significant travel-time inequities to trial centers and identifying optimization strategies to reduce excessive travel for underserved and rural populations); Kirkwood MK, Schenkel C, Hinshaw DC, et al., State of Geographic Access to Cancer Treatment Trials in the United

States: Are Studies Located Where Patients Live?, JCO Oncol. Pract. 21:427–437 (2025) (finding that nonmetropolitan counties are far less likely to host cancer clinical trials, forcing rural patients to travel farther for participation); Bruner DW, Pugh SL, Yeager KA, Bruner J, Curran W., Cartographic Mapping and Travel Burden to Assess and Develop Strategies to Improve Minority Access to National Cancer Clinical Trials, Int. J. Radiat. Oncol. Biol. Phys. 93:702–709 (2015) (using mapping to quantify travel burden to national trial sites and proposing strategies to mitigate long-distance barriers); Longacre CF, Neprash HT, Shippee ND, Tuttle TM, Virnig BA, Evaluating Travel Distance to Radiation Facilities Among Rural and Urban Breast Cancer Patients in the Medicare Population, J. Rural Health 36:334–346 (2020) (showing rural patients face substantially longer travel distances for cancer care, a barrier that similarly affects access to trial participation).

[13] Williams CP, Deng L, Caston NE, et al., Understanding the Financial Cost of Cancer Clinical Trial Participation, Cancer Med. 13(8):e7185 (2024).

[14] Id.

[15] Islami F, Baeker Bispo J, Lee H, et al. American Cancer Society's report on the status of cancer disparities in the United States, 2023. CA Cancer J Clin. 2024; 74(2): 136-166. doi:10.3322/caac.21812.

[16] Survey: Majority Would Participate in Clinical Trials if They Received Support to Offset Costs (2026) https://www.fightcancer.org/policy-resources/survey-majority-would-participate-clinical-trials-if-they-received-support-offset.

[17] Williams CP, Reh N, Chen M, et al., Financial Barriers to Breast Cancer Clinical Trial Participation: A Qualitative Study in the Deep South, Support. Care Cancer 33:771 (2025).

[18] See, e.g., OIG Advisory Opinion 98-6 (May 1, 1998) (permitting the remuneration at issue will "ensure that economically disadvantaged patients are not precluded from the study"); OIG Advisory Opinion 00-05 (Jun. 30, 2000), at 5 (same); OIG Advisory Opinion 06-05 (Apr. 26, 2006), at 3 (clinical trials "can impose substantial financial, logistical, and other burdens on patients and their families"); OIG Advisory Opinion 08-11 (Sep. 17, 2008), at 8 (permitting the remuneration at issue will "ensure that economically disadvantaged patients are not precluded from the study"); OIG Advisory Opinion 22-05 (Mar. 11, 2022), at 7 ("[a]ccording to Requestor, the out-of-pocket costs to participate in the Study would be cost prohibitive for many Medicare beneficiaries who otherwise would participate in the Study).

[19] Financial stress associated with oncology clinical trial participation, ASPE, 2025, accessed at: https://aspe.hhs.gov/reports/financial-stress-clinical-trial.

[20] Unger JM, Gralow JR, Albain KS, Ramsey SD, Hershman DL. Patient Income Level and Cancer Clinical Trial Participation: A Prospective Survey Study. JAMA Oncol. 2016;2(1):137–139. doi:10.1001/jamaoncol.2015.3924.

[21] Noel ODV, Akgul B, Bhandari M, Ramos F, Joshi G, Garg H, Dursun F, Mansour A. Clinical trial participation in kidney, bladder, and prostate malignancies in the United States: Sociodemographic distribution and impact on survival. Urol Oncol. 2026 Jun;44(6):176-188. doi: 10.1016/j.urolonc.2026.111065. Epub 2026 Mar 28. PMID: 41904094.

[22] Survey: Majority Would Participate in Clinical Trials if They Received Support to Offset Costs (2026) https://www.fightcancer.org/policy-resources/survey-majority-would-participate-clinical-trials-if-they-received-support-offset.

[23] 42 U.S.C. § 1320a-7b(b); 42 U.S.C. § 1320a-7a(a)(5), (i)(6); Clinical Trials RFI, 91 Fed. Reg. 37902 (June 24, 2026).

[24] Clinical Trials RFI, 91 Fed. Reg. 37902 (June 24, 2026) (noting 10 favorable advisory opinions addressing waiver or subsidization of Federal health care program cost-sharing obligations for clinical trial participants and no advisory opinions or guidance relating to other remuneration such as transportation costs, childcare costs, or stipends); see, e.g., OIG Advisory Op. No. 16-13 (Dec. 13, 2016) (concluding that waiving Medicare cost-sharing obligations for a government-funded HIV-prevention study and paying participants a stipend for their time and effort presented only a minimal risk of fraud and abuse where the study was not commercial or product-

specific and enrollment aimed to reach historically underrepresented populations); OIG Advisory Op. No. 22-05 (Mar. 11, 2022) (concluding that a device manufacturer's subsidy of Medicare cost-sharing obligations for a CMS-approved Category B IDE study presented a low risk of overutilization given enrollment caps, IRB oversight, and the absence of advertising); OIG Advisory Op. No. 23-11 (Dec. 21, 2023) (Favorable) (concluding that subsidizing up to $2,000 in Medicare cost-sharing obligations for a CMS-approved Category B IDE study was a reasonable means of promoting diverse enrollment and posed a low risk of overutilization).

[25] U.S. Dep't of Health & Human Servs., Office of the Assistant Secretary for Planning & Evaluation, Empowering Patients to Participate in Clinical Trials (July 2025), at 1; U.S. Dep't of Health & Human Servs., ASPE, Financial Stress Associated with Oncology Clinical Trial Participation (Jan. 2026).

[26] Clinical Trials RFI, 91 Fed. Reg. 37902 (June 24, 2026); FDA, Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators (Jan. 2018); Secretary's Advisory Committee on Human Research Protections, Attachment A—Addressing Ethical Concerns Offers of Payment to Research Participants (Sept. 30, 2019); NIH Office of Extramural Research, Allowable Costs Related to Participant Inclusion Activities (Nov. 29, 2023).

[27] Williams CP, Deng L, Caston NE, et al., Understanding the Financial Cost of Cancer Clinical Trial Participation, Cancer Med. 13(8):e7185 (2024).

[28] Williams CP, Deng L, Caston NE, et al., Understanding the Financial Cost of Cancer Clinical Trial Participation, Cancer Med. 13(8):e7185 (2024); Nipp RD, Powell E, Chabner B, Moy B, Recognizing the Financial Burden of Cancer Patients in Clinical Trials, Oncologist 20:572–575 (2015); U.S. Dep't of Health & Human Servs., ASPE, Empowering Patients to Participate in Clinical Trials (July 2025), at 1; U.S. Dep't of Health & Human Servs., ASPE, Use of Participant Compensation in U.S. Clinical Research Studies (July 2025).

[29] FDA, Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators (Jan. 2018); SACHRP, Attachment A—Addressing Ethical Concerns Offers of Payment to Research Participants (Sept. 30, 2019); 42 C.F.R. § 1001.952(bb).

[30] Protection of Human Subjects, 45 C.F.R. § 46.116 (2020).

[31] General requirements for informed consent, 21 C.F.R. § 50.20 (2026).

[32] Menikoff, J. 2022. Statement of Jerry Menikoff, OHRP Exploratory Workshop 2022: Beyond altruism - Exploring payment for research participation. September 15. p. 6. https://www.hhs.gov/ohrp/education-and-outreach/exploratory-workshop/2022-workshop/index.html.

[33] FDA (2018) Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators.https://www.fda.gov/regulatory-information/search-fda-guidance-documents/payment-and-reimbursement-research-subjects

[34] Abadie, R., Anderson, E., Eberts, J., Lynch, H. F., Fisher, J., Gelinas, L., … McNair, L. (2025). Pursuing Fair and Just Compensation for Research Participants: An Open Letter to the Research Ethics Community. *The American Journal of Bioethics*, *25*(7), 3–7.

[35] See OIG Advisory Op. No. 23-01 (2023) (concluding that a manufacturer's provision of financial assistance for transportation, lodging, and meals to financially needy pediatric patients receiving the manufacturer's drug presented a sufficiently low risk of fraud and abuse notwithstanding that no safe harbor applied to the arrangement); OIG Advisory Op. No. 24-13 (Dec. 26, 2024) (Favorable) (concluding that assistance for travel, lodging, meals, and associated expenses for patients receiving a cell therapy product was not used as a marketing tool where the manufacturer did not advertise the arrangement beyond providing treatment centers and referring physicians a general overview of available patient support resources and did not require exclusive use of its product) (both addressing analogous anti-steering concerns for manufacturer-funded travel and lodging support furnished in connection with treatment, rather than clinical trial participation); 42 C.F.R. § 1001.952(bb).

[36] FDA, Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators (Jan. 2018).

[37] See, e.g., OIG Advisory Op. No. 08-11 (Sept. 17, 2008) (concluding that waiving Medicare cost-sharing obligations for a government-sponsored oxygen therapy trial did not pose a significant risk of fraud and abuse where eligibility was based on objective, Steering-Committee-approved criteria and utilization was closely monitored under the study protocol); OIG Advisory Op. No. 16-13 (Dec. 13, 2016) (concluding that eligibility criteria tied to the study protocol, rather than to referral volume, supported a finding of minimal risk of fraud and abuse); OIG Advisory Op. No. 21-13 (Sept. 29, 2021) (concluding that a coinsurance subsidy for a clinical study presented a low risk of overutilization where subsidies were not advertised, participants had to satisfy the study's enrollment criteria and execute informed consent, and the arrangement was distinguishable from problematic seeding arrangements because it did not shift costs onto Federal health care programs); 42 C.F.R. § 1001.952(bb).

[38] Unger JM, Xiao H, Vaidya R, LeBlanc M. Patient Enrollment to Industry-Sponsored Versus Federally-Sponsored Cancer Clinical Trials. J Clin Oncol. 2024 Nov 20;42(33):3917-3925. doi: 10.1200/JCO.24.00843. Epub 2024 Sep 27. PMID: 39331494; PMCID: PMC11575909.

[39] Clinical Trials RFI, 91 Fed. Reg. 37902 (June 24, 2026); FDA, Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators (Jan. 2018); FDA, Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors (Aug. 2023).

[40] 42 C.F.R. § 1001.952(bb), (hh); Medicare and State Health Care Programs: Fraud and Abuse; Revisions to Safe Harbors Under the Anti-Kickback Statute, 85 Fed. Reg. 77684 (Dec. 2, 2020); SACHRP, Attachment A—Addressing Ethical Concerns Offers of Payment to Research Participants (Sept. 30, 2019).

[41] 42 C.F.R. § 1001.952(bb) (safe harbor conditions including documentation and cost-shifting limitations).

[42] FDA, Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators (Jan. 2018); SACHRP, Attachment A—Addressing Ethical Concerns Offers of Payment to Research Participants (Sept. 30, 2019); 42 U.S.C. § 1320a-7a(i)(6)(B).

[43] 42 U.S.C. § 1320a-7d(a)(2); Medicare and State Health Care Programs: Fraud and Abuse; Revisions to Safe Harbors Under the Anti-Kickback Statute, 85 Fed. Reg. 77684 (Dec. 2, 2020).

[44] 42 C.F.R. § 1001.952(bb); Medicare and State Health Care Programs: Fraud and Abuse; Revisions to Safe Harbors Under the Anti-Kickback Statute, 85 Fed. Reg. 77684, 77858–64 (Dec. 2, 2020); Shriver SP, Sahar L, Douangchai Wills VL, Adams DV, Fleury ME, Assessing populations with access to National Cancer Institute–funded sites using local distance-based service areas, Journal of Clinical and Translational Science 9:e218 (2025).

[45] 42 C.F.R. § 1001.952(ee)–(hh); Medicare and State Health Care Programs: Fraud and Abuse; Revisions to Safe Harbors Under the Anti-Kickback Statute, 85 Fed. Reg. 77684 (Dec. 2, 2020).

[46] 42 C.F.R. § 1003.110; Clinical Trials RFI, 91 Fed. Reg. 37902 (June 24, 2026); 42 U.S.C. § 1320a-7a(i)(6)(B) (illustrating that no parallel exception exists in the Federal anti-kickback statute for practices permissible under the Beneficiary Inducements CMP); OIG Advisory Op. No. 24-05 (2024) (concluding that a manufacturer's travel and lodging support for patients receiving a specialized cell therapy product satisfied the Promotes Access to Care Exception to the Beneficiary Inducements CMP because the support removed a barrier to accessing medically necessary care furnished only at a limited number of qualified treatment centers, even though no anti-kickback statute safe harbor applied to the arrangement); OIG Advisory Op. No. 24-13 (Dec. 26, 2024) (Favorable) (concluding that travel, lodging, and meal assistance for cell therapy patients presented a sufficiently low risk of fraud and abuse where the manufacturer did not require exclusive use of its product and did not advertise the arrangement as a marketing tool).

[47] Unger JM, Moseley A, Symington B, Chavez-MacGregor M, Ramsey SD, Hershman DL. Geographic Distribution and Survival Outcomes for Rural Patients With Cancer Treated in Clinical Trials. *JAMA Netw Open.* 2018;1(4):e181235. doi:10.1001/jamanetworkopen.2018.1235.

[48] Clinical Trials RFI, 91 Fed. Reg. 37902 (June 24, 2026); U.S. Dep't of Health & Human Servs., ASPE, Empowering Patients to Participate in Clinical Trials (July 2025), at 1; Holly Fernandez Lynch et al., Fair Payment and Just Benefits to Enhance Diversity in Clinical Research, J. Med. Ethics (2021).

[49] CMS, Medicare National Coverage Determinations Manual, Ch. 1, Part 4, § 310.1; OIG Advisory Opinion 98-6 (May 1, 1998) (explaining that the purpose of permitting the remuneration at issue was to induce participation in a government-sponsored scientific study, not to induce utilization of Medicare-covered services); OIG Advisory Op. No. 23-11 (Dec. 21, 2023) (Favorable) (concluding that a capped Medicare cost-sharing subsidy for a CMS-approved device study posed a low risk of overutilization because the subsidy was designed only to facilitate enrollment and prevent attrition, not to increase utilization of items or services).

[50] U.S. Dep't of Health & Human Servs., ASPE, Empowering Patients to Participate in Clinical Trials (July 2025), at 1; Williams RJ, Tse T, DiPiazza K, Zarin DA, Terminated Trials in the ClinicalTrials.gov Results Database: Evaluation of Availability of Primary Outcome Data and Reasons for Termination, PLoS ONE 10:e0127242 (2015); Carlisle B, Kimmelman J, Ramsay T, MacKinnon N, Unsuccessful Trial Accrual and Human Subjects Protections: An Empirical Analysis of Recently Closed Trials, Clin. Trials 12:77–83 (2015); ACS CAN, Barriers to Patient Enrollment in Therapeutic Clinical Trials for Cancer (2024).

[51] 42 U.S.C. §§ 1320a-7b(b), 1320a-7a(a)(5), 1320a-7d(b); 42 C.F.R. part 1008; see, e.g., OIG Advisory Op. No. 24-05 (2024) (noting the advisory opinion is issued only to the requestor and has no application to, or may not be relied upon by, any other individual or entity, illustrating the limited, case-by-case nature of advisory-opinion relief).

[52] Medicare Program; Modernizing and Clarifying the Physician Self-Referral Regulations, 84 Fed. Reg. 55766 (Oct. 17, 2019) (stating that HHS had identified the broad reach of the physician self-referral law, the AKS, and the Beneficiary Inducement CMP as potentially inhibiting beneficial arrangements that would advance the transition to value-based care); Medicare and State Health Care Programs: Fraud and Abuse; Request for Information Regarding the Anti-Kickback Statute and Beneficiary Inducements CMP, 83 Fed. Reg. 43607 (Aug. 27, 2018) (seeking input on ways OIG might modify or add safe harbors and CMP exceptions to foster arrangements promoting care coordination and advancing delivery-system goals).

[53] FDA, Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators (Jan. 2018); SACHRP, Attachment A—Addressing Ethical Concerns Offers of Payment to Research Participants (Sept. 30, 2019); Medicare and State Health Care Programs: Fraud and Abuse; Revisions to Safe Harbors Under the Anti-Kickback Statute, 85 Fed. Reg. 77684 (Dec. 2, 2020).

[54] See, e.g., OIG Advisory Op. No. 08-11 (Sept. 17, 2008) (concluding that eligibility criteria approved by a study's steering committee, rather than referral volume, minimized the risk of fraud and abuse in a government-sponsored oxygen therapy trial); OIG Advisory Op. No. 16-13 (Dec. 13, 2016) (concluding that a stipend for participant time and effort, calculated without regard to referrals and reviewed by an IRB, presented a minimal risk of fraud and abuse); OIG Advisory Op. No. 22-05 (Mar. 11, 2022) (concluding that a Medicare cost-sharing subsidy capped at a fixed enrollment number and not advertised to prospective subjects posed a low risk of overutilization).