February 9, 2026

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

Re: Solicitation of Proposals for New and Modified Safe Harbors and Special Fraud Alerts OIG-1125-N, ("Annual Solicitation")
90 Fed. Reg. 57016 (Dec. 9, 2025)

Dear Inspector General Bell:

The undersigned 25 organizations are committed to removing barriers to clinical trial access and thus urge the administration to create a new regulatory safe harbor to the federal health care program anti-kickback statute, 42 U.S.C. § 1320a-7b(b) ("AKS"). As discussed in detail below, we believe the adoption of this safe harbor is not only appropriate as a policy matter, but its adoption will not result in overutilization, improper patient steering, or any of the other ills that the AKS is intended to prevent.

I. Administration Efforts to Support Clinical Trials

We believe the adoption of a safe harbor for clinical trial participation is appropriate given the Administration's strong support for clinical trials. In a July 2025 Issue Brief entitled, "Empowering Patients to Participate in Clinical Trials," the Trump Administration made it clear that clinical trials are "the gold standard of clinical research and provide critical evidence for new treatments."[i]

Notwithstanding their importance, however, clinical trial sponsors struggle to enroll patients.[ii] Indeed, as the Administration notes in its July 2025 Issue Brief, "an estimated 30% of clinical trials conducted between 2011 and 2021 were suspended or terminated after failing to reach [their] enrollment target."[iii]

As the July 2025 Issue Brief further observes, 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."[iv] The July 2025 Issue Brief emphasizes that removing these barriers will "empower patients to participate in clinical trials, promote greater insights regarding how treatments/interventions work across the entirety of the U.S. population, and ensure clinical research dollars are used efficiently."[v]

The Trump Administration has been actively implementing the policies set forth in its July 2025 Issue Brief. Most notably, in December 2025, the Food and Drug Administration (FDA) published guidance for "Enhancing Participation in Clinical Trials- Eligibility Criteria, Enrollment Practices, and Trial Designs: Guidance for Industry" ("Industry Guidance").[vi] Consistent with the July 2025 Issue Brief, the Industry Guidance notes that notwithstanding the agency's decades-old promotion of "enrollment practices that would lead to clinical trials that better reflect the population most likely to use the drug" if approved, "challenges to participation in clinical trials remain, and certain groups continue to be underrepresented in many clinical trials."[vii]

Also consistent with the July 2025 Issue Brief, the Industry Guidance notes that among the barriers to greater clinical trial participation are the financial costs associated with such participation, such as those associated with travel, missing work, and dependent care. Further, the Guidance recognizes that these costs may be particularly burdensome for those in rural or remote locations.

Finally, and importantly, the Industry Guidance states that the "FDA does not consider reimbursement for reasonable travel expenses to and from the clinical trial site and associated costs such as airfare, parking, and lodging to raise issues regarding undue influence."[viii]

II. Background

Individuals who participate in clinical trials incur two types of costs: direct medical costs ("direct costs") and indirect ancillary costs ("indirect costs").

- Direct costs are the costs of care incurred by the participant in obtaining hospital, physician, laboratory, radiology and other health care items and services. An example of a direct (or routine) cost of care that a clinical trial participant might incur would be the payment of cost-sharing obligations, such as copayment and coinsurance amounts, attendant to receiving health care items and services from a provider, supplier, or practitioner that may be covered by commercial or government payers.[ix]

- Indirect costs are non-medical costs that the trial participant incurs pursuant to fulfilling trial participation requirements. For example, depending on the particular clinical trial and participant, indirect costs might include costs associated with travel, parking, lodging, childcare, and lost wages that the participant incurred as a result of attending appointments related to the clinical trial at issue.

In many cases, the indirect costs incurred by patients to participate in a clinical trial can be significant. 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.[x]

Not all indirect expenses are equal, of course. According to the same 2024 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."[xi]

This makes sense, as a new study found that nearly 38% of the U.S. population over 35 years old must drive over 50 miles to participate in a trial at an NCI-funded site, and almost 17% must travel 100 miles or more.[xii] These sites, in turn, are overwhelmingly located in urban areas, and while in many cases individuals live closer to other sites of cancer care, these other sites do not offer clinical trials as evidenced by the five-fold higher trial enrollment rate at NCI-designated cancer centers when compared to community cancer sites.[xiii]

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"[xiv]; 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."[xv] 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.[xvi] 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 about 40%, 30% and 20% higher, respectively, in rural areas when compared to urban areas.[xvii]

Under these circumstances, it is not surprising that a 2022 study found that almost 80 percent of cancer patients indicated they would be more likely to enroll in a clinical trial if sponsors supported them financially to offset non-medical costs.[xviii] Similarly, in a 2025 study, 86 percent of patients cited expenses as influencing their decision to participate in a clinical trial.[xix] For its part, the U.S. Department of Health and Human Services ("HHS"), Office of Inspector General ("OIG") has flagged this particular issue on multiple occasions over the past 25 years.[xx]

In 2024, the American Cancer Society Cancer Action Network (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.[xxi] 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.

Given the importance of clinical trials, and the economic barriers to ensuring their success, there is widespread support for arrangements pursuant to which clinical trial sponsors subsidize the indirect costs of clinical trial participants. Indeed, just last year, 64 individuals from the fields of philosophy, law, medicine, policy, public health, patient advocacy, and research ethics published an open letter "to highlight the growing recognition of the pitfalls of excessive concern over payment to research participants."[xxii] The authors note that

> [e]xperts in the field of research oversight, including institutional review boards/research ethics committees (IRB/RECs), now

> recognize that for adult participants capable of providing their own informed consent, instances of monetary undue influence are generally quite rare, underpayment is far more common and ethically concerning than overpayment, and that lowering payments threatens justice and fairness without providing substantive protection for participants.[xxiii]

Finally, this position is consistent with both the FDA's December 2025 Industry Guidance, which is discussed above, and the FDA's guidance for Institutional Review Boards ("IRBs") and clinical investigators, entitled "Payment and Reimbursement to Research Subjects" ("IRB Guidance").[xxiv] In its IRB guidance, the FDA makes two important points. First, the agency (again) emphasizes that it "does not consider reimbursement for travel expenses to and from the clinical trial site and associated costs"—including but not limited to airfare, parking, and lodging—"to raise issues regarding undue influence." Second, the guidance provides that with respect to all other remuneration, the IRB should review the amount, method and timing of such payments or reimbursements "to assure that neither are coercive or present undue influence."[xxv]

To summarize, participating in clinical trials often requires substantial travel. Such travel can be extremely expensive, especially so for those living in remote or other rural areas (where, to exacerbate matters, the incidence of cancer is highest). Public and private stakeholders view promoting representative clinical trials as a high priority; and these same stakeholders (i) have concluded that indirect costs create significant barriers to achieving representative clinical trials and (ii) support the removal of these barriers.

III. Proposed Safe Harbor

Notwithstanding the above consensus, many clinical trial sponsors are reluctant to cover indirect costs incurred by clinical trial participants. A principal reason for this reluctance is that offering such coverage to Medicare, Medicaid, and other federal health care program beneficiaries may implicate the AKS and/or the federal beneficiary inducement civil monetary law, 42 U.S.C. § 1320a-7a(a)(5) ("Beneficiary Inducement CMP"). To address this barrier, we propose the creation of a new regulatory safe harbor that, subject to a host of safeguards and limitations, would permit sponsors of clinical trials targeting cancer or other life-threatening diseases or conditions to cover certain indirect costs incurred by clinical trial participants without violating the AKS or Beneficiary Inducement CMP.

A. Text

Under the proposed safe harbor, 42 C.F.R. § 1001.952 would be amended to add a new section 1001.952(ll), which would provide as follows:

> (ll) **Coverage of Indirect Clinical Trial Costs**.

(1) As used in section 1128B of the Act, “remuneration” does not include indirect cost payments or indirect cost stipends offered by the sponsor of an approved clinical trial to a human subject participating in that approved clinical trial if the conditions in paragraphs ll(1)(i) through (iv) of this section are met.

(i) The indirect cost payment or indirect cost stipend is provided pursuant to a written protocol that has been reviewed and approved in advance by the Institutional Review Board responsible for the approved clinical trial.

(ii) In the case of remuneration in the form of indirect cost payments:

(a) the written protocol specifies

(i) each category of indirect costs for which payment will be made (e.g., travel, lodging, parking, etc.),

(ii) with respect to each category, whether the payment will be made to the human subject (in the form of reimbursement) or directly to the vendor providing the item or service to the human subject, and

(iii) any monetary caps or other limitations that will apply to such payments; and

(b) the purpose, amount, date, and method of payments made to or on behalf of each human subject is contemporaneously documented by the sponsor.

(iii) In the case of remuneration in the form of an indirect cost stipend:

(a) the written protocol specifies

(a) the amount of the stipend,

(b) the period (e.g., one month) or activity (e.g., one visit) the stipend covers,

(c) the indirect cost categories the stipend covers (e.g., travel and lodging), and

(d) the methodology used to calculate the stipend; and

(b) the payment amount and date of each stipend provided to each human subject is contemporaneously documented by the sponsor.

(iv) The documentation required by paragraph ll(1) is made available to the Secretary upon request.

(2) For purposes of paragraph (ll) of this section:

(i) *Approved clinical trial* has the meaning set forth in section 2709(d) of the Public Health Service Act.[xxvi]

(ii) *Human subject* has the meaning set forth in 21 C.F.R. § 56.102(e).[xxvii]

(iii) *Indirect cost payment* means a payment that is made directly to a human subject, or to a vendor on behalf of a human subject, that covers the actual, non-medical costs incurred by a human subject relating exclusively to their participation in an approved clinical trial.

(iv) *Indirect cost stipend* means a flat, predetermined dollar amount that is intended to cover, for a designated period of time (e.g., one month) or in connection with a specified activity (e.g., one visit), the actual, non-medical costs incurred by a human subject relating exclusively to their participation in an approved clinical trial.

(iv) *Institutional Review Board (IRB)* has the meaning set forth in 21 C.F.R. § 56.102(g).[xxviii]

(v) *Life-threatening disease or condition* has the meaning set forth in section 2709(e) of the Public Health Service Act.[xxix]

(vi) *Sponsor* has the meaning set forth in 21 C.F.R. § 56.102(j).[xxx]

B. Explanation

Before turning to how the proposed safe harbor fares with respect to the various factors enumerated in the Annual Solicitation, we would like to highlight the safeguards built into the proposed safe harbor.

First, the proposed safe harbor would not apply to all clinical trials. The safe harbor would apply only to "approved clinical trials" as defined in section 2709(d) of the Public Health Service Act ("PHSA"). Among other limitations, that definition only includes clinical trials that are conducted in relation to the "prevention, detection, or treatment" of a "life-threatening disease or condition" and, pursuant to section 2709(e) of the PHSA, a disease or condition only qualifies as "life-threatening" if "the likelihood of death is probable unless the course of the disease or condition is interrupted." Simply put, the universe of clinical trials to which the proposed safe harbor would apply would be limited.

Second, the proposed safe harbor would protect only a narrow category of remuneration. Specifically, the safe harbor is designed to protect only the reimbursement of those actual, non-medical costs incurred by a human subject that relate exclusively to their participation in an approved clinical trial.

Thus, the proposed safe harbor would not protect any remuneration that might incentivize a patient to purchase or order any health care item or service. For example, the proposed safe harbor would not protect remuneration in the form of a waiver of a patient's cost-sharing obligations.

Further, the proposed safe harbor would not protect the coverage of all non-medical costs. For example, costs associated with traveling to a clinical trial site that is far from the participant's residence (such as lodging, fuel, and parking) might be covered by the safe harbor. However, many other costs (such as toiletries, clothing, and entertainment) would not be covered.

Third, every approved clinical trial (as defined in the proposed safe harbor) is subject to the oversight of an IRB, and every IRB has a preexisting legal obligation to ensure that the study in question has the safeguards necessary to protect participants from either "coercion or undue influence."[xxxi] As an added safeguard, in order to receive protection under the proposed safe harbor, indirect cost payments and indirect cost stipends must be provided pursuant to a detailed written protocol that has been reviewed and approved in advance by the relevant IRB.

Fourth, in addition to the written protocol approved by the IRB, the safe harbor requires documentation relating to both indirect cost payments and indirect cost stipends. These documentation requirements ensure that the government is able to confirm that all payments meet the definition of "indirect cost payments" or "indirect cost stipends," as applicable, and that the arrangement otherwise meets the conditions of the safe harbor.

C. Discussion

As set forth in the Annual Solicitation, the OIG considers a number of factors in reviewing proposals for additional safe harbors, including the extent to which the proposals may result in an increase or decrease in (i) overutilization of health care services, (ii) costs to Federal health care programs resulting from such overutilization, (iii) patient freedom of choice among health care providers, (iv) competition among health care providers, (v) access to health care services, (vi) the quality of health care services, and (vii) the ability of health care facilities to provide services in medically underserved areas or to medically underserved populations. OIG also considers "the existence (or nonexistence) of any potential financial benefit to health care professionals or providers that may influence their decision whether to" (i) "order a health care item or service" or (ii) "arrange for a referral of health care items or services to a particular practitioner or provider."

1. Overutilization; Program Costs

The proposed safe harbor will not result in overutilization—that is, the ordering of items or services that are not medically necessary. As a threshold matter, whether participating in a clinical trial or not, patients who have cancer or another life-threatening condition typically will receive routine care, and both Medicare and Medicaid cover the costs associated with such routine care whether they are incurred in or outside a clinical trial. Further, the proposed safe harbor does not protect any remuneration that is provided to any physician or other provider, supplier, or practitioner who is able to order health care items or services. To the contrary, the only person who will receive remuneration under the proposed safe harbor is the human subject participating in the clinical trial at issue, and that individual is not able to order health care items or services. Simply put, and like the proposed arrangement in OIG Advisory Opinion 98-6, the purpose of the proposed safe harbor here is "to induce participation in a scientific study, not to induce utilization of Medicare-covered services."[xxxii]

Because the proposed safe harbor will not result in overutilization, it cannot (by definition) result in any inappropriate increase in federal health care program costs. It is true, of course, that a drug or device that is the subject of a clinical trial may, depending on a host of factors, ultimately be approved by the FDA and covered and reimbursed by Medicare, Medicaid and/or other government health care programs. But any increase in program costs as a result of these approval, coverage, and reimbursement decisions would neither be the result of overutilization (again, the ordering of medically unnecessary items or services) nor attributable to the remuneration permitted by the proposed safe harbor (i.e., the coverage of indirect costs incurred by clinical trial participants suffering from life-threatening conditions).

2. Patient Freedom of Choice

With respect to patient freedom of choice, the government's principal concern is the steering of patients to particular providers not because the providers are the most convenient for the patient or offer the highest quality items or services, but because the provider is paying the referring individual or entity a kickback. For example, where Lab A offers a physician $25 for each referral of a Medicare or Medicaid beneficiary, the physician may steer patients to Lab A, even though Lab B and Lab C are more convenient for the patient and offer higher quality services than Lab A. The proposed safe harbor will not result in improper patient steering for several reasons.

As a threshold matter, the proposed safe harbor will not protect incentives offered to patients by providers, suppliers or practitioners to obtain medical care. For example, were a hospital or physician to offer to waive the cost-sharing obligations of a Medicare beneficiary participating in an approved clinical trial, this remuneration would not be protected under the proposed safe harbor.

Further, by defining the terms "indirect cost payments" and "indirect cost stipends" to cover only "actual, non-medical costs incurred by a human subject relating exclusively to their participation in an approved clinical trial," the safe harbor effectively ensures that the remuneration provided to a given patient will do nothing more than put that patient in precisely the same economic position they would have been in had they decided not to participate in the clinical trial. Put somewhat differently, while the safe harbor might incentivize a patient to participate in an approved clinical trial by removing any economic disincentive to do so, the safe harbor will not incentivize a patient to seek care that is not medically necessary or to seek medically necessary care from any particular provider, supplier, or practitioner.

Finally, as an added safeguard, all indirect cost payments and indirect cost stipends must be documented and provided consistent with the terms and conditions of a written protocol that has been reviewed and approved in advance by the relevant IRB, which (as noted above) has a preexisting legal obligation to ensure that the study in question has the safeguards necessary to protect participants from either "coercion or undue influence."

3. Provider Competition

With respect to unfair competition, the government's principal concern is that where referrals are controlled by those (e.g., physicians) receiving remuneration from a provider (e.g., Lab A), the medical marketplace suffers because new competitors (e.g., Labs B and C) may no longer be able to win business with superior quality, service, or price. For precisely the same reasons the proposed safe harbor will not result in any improper patient steering, it also will not result in any unfair competition. Simply put, the safe harbor does not provide any economic incentive to any patient to obtain health care items or services from any particular provider, supplier, or practitioner. As such, the proposed safe harbor will have no impact on the ability of providers, suppliers or practitioners to compete against one another based on quality, service, or price (much less an impact that could be characterized as unfair).

4. Health Care Access and Quality; Underserved Areas and Populations

For all the reasons set forth above, promulgation of the proposed safe harbor should (i) increase access to health care services, (ii) increase the quality of health care services, and (iii) increase the ability of health care facilities to provide services in medically underserved areas or to medically underserved populations. Again, the objective of the proposed safe harbor is to remove a significant economic barrier to achieving representative clinical trials, which, as the Trump Administration has emphasized, are "the gold standard of clinical research and provide critical evidence for new treatments." Indeed, with respect to cancer patients living in rural areas, where cancer rates are higher, studies have shown that while such patients traditionally have had poorer treatment outcomes when compared to their urban counterparts, this disparity is erased when rural patients are enrolled in clinical trials.[xxxiii]

5. Provider Influence

Finally, as to "the existence (or nonexistence) of any potential financial benefit to health care professionals or providers that may influence their decision whether to" (i) "order a health care item or service" or (ii) "arrange for a referral of health care items or services to a particular practitioner or provider," the proposed safe harbor would not protect any financial benefit that is provided to any health care provider, supplier, or practitioner. Again, the safe harbor would only protect a narrow category of remuneration ("indirect cost payments" and "indirect cost stipends") provided to a narrow category of individuals ("human subjects") under a narrow set of circumstances ("approved clinical trials").

III. Conclusion

As the OIG notes in the Annual Solicitation, the agency "seeks to identify and develop safe harbors that protect beneficial and innocuous arrangements and safeguard Federal health care programs and their beneficiaries from the harms caused by fraud and abuse." We believe that the narrowly tailored safe harbor it proposes squarely meets this test:

- for all the reasons set forth in Section II, by effectively eliminating a significant economic barrier to the participation of patients in clinical trials, the safe harbor will help achieve a priority of the Trump Administration—"empower[ing] patients to participate in clinical trials, promot[ing] greater insights regarding how treatments/interventions work across the entirety of the U.S. population, and ensur[ing] clinical research dollars are used efficiently"; and

- for all the reasons set forth in Section III, this objective can be achieved without causing overutilization, a concomitant increase in program costs, improper patient steering, unfair competition, or any of the other types of fraud or abuse that the AKS is intended to prevent.

The undersigned organizations would like to thank the OIG again for this opportunity to propose a new AKS safe harbor. Please feel free to contact Mark.Fleury@cancer.org, policy

principal, ACS CAN, if we can answer any questions the agency might have or provide any additional information the agency might need relating to our proposed safe harbor.

Sincerely,

American Cancer Society Cancer Action Network (ACS CAN)
American Association for Cancer Research (AACR)
American Lung Association
American Society for Radiation Oncology (ASTRO)
Association of American Cancer Institutes (AACI)
Association for Clinical Oncology (ASCO)
Blood Cancer United
Color of Gastrointestinal Illnesses (COGI)
Digestive Disease National Coalition (DDNC)
Fight CRC
Foundation for Sarcoidosis Research
Friends of Cancer Research (FOCR)
Global Liver Institute
International Myeloma Foundation
LUNGevity Foundation
Melanoma Research Foundation
National Brain Tumor Society (NBTS)
National Cancer Registrars Association (NCRA)
National Comprehensive Cancer Network (NCCN)
The National Pancreas Foundation
Oncology Nursing Society (ONS)
Ovarian Cancer Research Alliance (OCRA)
Pennsylvania Prostate Cancer Coalition (PPCC)
Susan G. Komen
Triage Cancer

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[i] U.S. Dep't of Health & Human Servs., Office of the Assistant Secretary for Planning & Evaluation (ASPE), *Empowering Patients to Participate in Clinical Trials* at 1 (July 2025), https://aspe.hhs.gov/sites/default/files/documents/32f96e701a972323b4a21f99d36730ab/Empowering-Patients-%20through-Clinical-Trials-%203.13.25_clean.pdf (hereinafter July 2025 Issue Brief).

[ii] *See*, e.g., Sharon P. Shriver et al., *Assessing populations with access to National Cancer Institute–funded sites using local distance-based service areas*, 9 Clin. Transl. Sci. 1-9, (2025), https://pmc.ncbi.nlm.nih.gov/articles/PMC12529631/pdf/S2059866125101489a.pdf (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); Nicole L. Stout et al., *Improving Rural Clinical Trial Enrollment: Recommendations from the Rural Health Working Group of the Alliance Clinical Trials Network*, 42 J. Clin. Oncol. 1722–1725, (2024), https://pmc.ncbi.nlm.nih.gov/articles/PMC11095896/pdf/jco-42-1722.pdf (identifying persistent enrollment challenges tied to long travel times, site location, staffing, and operational constraints in rural U.S. settings for

cancer care and proposing remedies to improve accrual via improved community outreach); Rebecca J. Williams et al., *Terminated Trials in the ClinicalTrials.gov Results Database: Evaluation of Availability of Primary Outcome Data and Reasons for Termination*, 10 PLoS ONE, (2015), https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0127242&type=printable (finding "insufficient rate of accrual" a leading reason for termination of registered trials with posted results); Benjamin Carlisle et al., *Unsuccessful Trial Accrual and Human Subjects Protections: An Empirical Analysis of Recently Closed Trials*, 12 Clin. Trials 77–83, (2015), https://pmc.ncbi.nlm.nih.gov/articles/PMC4516407/pdf/nihms4853.pdf (documenting unsuccessful accrual as a recurrent cause of premature closure and identifying features associated with slow enrollment); and Carrie Lee et al., *Clinical Trial Metrics: The Complexity of Conducting Clinical Trials in North American Cancer Centers*, 17 JCO Oncol. Pract. 77–93, (2021), https://pmc.ncbi.nlm.nih.gov/articles/PMC8202063/pdf/op-17-e77.pdf (describing accrual and operational complexities at North American cancer centers that impede on-time target enrollment).

[iii] July 2025 Issue Brief, supra note i, at 1 (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).

[iv] July 2025 Issue Brief, supra note i, at 1. *See also* Courtney P. Williams et al., *Understanding the Financial Cost of Cancer Clinical Trial Participation*, 13 Cancer Med. 7185, (2024), https://pmc.ncbi.nlm.nih.gov/articles/PMC11022148/pdf/CAM4-13-e7185.pdf (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); Courtney P. Williams et al., *Clinical trial-related financial considerations from Barriers to Breast Cancer Clinical Trial Participation: A Qualitative Study in the Deep South-patients with breast cancer who previously declined trial participation*, 33 Supportive Care Cancer 771, (2025), https://pmc.ncbi.nlm.nih.gov/articles/PMC12334509/pdf/520_2025_Article_9823.pdf (patients who declined trials cited direct and indirect expenses, such as travel, lodging, parking, food, and missed work, confusion about insurance coverage and recurrent cost sharing also noted, lack of trust in clinical trials, and financial compensation for trial preparation); U.S. Dep't of Health & Human Servs., ASPE, *Use of Participant Compensation in U.S. Clinical Research Studies* (July 2025), https://aspe.hhs.gov/sites/default/files/documents/2a53eba5b12d49257e5062fef1d60fd9/Compensation%20Issue%20Brief%20Final.pdf (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); Ryan D. Nipp RD et al., Powell E, Chabner B, Moy B, *Recognizing the Financial Burden of Cancer Patients in Clinical Trials*, 20 Oncologist 572–575 (2015), https://pmc.ncbi.nlm.nih.gov/articles/PMC4571792/pdf/theoncologist_1568.pdf (reporting substantial "indirect" burdens including travel and lodging—often hundreds of dollars per month—and urging noncoercive financial assistance to mitigate access barriers); 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 1242–1249, (2018), https://pmc.ncbi.nlm.nih.gov/articles/PMC6263122/pdf/onco12465.pdf (documenting significant travel distances and burdens—greatest for some NIH-sponsored and phase I studies—underscoring indirect cost barriers to enrollment); and 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. 9 Med. 1200–1206 (2023), https://pmc.ncbi.nlm.nih.gov/articles/PMC9713084/pdf/11606_2022_Article_7801.pdf (showing that travel, parking, lodging, and caregiving costs substantially influence willingness to participate and that reimbursement can mitigate burden).

[v] July 2025 Issue Brief, supra note i, at 1.

[vi] U.S. Food & Drug Administration, Center for Drug Evaluation and Research (CDER), and the Center for Biologics Evaluation and Research (CBER), *Enhancing Participation in Clinical Trials — Eligibility Criteria, Enrollment Practices, and Trial Designs: Guidance for Industry* (Dec. 2025), https://www.fda.gov/media/190162/download.

[vii] *Id.* at 5.

[viii] *Id.* at 9.

[ix] Centers for Medicare & Medicaid Services, Medicare National Coverage Decisions Manual, Ch. 1, Part 4, §310.1.

[x] *See*, Williams, *Understanding the Financial Cost of Cancer Clinical Trial Participation*, supra note iv. *See also*, Nipp, supra note iv, (reporting average indirect, nonmedical costs of roughly $600 per month for trial participants); Ryan W. Huey et al., *Patient-Reported Out-of-Pocket Costs and Financial Toxicity During Early-Phase Oncology Clinical Trials*, 26 Oncologist 588–596 (2021) (finding that 48% of patients in early-phase oncology trials incurred ≥$1,000 per month out-of-pocket); Ryan D. Nipp et al., *Financial Burden of Cancer Clinical Trial Participation and the Impact of a Cancer Care Equity Program*, 21 Oncologist 467–474 (2016) https://pmc.ncbi.nlm.nih.gov/articles/PMC4828126/pdf/theoncologist_15481.pdf (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); July 2025 Issue Brief, supra note i, at 1 (noting survey evidence that cancer trial participants commonly need about $200–$1,000 per month to offset trial-related expenses); and Williams et al., *Clinical trial-related Financial considerations from Deep-South-patients with Barriers to Breast Cancer who previously declined Clinical Trial Participation*, supra note iv (patients suggested compensation in the range of $50–$700 per month to cover travel, parking, lodging, food, and missed work).

[xi] *See*, Williams, *Understanding the Financial Cost of Cancer Clinical Trial Participation*, supra note iv; *See also*, Williams, *Clinical trial-related Financial considerations from Deep-South-patients with Breast Cancer who previously declined Trial Participation*, supra note iv (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, supra note iv (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); July 2025 Issue Brief, supra note i (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); *Use of Participant Compensation in U.S. Clinical Research*, supra note iv (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, *Recognizing the Financial Burden of Cancer Patients in Clinical Trials*, supra note iv (documents substantial indirect costs for trial participants—often hundreds of dollars per month—driven by travel and lodging).

[xii] Shriver, supra note ii.

[xiii] Josepha M. Unger et al., *National Estimates of the Participation of Patients With Cancer in Clinical Research Studies Based on Commission on Cancer Accreditation Data*, 42 J Clin Oncol. 2139-2148, (2024), https://pmc.ncbi.nlm.nih.gov/articles/PMC11191051/pdf/jco-42-2139.pd.

[xiv] *See*, Williams, *Understanding the Financial Cost of Cancer Clinical Trial Participation*, supra note iv; Shriver, supra note ii (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); July 2025 Issue Brief, supra note i (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, supra note ii (describing persistent rural

enrollment barriers tied to long travel distances to trial sites and limited local research infrastructure); Borno, supra note iv (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); Hassal Lee et al., *Analysis and Optimization of Equitable U.S. Cancer Clinical Trial Center Access by Travel Time*, 10 JAMA Oncol. 652–657 (2024), https://jamanetwork.com/journals/jamaoncology/fullarticle/2816796 (demonstrating significant travel-time inequities to trial centers and identifying optimization strategies to reduce excessive travel for underserved and rural populations); M. Kelsey Kirkwood et al., *State of Geographic Access to Cancer Treatment Trials in the United States: Are Studies Located Where Patients Live?*, 21 JCO Oncol. Pract. 427–437 (2025), https://pmc.ncbi.nlm.nih.gov/articles/PMC11925346/pdf/op-21-427.pdf (finding that nonmetropolitan counties are far less likely to host cancer clinical trials, forcing rural patients to travel farther for participation); Deborah Watkins et al., *Cartographic Mapping and Travel Burden to Assess and Develop Strategies to Improve Minority Access to National Cancer Clinical Trials*, 93 Int. J. Radiat. Oncol. Biol. Phys. 702–709 (2015), https://pmc.ncbi.nlm.nih.gov/articles/PMC4605855/pdf/nihms707213.pdf (using mapping to quantify travel burden to national trial sites and proposing strategies to mitigate long-distance barriers); Coleen F. Longacre, et al., *Evaluating Travel Distance to Radiation Facilities Among Rural and Urban Breast Cancer Patients in the Medicare Population*, 36 J. Rural Health 334–346 (2020), https://onlinelibrary.wiley.com/doi/epdf/10.1111/jrh.12413 (showing rural patients face substantially longer travel distances for cancer care, a barrier that similarly affects access to trial participation).

[xv] Williams, *Understanding the Financial Cost of Cancer Clinical Trial Participation*, supra note iv.

[xvi] *Id*.

[xvii] Farhad Islami et al., *American Cancer Society's report on the status of cancer disparities in the United States, 2023*. 74 CA Cancer J Clin. 136-166 (2024), https://acsjournals.onlinelibrary.wiley.com/doi/epdf/10.3322/caac.21812.

[xviii] Devon V. Adams et al., *Association of Remote Technology Use and Other Decentralization Tools With Patient Likelihood to Enroll in Cancer Clinical Trials*, 5 JAMA Network Open (2022) https://acsjournals.onlinelibrary.wiley.com/doi/epdf/10.3322/caac.21812.

[xix] Williams, *Clinical trial-related financial considerations from Barriers to Breast Cancer Clinical Trial Participation: A Qualitative Study in the Deep South-patients with breast cancer who previously declined trial* participation, supra note iv.

[xx] *See*, e.g., OIG Advisory Opinion No. 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 No. 00-05 (Jun. 30, 2000), at 5; OIG Advisory Opinion No. 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 No. 08-11 (Sep. 17, 2008), at 8 (permitting the remuneration at issue will "ensure that economically disadvantaged patients are not precluded from the study"); and OIG Advisory Opinion No. 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").

[xxi] U.S. Dep't of Health & Human Services, ASPE, *Financial Stress Associated with Oncology Clinical Trial Participation* (Jan. 2026), https://aspe.hhs.gov/reports/financial-stress-clinical-trial

[xxii] Roberto Abadie et al., *Pursuing Fair and Just Compensation for Research Participants: An Open Letter to the Research Ethics Community*, 25 Am. J. Bioethics (2025), at 1, https://www.tandfonline.com/doi/full/10.1080/15265161.2025.2506328.

[xxiii] *Id*.

[xxiv] Food & Drug Admin., *Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators* (Jan. 2018), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/payment-and-reimbursement-research-subjects.

[xxv] *Id*. *See also*, Scott D Halpern et al., *Effectiveness and Ethics of Incentives for Research Participation: 2 Randomized Clinical Trials*, 181 JAMA Internal Med. 1479 (2021), https://pmc.ncbi.nlm.nih.gov/articles/PMC8453363/ (Indeed research suggests that even the provision of cash incentives to participate in clinical trials does not result in undue or unjust inducements).

[xxvi] 42 U.S.C. § 300gg-8(d) (Public Health Service Act (PHSA) § 2709(d)), provides:

> *"(d) Approved clinical trial defined*
>
> *(1) In general*
>
> *In this section, the term "approved clinical trial" means a phase I, phase II, phase III, or phase IV clinical trial that is conducted in relation to the prevention, detection, or treatment of cancer or other life-threatening disease or condition and is described in any of the following subparagraphs:*
>
> *(A) Federally funded trials. The study or investigation is approved or funded (which may include funding through in-kind contributions) by one or more of the following:*
>
> *(i) The National Institutes of Health.*
>
> *(ii) The Centers for Disease Control and Prevention.*
>
> *(iii) The Agency for Health Care Research and Quality.*
>
> *(iv) The Centers for Medicare & Medicaid Services.*
>
> *(v) cooperative group or center of any of the entities described in clauses (i) through (iv) or the Department of Defense or the Department of Veterans Affairs.*
>
> *(vi) A qualified non-governmental research entity identified in the guidelines issued by the National Institutes of Health for center support grants.*
>
> *(vii) Any of the following if the conditions described in paragraph (2) are met:*
>
> *(I) The Department of Veterans Affairs.*
>
> *(II) The Department of Defense.*
>
> *(III) The Department of Energy.*
>
> *(B) The study or investigation is conducted under an investigational new drug application reviewed by the Food and Drug Administration.*
>
> *(C) The study or investigation is a drug trial that is exempt from having such an investigational new drug application."*
>
> *(2) Conditions for departments*
>
> *The conditions described in this paragraph, for a study or investigation conducted by a Department, are that the study or investigation has been reviewed and approved through a system of peer review that the Secretary determines-*

(A) to be comparable to the system of peer review of studies and investigations used by the National Institutes of Health, and

(B) assures unbiased review of the highest scientific standards by qualified individuals who have no interest in the outcome of the review.

[xxvii] 21 C.F.R. § 56.102(e) (2024) provides: "*Human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient."

[xxviii] 21 C.F.R. § 56.102(g) (2024) provides: "*Institutional Review Board (IRB)* means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase institutional review committee as used in section 520(g) of the act."

[xxix] Section 2709(e) (2024) of the PHSA defines a "life threatening condition" as "any disease or condition from which the likelihood of death is probable unless the course of the disease or condition is interrupted."

[xxx] 21 C.F.R. § 56.102(j) (2024) provides: "*Sponsor* means a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators."

[xxxi] 21 C.F.R. § 56.111(b) (2024) provides: "When some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study to protect the rights and welfare of these subjects."

[xxxii] *See*, OIG Advisory Opinion No. 98-6, at 8 (May 1, 1998), at 8; OIG Advisory Opinion No. 00-05, at 4 (Jun. 30, 2000) (the purpose of the remuneration at issue "is to induce participation in a HCFA-sponsored scientific study, not to induce utilization of Medicare covered services."), and OIG Advisory Opinion No. 23-11 at 7 (Dec. 21, 2023) ("the Proposed Arrangement would pose a low risk of overutilization or inappropriate utilization of items and services payable by a Federal health care program. Because the cost-sharing subsidies are specifically designed to facilitate enrollment of individuals in the Study and help prevent attrition during the course of the Study, it is possible that overall utilization of items and services may increase, but there is nothing to suggest that such an increase would be inappropriate").

[xxxiii] *See*, Islami, supra note xv; Unger, supra note xi.