

Expanding Equity and Innovation in Pharmaceutical Law and Drug Development: Paying Clinical Trial Participants for their Data

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Abstract:

Bringing a drug to market is exceedingly expensive and exposes pharmaceutical manufacturers to significant legal risk. But when companies are successful, their profits make the PowerBall jackpot look like petty cash. Staggering rewards measure in the billions or millions for the firms, CEOs, pharmacies, drug benefit managers, data brokers, and many more actors in the pharmaceutical-to-patient pipeline. The only individuals who don't get paid handsomely are the clinical trial participants, whose voluntary participation and data helped make those successes possible. It is long past time that we reform the legal and regulatory roadblocks to paying clinical trial participants in the United States for the fair value of their data—for it is precisely their information (and personal sacrifice) that makes so many others in our country wealthy beyond imagination.

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INTRODUCTION

On average, pharmaceutical manufacturers can spend nearly \$900 million on research and development for a new drug.¹ Beyond the staggering cost, it typically takes over nine years to bring the product to market.² And success in bringing a drug to market is rare: only 8.5% of drugs are successfully developed, approved, and sold, providing drug companies an income stream to recoup the enormous up-front costs of development.³

Clinical trials play a critical role in this process. The failure to recruit and retain an appropriate number of clinical trial participants increases costs and delays drug development timelines. Pharmaceutical companies spend a significant portion of their drug development resources on clinical trial participant recruitment, losing a significant amount with each delay. This Article proposes a unique solution to the problem: paying participants directly for their data. Unfortunately, substantial legal and regulatory hurdles line the path to creating this new reality.

Part I of this Article outlines the challenge of participant recruitment and retention in clinical trials and describes how current legal constraints and faulty payment standards do not promise reprieve. The most important legal constraint is the requirement that payment to participants cannot present an “undue influence.” While it is ethically important to refrain from unduly influencing participants, payment is currently severely limited—well beyond what is necessary to avoid undue influence. Financial compensation standards in clinical trials, including reimbursement for out-of-pocket costs, compensation for lost economic opportunities, appreciation payments, and incentive payments, can significantly enhance participant recruitment and retention without unduly influencing participants. Legalizing direct payment for patients’ data would be a game-changing solution.

Part II discusses how clinical trials are increasingly using participant data to address challenges in recruitment and retention, enhance data collection, and

1. See Aylin Sertkaya et al., *Costs of Drug Development and Research and Development Intensity in the U.S., 2000-2018, Table 2*, 7 JAMA NETWORK OPEN e2415445 (2024), <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2820562> [https://perma.cc/QTZ8-WBVZ].

2. Dean Brown et al., *Clinical Development Times for Innovative Drugs*, 21 NATURE REVIEWS: DRUG DISCOVERY 793 (2022). This paper focuses on drug development, but our recommendations also apply to medical device development. In comparison to drug development, the average cost to develop and bring a new medical device to market is over \$500 million. Aylin Sertkaya et al., *Estimated Cost of Developing a Therapeutic Complex Medical Device in the US*, 5 JAMA NETWORK OPEN e2231609 (2022).

3. See Sertkaya, *supra* note 1, Table 2.

cater to the growing market for clinical data. Clinical trials are more data-intensive than ever, using decentralized methods, passive data collection, metadata applications, integration with real-world data (RWD), and artificial intelligence (AI) and machine learning (ML) solutions. The new methods for gathering clinical data and the emerging markets for using it demonstrate the need to pay clinical trial participants for the value of their data. Current payment methods fail to do so, stymie needed efforts to recruit representative patient populations and undermine fairness and equity in the payments that participants receive.

Part III describes the role of using fair market value (FMV) to value data in clinical trials. FMV is necessary in clinical trial negotiations to avoid legal liability and to ensure fair compensation for research sites. Specifically, FMV operates as a defense against legal issues under laws like the Stark Law and the federal Anti-Kickback Statute.⁴ While various methods, including Medicare pricing and benchmark pricing, can estimate FMV, the best approximation often comes from negotiations between healthcare institutions and insurers. Due to the widespread use of FMV in clinical trial payments, FMV should be used to determine clinical trial participant compensation as well.

Part IV outlines methods and considerations for developing an FMV calculator that would pay clinical trial participants the true value of their data. Various clinical data valuation methods are considered: the market approach uses comparable data in the marketplace; the cost approach determines the cost of data recreation; and the income approach utilizes future income resulting from the use of patient data to assess its value. However, additional considerations are necessary, including that trial data are more valuable than mere clinical data due to their specialized nature, the intensity of data collection methods, and the presence of data management and sharing (DMS) plans. Moreover, fundamental fairness and respect for patient autonomy dictate that participants' valuation of their own data should play a vital role in this compensation process.

Finally, Part V advocates for the legislative and regulatory reform required to implement an FMV calculator necessary to pay clinical trial participants for the value of their data. We argue that doing so would allow clinical trial sponsors to see greater efficiencies in their drug development timelines and data management. We further advocate for federal regulatory agencies to issue official guidance and develop reliable standards so that institutional review boards (IRBs) will approve this innovative payment method.

In sum, this Article advocates for a future where drug development will be not only more efficient but also more fair, equitable, and inclusive for all

4. Stark Law, 42 U.S.C. § 1395nn; Anti-Kickback Statute, 42 U.S.C. § 1320a-7b(b).

participants involved, not just those occupying the C-suite. It is long past time that we reform the legislative and regulatory hurdles that stand in the way of achieving this vision.

I. CURRENT LEGAL CONSIDERATIONS AND PAYMENT STANDARDS FAIL TO IMPROVE RECRUITMENT AND RETENTION OF CLINICAL TRIAL PARTICIPANTS

A. Failure to Recruit and Retain Participants in Clinical Trials

Most law and public policy decisionmakers are aware of the high cost and lengthy timelines for drug development and the rarity of success in the United States. A recent study showed that, on average, pharmaceutical companies spend nearly \$900 million on research and development for a new drug.⁵ Further, only 8.5% of drugs will successfully be developed, approved, and sold.⁶ On average, it takes over nine years to develop an innovative drug,⁷ and clinical trial participant recruitment and retention is a major challenge. About 11% of clinical research sites fail to enroll a single patient, and 37% of sites under-enroll participants.⁸ Clinical trial participant recruitment and retention is critical to the drug development process, and delays or failures to recruit and retain participants are costly to pharmaceutical companies. For every day of delay, drug companies lose about \$500,000 in future revenues.⁹

There are many barriers to recruitment and retention, including a high commitment burden on participants and underpayment for study burden and risks. Barriers to recruitment and retention include poor communication with participants, elements of the trial protocol—including visit frequency, time commitment, study length, and transportation—that are burdensome to participants, restrictive inclusion criteria, and financial barriers.¹⁰ In response,

5. See Sertkaya, *supra* note 1, Table 2.

6. *Id.*

7. Brown et al., *supra* note 2, at 794.

8. See KIMBERLY RAY & BERNADETTE TOSTI, TRANSFORMING PATIENT RECRUITMENT THROUGH PATIENT AND SITE ENGAGEMENT (2017), <https://www.iqvia.com/-/media/iqvia/pdfs/library/infographics/transforming-patient-recruitment-through-patient-and-site-engagement.pdf> [<https://perma.cc/6AY7-YQ5Z>].

9. See Zachary Smith et al., *New Estimates on the Cost of a Delay Day in Drug Development*, THERAPEUTIC INNOVATION & REGULATORY SCI. (2024), <https://link.springer.com/article/10.1007/s43441-024-00667-w> [<https://perma.cc/S9RK-XNAX>].

10. See Bernadette Boden Albala, *Examining Barriers and Practices to Recruitment and Retention in Stroke Clinical Trials*, 48 STROKE 2232 (2015); Joshua Grill & Jason Karlawish, *Addressing the Challenges to Successful Recruitment and Retention in Alzheimer's Disease Clinical Trials*, ALZHEIMER'S RSCH. & THERAPY 2, 34 (2010), <https://doi.org/10.1186/alzrt58> [<https://perma.cc/FFM9-W8BF>]; Amany Keruakous et al., *Research Staff Perspectives on Cancer Clinical Trials and Barriers to Recruitment: A Qualitative Research*, 13 CUREUS e17202. (2021);

many interventions to address subject recruitment and retention focus on statistical methodology to account for missing participants, improvements in patient tracking, and enhanced communication.¹¹ However, new approaches to paying participants adequately to compensate for the burdens of clinical trial participation are sorely lacking. Resources are spent on recruiting participants, but those resources aren't going to participants.

Monetary payments impact patient recruitment and retention in clinical trials. Numerous studies list payment as an “important factor” in recruiting and retaining participants.¹² For example, Courtney Williams found that “over half (55%) of respondents reported at least one cost-related consideration as ‘very influential’ to trial participation, including . . . payment for participation, or support for participation.”¹³ In addition, in a meta-analysis of randomized controlled trials, Basel Abdelazeem found that payment increased participant consent and response rates.¹⁴ In fact, a review of clinical trials involving healthy volunteers cited financial reward as the *primary* motivation for participation.¹⁵ Even the few studies concluding that payment was not an overwhelming or decisive factor found that payment was still somewhat influential.¹⁶

Jessica Langbaum et al., *Recommendations to Address Key Recruitment Challenges of Alzheimer’s Disease Clinical Trials*, 19 ALZHEIMER’S & DEMENTIA 696 (2023), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9911558/> [<https://perma.cc/4HCW-8K92>].

11. See Lawrence Fisher et al., *AASAP: A Program to Increase Recruitment and Retention in Clinical Trials*, 86 PATIENT EDUC. & COUNSELING 372 (2012), <https://www.sciencedirect.com/science/article/pii/S0738399111003697> [<https://perma.cc/4L97-GL5E>].

12. See Carmen Breikopf et al., *Perceptions of Reimbursement for Clinical Trial Participation*, 6 J. EMPIRICAL RSCH. ON HUMAN RSCH. ETHICS 31 (2011); Leanne Stunkel & Christine Grady, *More Than the Money: A Review of the Literature Examining Healthy Volunteer Motivations*, 32 CONTEMP. CLINICAL TRIALS 342 (2011), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4943215> [<https://perma.cc/F2GX-PSXQ>].

13. Courtney Williams et al., *Influence of Cost-Related Considerations on Clinical Trial Participation: Results from the 2020 Health Information National Trends Survey (HINTS)*, 38 J. GENERAL INTERNAL MEDICINE 1200 (2023), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9713084> [<https://perma.cc/75AD-SQWV>].

14. Basel Abdelazeem et al., *The Effectiveness of Incentives for Research Participation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials*, 17 PLOS ONE e0267534 (2022), <https://doi.org/10.1371/journal.pone.0267534> [<https://perma.cc/WF6U-5A97>].

15. Stunkel & Grady, *supra* note 12.

16. Catherine Houghton et al., *Factors that Impact on Recruitment to Randomized Trials in Health Care: A Qualitative Evidence Synthesis*, 10 COCHRANE DATABASE OF SYSTEMATIC REVIEWS MR000045 (2020), <https://pubmed.ncbi.nlm.nih.gov/33026107> [<https://perma.cc/3KMU-DJWZ>]. Payment “was not seen as a very important factor that influences their decision.”); Ajay D. Wasan, *Reasons for Participation in Pain Research: Can They Indicate a Lack of Informed Consent*, 10 PAIN MEDICINE 111 (2009), <https://academic.oup.com/painmedicine/article/10/1/111/1833905> [<https://perma.cc/XPT9-57P5>] (only 19% of participants said payment was an important factor in their participation); Hala T. Borno, *Accelerating Cancer Clinical Trial Recruitment Through a*

B. Clinical Trial Sponsors May Pay Participants

Financial considerations and reimbursement already pervade clinical trials. While the participant's insurer typically pays for patient care costs, including doctor visits, hospital stays, standard treatments, treatments to improve symptoms or side effects, lab tests, and imaging, industry-sponsored clinical trial costs may be paid for by a research sponsor.¹⁷ A research sponsor—typically a pharmaceutical, medical device, or diagnostic company—negotiates with the research site to determine the cost of administering the clinical trial.

Drugs in development typically go through at least three phases of clinical trials, each with different risks and benefits to study participants. Phase I clinical trials are the first time that a drug is tested in humans.¹⁸ A small group of participants is used primarily to determine whether there are adverse effects associated with the drug.¹⁹ Next, Phase II clinical trials test a drug in a larger group of participants to determine whether the drug alleviates the health condition under study.²⁰ Finally, Phase III clinical trials test a drug in an even larger group of participants to test the drug's efficacy compared to that of a commonly used alternative drug.²¹

Participants are usually paid for their clinical trial participation. The compensation depends on the amount of time the participant devotes to clinical trial activities and the inconvenience of clinical trial procedures, which can be greater in earlier trial phases.²² For example, ICON, a noted clinical research organization (CRO), offered \$6,050 for healthy volunteers to participate in a clinical trial including one screening visit, one stay of four nights, and six

Financial Reimbursement Program Integrated with Patient Navigation: An Interrupted Time Series Analysis, 30 J. CANCER POL'Y 100305 (2021), <https://doi.org/10.1016/j.jcpo.2021.100305> [<https://perma.cc/M2GS-KQ3M>].

17. *Who Pays for Clinical Trials?*, NAT'L CANCER INST. (June 17, 2024), <https://www.cancer.gov/research/participate/clinical-trials/paying> [<https://perma.cc/NSQ7-KRDS>]; Andrew Snyder, *Fair Market Value Conundrum: Solutions for Sponsors and Sites*, APPLIED CLINICAL TRIALS (Apr. 10, 2014), <https://www.appliedclinicaltrials.com/view/fair-market-value-conundrum-solutions-sponsors-and-sites> [<https://perma.cc/GQ5Y-2TKC>].

18. *See FAQs About Clinical Studies*, NAT'L INST. HEALTH (Feb. 13, 2024), <https://clinicalcenter.nih.gov/participate/faqaboutcs.html> [<https://perma.cc/5HZ8-JD6J>].

19. *Id.*

20. *Id.*

21. *Id.*; *see also Step 3: Clinical Research*, U.S. FOOD & DRUG ADMIN. (Jan. 1, 2018), <https://www.fda.gov/patients/drug-development-process/step-3-clinical-research> [<https://perma.cc/BUN2-5GPM>].

22. *FAQs About Clinical Studies*, *supra* note 18.

outpatient visits.²³ In comparison, the CRO Fortrea paid \$13,006 to participants to test a drug treatment of atopic dermatitis involving one stay of fourteen nights and eleven follow-up visits.²⁴ Potential study participants can browse trials sorted by the amount of compensation on websites such as studyscavenger.com, which lists healthy volunteer study opportunities from multiple trial centers. Entities like ICON also promote their studies and associated compensation on social media. However, even if they are paid, clinical trial participants do not typically receive significant sums of money.²⁵ One study reported by Jill Fisher followed 131 participants of Phase I clinical trials over three years and determined that participants received an average of \$4,000 per year.²⁶ But \$4,000 is hardly enough to pay for one month of life's expenses and is woefully inadequate to encourage enrollment by poor or unhealthy patients who might benefit the most from participation.

C. Legal Considerations for Participant Payment

Paying participants for their involvement in a clinical trial is subject to federal statutes and regulations. Any type of payment implicates informed consent law, tax considerations, the Anti-Kickback Statute (AKS), and the Beneficiary Inducements Civil Monetary Penalty (CMP). According to informed consent principles, payments must be made without coercion and undue influence, must be just and fair, should be pro-rated, and must be approved by an IRB.²⁷ Higher payment increases the risk not only of undue influence but also of participant tax liability,²⁸ as money paid to participants can count as "earnings", and sponsors must report payments over \$600 to a single participant to the Internal Revenue Service (IRS). Both sponsors and participants must also be wary of making what might be considered an "illegal payment" under the federal

23. Healthy Volunteers, ICON, <https://web.archive.org/web/20240912154637/https://iconstudies.com/Lenexa/Clinical-Research-Study/482>.

24. *1 Stay of 14 Nights and 11 Follow-Up Visits: Study Number 8524-870*, FROTERA, <https://www.fortreaclinicaltrials.com/en-us/clinical-research/8524-870-1-stay-14-nights-11-follow-visits-1> [<https://perma.cc/B357-MS8L>].

25. See Jill Fisher et al., *Phase I Trial Compensation: How Much do Healthy Volunteers Actually Earn from Clinical Trial Enrollment?* 18 *CLINICAL TRIALS* 477-88 (2021), <https://pubmed.ncbi.nlm.nih.gov/33938244> [<https://perma.cc/3KJL-LM93>].

26. *Id.*

27. *FDA Information Sheet: Payment and Reimbursement to Research Subjects*, U.S. FOOD & DRUG ADMIN. (Jan. 25, 2018), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/payment-and-reimbursement-research-subjects> [<https://perma.cc/9ZFS-NPL8>].

28. *About Form 1099-MISC, Miscellaneous Information*, INTERNAL REVENUE SERV. (Feb. 19, 2025), <https://www.irs.gov/forms-pubs/about-form-1099-misc> [<https://perma.cc/YZ4D-CUR5>].

AKS and CMP.²⁹ Physicians who pay or accept kickbacks can face penalties of up to \$50,000 per kickback, plus three times the amount of the remuneration received.³⁰

1. Informed Consent and Undue Influence

Payment practices and recommendations for clinical trials fall against the backdrop of informed consent law. Informed consent has been part of health care law since the early 1900s, when Judge Benjamin Cardozo stated in the seminal case *Schloendorff v. NY Hospital* that “[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient’s consent, commits an assault, for which he is liable in damages.”³¹ Under contemporary informed consent regulations, “[a]n investigator shall seek informed consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.”³² Of course, coercion or undue influence threaten a patient’s bodily autonomy and their ability to provide informed consent.

Federal regulations on payment to clinical trials participants reflect these bedrock principles of informed consent law. The Food and Drug Administration (FDA) states that payment for participation in clinical trials should be “just and fair,” not “coercive or present undue influence,” pro-rated, and approved by an IRB.³³ Payment is pro-rated when “credit . . . accrues as the study progresses” and is not “contingent upon the subject completing the entire study.”³⁴ Pro-rating payments reduces the likelihood of undue influence because payment delayed until study completion “could unduly influence a subject’s decision to exercise his or her right to withdraw at any time.”³⁵ This echoes one of the required

29. See 42 U.S.C. § 1320a-7b(b) (criminal penalties for acts involving Federal Healthcare Programs); 42 U.S.C. § 1320a-7a(a) (civil monetary penalties); Emily Largent et al., *Paying Clinical Trial Participants: Legal Risks and Mitigation Strategies*, 38 J. CLINICAL ONCOLOGY 533 (2019).

30. See *Fraud & Abuse Laws*, U.S. DEP’T OF HEALTH & HUM. SERV., OFF. OF INSPECTOR GEN., <https://oig.hhs.gov/compliance/physician-education/fraud-abuse-laws> [https://perma.cc/BG23-EQZF].

31. *Schloendorff v. New York Hospital*, 211 N.Y. 125 (N.Y. 1914).

32. 45 C.F.R. § 46.116(a)(2); 21 C.F.R. § 50.20.

33. See *Payment and Reimbursement to Research Subjects*, *supra* note 27.

34. *Id.*

35. *Informed Consent FAQs*, OHRP, U.S. DEP’T OF HEALTH & HUM. SERV., OFF. FOR HUM. RSCH. PROT., <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html> [https://perma.cc/2LVK-F4CY].

elements of informed consent, which is that clinical trial investigators include a statement saying that the “subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.”³⁶

To increase the likelihood that clinical trials will conform to FDA regulations, an IRB must approve clinical trials on a case-by-case basis.³⁷ IRBs have discretion to determine whether the proposed payment for participation in a clinical trial is coercive, presents undue influence, and is “just and fair.”³⁸ Further, clinical trial sponsors are required to assure the FDA that they will conform to the IRB’s protocol.³⁹

IRBs take their charge seriously and actively review participant payments for coercion or undue influence.⁴⁰ Coercion is relatively rare and “refer[s] to situations that involve a threat to harm someone or violate a person’s rights.”⁴¹ However, “undue influence” is a lower bar to meet and occurs when “an offer of something desirable influences decision making in *inappropriate* ways.”⁴² The U.S. Department of Health and Human Services Office for Human Research Protections (OHRP) offers a similar definition. According to the OHRP, a payment is unduly influential when it “could compromise a prospective subject’s examination and evaluation of the risks or affect the voluntariness of his or her choices.”⁴³ Therefore, like an employer offering payment to attract talent, “payment may *appropriately* influence the decision to participate in IRB-approved research.”⁴⁴ Ethics scholars recommend that investigators provide a justification for the payment amount, prioritize reimbursement and compensation before incentives, and increase safeguards to prevent undue influence as payment amounts increase.⁴⁵ In addition, IRBs must ensure that the study has safeguards “to protect the rights and welfare” of vulnerable populations, including “children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.”⁴⁶

36. 45 C.F.R. § 46.116(a)(2); 45 C.F.R. § 46.116(b)(8); 21 C.F.R. § 50.20.

37. 45 C.F.R. § 46.109; 21 C.F.R. § 56.103.

38. *Informed Consent FAQs*, *supra* note 35.

39. 21 C.F.R. § 312.23(a)(1)(iv).

40. See Luke Gelinas et al., *A Framework for Ethical Payment to Research Participants*, 378 *NEW ENG. J. MED.* 766–67 (2018).

41. *Id.*

42. *Id.* (emphasis added).

43. *Informed Consent FAQs*, *supra* note 35.

44. Gelinas, *supra* note 40 (emphasis added).

45. *Id.*

46. 45 C.F.R. 46.111(b). For a list of regulations regarding the function of IRBs, see Christine Grady, *Institutional Review Boards*, 148 *Chest* 1148 (2015), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4631034/> [<https://perma.cc/54PP-KF22>].

2. Tax Implications

In addition, tax laws and regulations affect recruitment and retention by restricting the amount that can be paid to participants and by requiring participants to disclose personal information. Study sponsors must report payments to any given participant of over \$600 per year to the IRS.⁴⁷ Reporting to the IRS requires the sponsor to report participant social security numbers and other personal information.⁴⁸ As a result, individuals without social security numbers or people who do not want to report their personal information, including undocumented immigrants, are excluded from receiving more than \$600 per year from a clinical trial.⁴⁹ In addition, payment mechanisms are more burdensome for research participants who are foreign nationals. The IRS requires such individuals to complete Form 1042-S and requires a mandatory 30% income tax withholding up front.⁵⁰

3. Anti-Kickback Statute and Beneficiary Inducements Civil Monetary Penalty

Both the federal AKS and CMP regulate the clinical research market by restricting allowable payments. A clinical trial sponsor would be liable under the AKS and CMP if they induced participants covered under a federally funded health care program to participate in a clinical trial with the goal of securing a publicly insured population who would use their product once approved.⁵¹ Therefore, higher payment to clinical trial participants with government health insurance increases the risk of illegal inducement. Under the AKS and CMP, clinical trial sponsors cannot pay participants with governmental health insurance a “remuneration” to induce them to use their product.⁵² Under the AKS, “‘remuneration’ includes the transfer of anything of value, directly or indirectly, overtly or covertly, in cash or in kind.”⁵³ For the purposes of the CMP,

47. *About Form 1099-MISC*, *supra* note 28; Largent et al., *supra* note 39.

48. Largent et al., *supra* note 39.

49. *The Payment Plan*, UNIV. OF WASH. HUM. SUBJ. DIV., (Mar. 24, 2024), <https://www.washington.edu/research/hsd/guidance/subject-payment/#5c> [<https://perma.cc/US97-AMTV>]; James M. DuBois, *Crossing a Boundary?*, 46 *MONITOR ON PSYCH.* 70 (2015), <https://www.apa.org/monitor/2015/02/ethics> [<https://perma.cc/29A6-B4US>].

50. *Id.*

51. *See* 42 U.S.C. § 1320a-7b(b) (criminal penalties for acts involving Federal health care programs); 42 U.S.C. § 1320a-7a(a) (civil monetary penalties).

52. 42 U.S.C. § 1320a-7b(b) (criminal penalties for acts involving Federal health care programs); 42 U.S.C. § 1320a-7a(a) (civil monetary penalties)

53. *OIG Advisory Opinion No. 23-11 (Favorable)*, U.S. DEP’T OF HEALTH & HUM. SERV. (Dec. 21, 2023), <https://oig.hhs.gov/documents/advisory-opinions/1143/AO-23-11.pdf>

“‘remuneration’ [also] includes the waiver of coinsurance and deductible amounts (or any part thereof), and transfers of items or services for free or for other than fair market value.”⁵⁴

The Department of Health and Human Services Office of the Inspector General (OIG) has discretion over the enforcement of federal AKS and CMP⁵⁵ and may issue advisory opinions in advance of a questionable practice at request.⁵⁶ While OIG opinions are narrowly tailored to the case at hand, “every OIG advisory opinion addressing research [between 1997 and 2019] permitted the requestors’ proposed remuneration arrangements.”⁵⁷ In addition, OIG allows remuneration if it “accommodates the needs—typically recruitment and retention of participants—and advances the scientific validity of a government-sanctioned or government-sponsored study under conditions that limit the risk of overuse of a federal health care program, including that any clinical care billed to such a program is dictated by a well-developed trial protocol.”⁵⁸

For example, in 2023, a clinical trial sponsor requested an OIG opinion approving Medicare payment of up to \$2,000 for clinical services rendered during a randomized controlled trial testing a rechargeable, implantable pulse generator in heart failure patients.⁵⁹ The OIG determined that the proposed arrangement was a “remuneration” under the federal AKS and CMP, but that the OIG would not impose sanctions upon the sponsor because the proposed arrangement reasonably promoted enrollment, posed a low risk of overutilization of services, was approved by the Center for Medicare and Medicaid Services (CMS), and did not show characteristics that the sponsor wanted to lock in future utilization of the service.⁶⁰

Thus, the AKS and CMP should rarely inhibit payment to clinical trial

[<https://perma.cc/SM4M-W72J>]; 42 U.S.C. § 1320a-7b(b) (criminal penalties for acts involving Federal health care programs).

54. 42 U.S.C. § 1320a-7a(i)(6).

55. 42 C.F.R. § 1001.951.

56. See *OIG Enforcement Policy Statement Regarding OIG’s Assessment of Advisory Opinion Requests*, U.S. DEP’T OF HEALTH & HUM. SERV. (Jan. 6, 2022, updated Jan. 13, 2022), https://oig.hhs.gov/documents/advisory-opinions/1016/OIG_Enforcement_Policy_Statement_Regarding_OIGs_Assessment_of_Advisory_Opinion_SLiQXkK.pdf [<https://perma.cc/573L-JDK3>]. Advisory opinions can be found at *Browse Advisory Opinions*, U.S. DEP’T OF HEALTH & HUM. SERV., <https://oig.hhs.gov/compliance/advisory-opinions/browse> (last visited Mar. 20, 2025). More information is available at *Advisory Opinion Process*, U.S. DEP’T OF HEALTH & HUM. SERV., <https://oig.hhs.gov/compliance/advisory-opinions/process> [<https://perma.cc/9NAH-NSLQ>].

57. See Largent et al., *supra* note 29.

58. *Id.*

59. *OIG Enforcement Policy Statement Regarding OIG’s Assessment of Advisory Opinion Requests*, *supra* note 56.

60. *Id.*

participants. Not only does OIG typically allow remuneration in the clinical trial context, but inclusion and exclusion criteria for a patient population are highly selective, limiting the likelihood that federal regulators will determine that a payment is considered an illegal remuneration.⁶¹ Nevertheless, these statutes are important to consider when designing more effective methods of direct clinical trial participant payment.

D. Participant Compensation Standards

1. Financial Compensation

In addition to legal requirements, other standards guide payment to clinical trial participants. To meet FDA and statutory guidelines and pass muster with an IRB, sponsors must choose from several standard categories of monetary payment for participants of clinical trials, including “reimbursement,” “compensation,” “appreciation,” and “incentives.”⁶² “Reimbursement” includes payment for out-of-pocket costs incurred for participating in a clinical trial, such as travel, parking, lodging, and additional medical expenses, and is “intended to minimize the financial impact of study participation.”⁶³ The FDA does not consider reimbursement to raise issues of undue influence.⁶⁴ However, because participants are simply reimbursed for costs they would have incurred during their participation in the study, reimbursement does not “make research participation more attractive than alternatives” and may fail to adequately increase recruitment and retention.⁶⁵

Second, “compensation” includes payment for lost economic opportunities, such as missed work.⁶⁶ Under the compensation theory, participants will choose to participate in research when they are paid *more* than the “opportunity costs associated with research participation.”⁶⁷ Because “participants all have different capacities to generate income outside of research,” the Secretary’s Advisory

61. U.S. FOOD & DRUG ADMIN., PUBLIC WORKSHOP: EVALUATING INCLUSION AND EXCLUSION CRITERIA IN CLINICAL TRIALS 1 (2018), <https://www.fda.gov/media/134754/download> [<https://perma.cc/MW3T-WFRH>].

62. *Attachment A - Addressing Ethical Concerns Offers of Payment to Research Participants*, U.S. DEP’T OF HEALTH & HUM. SERV., OFF. FOR HUM. RSCH. PROT., SECRETARY’S ADVISORY COMMITTEE ON HUMAN RESEARCH PROTECTIONS (Oct. 18, 2019), <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-september-30-2019/index.html> [<https://perma.cc/JT9A-865T>].

63. *Id.*

64. *FDA Information Sheet: Payment and Reimbursement to Research Subjects*, *supra* note 27.

65. *Attachment A*, *supra* note 62; Grady, *supra* note 46, at 1149.

66. *Attachment A*, *supra* note 62.

67. *Id.*

Committee on Human Research Protections (SACHRP) suggests that everyone is compensated equally, and compensation “acknowledge the importance of [the participants’] contributions to research and the sacrifices associated with participation.”⁶⁸ While compensation generally raises few concerns about undue influence because participants are compensated for the economic opportunities they lose by participating in research,⁶⁹ equal compensation among people with different opportunity costs could create a greater risk of undue influence for people with lower incomes.⁷⁰ Further, because the compensation model does not increase compensation above participants’ opportunity costs, it may have a limited impact on recruitment and retention.⁷¹

Payments of “appreciation” are used to thank participants for their contribution.⁷² Because payments of appreciation are generally small, they also have little ability to improve recruitment and retention.⁷³

Finally, an “incentive” is an extra payment for completing the study “beyond what participants might be owed as a matter of fairness.”⁷⁴ Incentives present a greater opportunity for undue influence because they are greater than other forms of payment, but it is possible to provide incentives without unduly influencing participants.⁷⁵ SACHRP believes that “incentive payments that may be unduly influential can be managed without necessarily lowering or eliminating them” because incentive payments are important to increase recruitment, the payment does not blind participants to risk, and providing lower payments would risk attracting only those of lower socioeconomic status.⁷⁶ To reduce concerns over incentive payments, SACHRP further recommends several approaches, including facilitating active rather than passive participant consent through in-depth review, providing “teach-back” opportunities to ensure that participants understand the study risks and obligations, incorporating a waiting period for participants, helping participants understand the conflicts between current interests and future interests, and granting support to participants who demonstrate a belief that they are being coerced.⁷⁷

In addition to these payment types, the mechanisms for clinical trial

68. *Id.*

69. *Id.*

70. Grady, *supra* note 46, at 1149.

71. *Id.*

72. *Attachment A, supra* note 62.

73. *Id.* (“Because of their minimal nature, [appreciation] payments are unlikely to influence decisions about study participation”).

74. *Attachment A, supra* note 62.

75. *Id.*

76. *Id.*

77. *Id.*

payments also vary and can be used to encourage recruitment and retention. Participants may be paid through a stipend, a fixed amount received after completion of a clinical trial step.⁷⁸ Patients may also be paid through reimbursement after a purchase has been made and a receipt submitted, including for meals, mileage, tolls, parking, and incidentals.⁷⁹ Third, wage reimbursement may be offered. Like the expense reimbursement mechanism, wage reimbursement pays participants for missed time at work due to participation in the clinical trial if the participant submits proof of attendance at a clinical visit and evidence of their employment and the salary they otherwise would have earned.⁸⁰

In recent years, alternative payment mechanisms have been implemented to encourage participant retention. One such example is micropayment, where a participant receives payments at regular intervals through a study to keep study participants engaged.⁸¹ In one clinical trial, participants reported that receiving micropayments effectively reminded them to fulfill their duties as a participant.⁸²

2. Non-Financial Compensation

Clinical trial sponsors have experimented with non-financial compensation for trial participants to improve recruitment and retention. Often the nature of the study provides a benefit to participation. For instance, participants may receive a direct benefit from the intervention, a collateral or indirect benefit such as a free physical examination, and an aspirational benefit such that the participant feels as though their participation provided a benefit to society.

In addition, clinical trials have used non-financial methods in conjunction with payment to participants. For example, Hala Borno details how a cancer treatment center offered patient navigation services to help participants considering entry into a clinical trial understand, complete, and submit

78. Suzanne Hamberger, *Do You Know Which Patient Payment Mechanism is Right for Your Clinical Trial?*, CLINCIERGE (Feb. 17, 2021), <https://web.archive.org/web/20230324062623/https://www.clincierge.com/do-you-know-which-patient-payment-method-is-right-for-your-clinical-trial>.

79. *Id.*

80. *Id.*

81. *Case Study: SmartSignals eCOA, SIGNANT HEALTH*, <https://43712937.fs1.hubspotusercontent-na1.net/hubfs/43712937/Marketing%20Assets/Case%20Studies/Case%20Study%20-%20Signant%20SmartSignals%20eCOA%20Integration%20with%20Clinical%20Research%20Payments%20Solution.pdf> [https://perma.cc/8QU9-FVK5].

82. *Id.*

documents associated with receiving financial reimbursement.⁸³ The intervention successfully increased participation in clinical trials.⁸⁴

But none of the prevailing methods of compensation, either monetary or non-monetary, account for the true value of clinical trial participant data, including the privacy risks of providing data to clinical trial investigators. In addition, as discussed next, these methods fall short of being “just and fair,” investigators could pay participants more without creating an “undue influence,” and these methods fail to achieve the FDA’s diversity goals.

E. Challenges with Current Payment Practices

1. Concerns Over Undue Influence Artificially Limit Participant Payment Under Current Payment Standards

Concerns that monetary payments could create “undue influence” limit participant payment under current standards of reimbursement, compensation, appreciation, and incentive. Undue influence is difficult to measure precisely,⁸⁵ and scholars place different levels of emphasis on the role of undue influence in compensating participants. Dr. Mansi Pandya emphasizes that payment of any kind risks creating undue influence, especially for vulnerable populations, and that it encourages commodification.⁸⁶ Vulnerability, according to Pandya, “is characterized as limited autonomy of the individual in making a decision.”⁸⁷ Populations who could have limited autonomy in decision-making include children, people with mental health disabilities, people living in poverty, people with low literacy, and people in prison.⁸⁸ For children and people with mental health disabilities, the concern is that the individuals have limited autonomy to make decisions for themselves and that their guardians are not themselves exposed to the risk of the clinical trial, resulting in a greater likelihood that they

83. Hala Borno et al., *Accelerating Cancer Clinical Trial Recruitment Through a Financial Reimbursement Program Integrated with Patient Navigation*, 30 J. CANCER POL’Y 1, 2 (2021), <https://www.sciencedirect.com/science/article/pii/S2213538321000369?via%3Dihub#bib0165> [<https://perma.cc/AEV3-RWB8>].

84. *Id.* at 5.

85. *See Informed Consent FAQs*, *supra* note 35.

86. Mansi Pandya & Chetna Desair, *Compensation in Clinical Research: The Debate Continues*, 4 PERSP. IN CLINICAL RSCH. 70, 71 (2013), https://journals.lww.com/picp/fulltext/2013/04010/compensation_in_clinical_research_the_debate.17.aspx#O4-17-4 [<https://perma.cc/QRZ5-NDQL>].

87. *Id.* at 71.

88. *Id.*; *see* Paul P. Christopher, *Enrolling in Clinical Research While Incarcerated: What Influences Participants’ Decisions?*, 47 HASTINGS CTR. REP. no. 21, at 12 (2017), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5356487/pdf/nihms841246.pdf> [<https://perma.cc/4YA3-2DBD>].

could be heavily influenced by financial compensation.⁸⁹ In addition, people in poverty and with low literacy may be more heavily influenced by financial compensation because they need money or cannot properly understand the risks associated with participation.⁹⁰ Research suggests that people who had spent a longer time in prison or had a lower level of education were most vulnerable to undue influence related to payment for clinical trials.⁹¹

However, overly restricting payment due to undue influence concerns can have unintended negative consequences, including by deterring participation. First, withholding payment deprives people of their economic rights, is an affront to their autonomy to determine what tradeoffs they are willing to take, and ignores cost-benefit analysis.⁹² IRBs condition approval “on a threshold determination that a study has a favorable risk-benefit ratio” without considering payment.⁹³ If the study has a favorable risk-benefit ratio without payment, adding the benefit of payment will have little impact on the participant’s risk-benefit analysis.⁹⁴ In addition, clinical trial participants are informed of the risks of research and the treatment of their body as a research commodity.⁹⁵ In one study interviewing participants in Phase I clinical trials, researchers Rebecca Walker and Jill Fisher concluded that framing payment as an “incentive” should be allowed precisely because “payment rhetorics that avoid body commodification have the double effect of also limiting participants’ economic rights.”⁹⁶

Second, payment can be an affirmative signal of risk.⁹⁷ Cynthia Cryder argues that high payments for participation in a clinical trial “may help alert

89. Pandya & Desair, *supra* note 86, at 71-72. Regarding the vulnerability of children, see ETHICAL CONDUCT OF CLINICAL RESEARCH INVOLVING CHILDREN (Marilyn J. Field & Richard E Behrman eds., 2004), <https://www.ncbi.nlm.nih.gov/books/NBK25557/> [<https://perma.cc/6V6M-ZLBF>].

90. Pandya & Desair, *supra* note 86, at 72.

91. Ravi Divya et al., *Financial Payments for Participating in Research while Incarcerated: Attitudes of Prisoners*, 40 ETHICS & HUM. RSCH. 1 (2018).

92. See Emily A. Largent & Holly Fernandez Lynch, *Paying Research Participants: The Outsized Influence of “Undue Influence,”* 39 IRB 1–9 (2017), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5640154/pdf/nihms877093.pdf> [<https://perma.cc/VFS5-KEFV>]; Rebecca Walker & Jill Fisher, “My Body is One of the Best Commodities”: Exploring the Ethics of Commodification in Phase I Healthy Volunteer Clinical Trials, 29 KENNEDY INST. ETHICS J. 305, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6989025/pdf/nihms-1059559.pdf> [<https://perma.cc/EM4P-L8KZ>].

93. Largent & Fernandez Lynch, *supra* note 92, at 4.

94. *Id.* at 4-5.

95. Walker & Fisher, *supra* note 92.

96. *Id.*

97. Cynthia E. Cryder et al., *Informative inducement: Study Payment as a Signal of Risk*, 70 SOC. SCI. & MED. 455-64 (2010), <https://pubmed.ncbi.nlm.nih.gov/19926187/> [<https://perma.cc/VU7B-PRXQ>].

participants that study procedures do not necessarily favor their individual interests, and thus may prompt vigilance about a study's risks."⁹⁸ In fact, empirical research demonstrates that participants use the payment amount as a proxy for the risk involved in the study.⁹⁹ One study showed that when a payment was higher, participants became more vigilant in learning about the study's risks.¹⁰⁰

Third, the undue influence standard creates a harmful and paternalistic implication that vulnerable populations have minimal autonomy or lack the competence to evaluate the risk of participating in a clinical trial.¹⁰¹ The over-protective nature of the undue influence standard consequently may lead IRBs to mistakenly limit participation for people who can fully consider the risks and benefits for themselves.¹⁰²

Finally, there is some evidence that participant payment does not risk creating undue influence. Research by Scott Halpern has demonstrated that moderate payment levels do not unduly influence hypothetical study participants.¹⁰³ The study showed that, while some participants are more willing to participate with higher payment, payment does not cloud participants' judgment of risk.¹⁰⁴ In another study, some participants reported that financial incentives did not unduly influence their decision to participate in a clinical trial.¹⁰⁵ Incarcerated participants in a prison study reported that they did not believe payment would unduly influence their decision-making in a hypothetical clinical trial.¹⁰⁶ Finally, under current payment standards, clinical trial sponsors

98. *Id.* at 456.; see also Neal Dickert & Christine Grady, *What's the Price of a Research Subject? Approaches to Payment for Research Participation*, 341 *NEW ENG. J. MED.* 198, 199 (1999). Dickert & Grady lay out three models for payment: 1) a market model, 2) wage payment, and 3) reimbursement. The FMV model might be viewed as a methodology for valuing one of those, or as a fourth model, building upon their framework twenty-five years later.

99. Cryder et al., *supra* note 97, at 460.

100. *Id.*

101. Ana S. Iltis, *Payments to Normal Healthy Volunteers in Phase I Trials: Avoiding Undue Influence While Distributing Fairly the Burdens of Research Participation*, 34 *J. MED. & PHIL.* 68, 82 (2009).

102. Emily Largent et al., *Misconceptions About Coercion and Undue Influence: Reflections on the Views of IRB Members*, 27 *BIOETHICS* 500, 506 (2013).

103. Scott D. Halpern et al., *Empirical Assessment of Whether Moderate Payments Are Undue or Unjust Inducements for Participation in Clinical Trials*, 164 *ARCHIVES INTERNAL MED.* 801, 801 (2004).

104. *Id.*

105. Emily A. Largent et. al., *Participants' Perspectives on Payment for Research Participation: A Qualitative Study*, 44 *ETHICS & HUM. RSCH.* 14, 17-18 (2022).

106. Divya et al., *supra* note 91, at 4. We note that factors other than payment may create undue influence. The presence of authority figures and individuals' preexisting ability to access care may influence participants' decision to participate as much as or more than payment. See

must still provide a significantly compelling rationale behind the payment of money to prevent undue influence concerns from arising in the IRB approval process.

2. *The Failure to Adequately Compensate Participants Reduces Diversity and Hinders Representative Research*

This Article defines diversity in clinical trial participation to mean that clinical researchers achieve the appropriate representation of population groups in a study.¹⁰⁷ According to the National Academies of Science, Engineering, and Medicine, “[a]n equitable clinical research enterprise would include trials and studies that match the demographics of the disease burden under study.”¹⁰⁸ Underrepresented populations in clinical research include “women[,] . . . racial and ethnic minority population groups[,] . . . older adults, pregnant and lactating individuals, LGBTQIA+ populations, and persons with disabilities.”¹⁰⁹ The representation of white women has significantly improved, but “racial and ethnic subgroups of women remain underrepresented.”¹¹⁰

The failure to adequately compensate clinical trial participants reduces participant diversity by excluding economically disadvantaged groups,¹¹¹ which runs directly in contravention of the FDA’s published diversity recommendations.¹¹² In response to statutory authority granted by the Food and Drug Omnibus Reform Act of 2022,¹¹³ FDA draft guidance issued in June 2024 recommends that clinical trial sponsors develop a “Diversity Action Plan.”¹¹⁴

David Borasky, *Paying Subjects to Take Part in Research: A New Perspective on Coercion and Undue Influence*, 33 *CLINICAL RESEARCHER* (2019).

107. See NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE, *IMPROVING REPRESENTATION IN CLINICAL TRIALS AND RESEARCH: BUILDING RESEARCH EQUITY FOR WOMEN AND UNDERREPRESENTED GROUPS 1* (2022).

108. *Id.*

109. *Id.*

110. *Id.* at 3.

111. Barbara E. Bierer et al., *Fair Payment and Just Benefits to Enhance Diversity in Clinical Research*, 5 *J. CLINICAL & TRANSLATIONAL SCI.* e1591 (2021), <https://pubmed.ncbi.nlm.nih.gov/34527298> [<https://perma.cc/PTT3-56W3>]

112. U.S. FOOD & DRUG ADMIN., *ENHANCING THE DIVERSITY OF CLINICAL TRIAL POPULATIONS—ELIGIBILITY CRITERIA, ENROLLMENT PRACTICES, AND TRIAL DESIGNS GUIDANCE FOR INDUSTRY* (2020) <https://www.fda.gov/media/127712/download> [<https://perma.cc/3RC3-676N>]; Press Release, U.S. Food & Drug Admin., *FDA Guidance Provides New Details on Diversity Action Plans Required for Certain Clinical Studies* (June 26, 2024), <https://www.fda.gov/news-events/press-announcements/fda-guidance-provides-new-details-diversity-action-plans-required-certain-clinical-studies> [<https://perma.cc/86BG-7PNB>].

113. 21 U.S.C. § 355(z).

114. FDA Guidance Provides New Details on Diversity Action Plans Required for Certain Clinical Studies, *supra* note 112.

Diversity Action Plans “must specify the sponsor’s rationale and goals for clinical study enrollment (separated by the age group, ethnicity, sex and race of clinically relevant study populations) and describe how the sponsor intends to meet those goals.”¹¹⁵ However, Diversity Action Plans are only necessary for “Phase 3 clinical studies” or “other pivotal clinical studies of a drug or biological product” as appropriate.¹¹⁶

Recent shifts in federal policy have created uncertainty around diversity action plans (DAPs).¹¹⁷ But regardless of electoral winds, the scientific need for representative research remains.¹¹⁸ Diversity in trial participation advances valid, generalizable results.¹¹⁹ Trials that reflect the target population improve accuracy across genetic, environmental, and social factors. They reduce risk for underrepresented groups, support precision medicine,¹²⁰ and increase regulatory and market confidence.¹²¹ Representative research is not a political formality; it is a necessary condition for credible, usable science.

The prevailing challenge to increasing diversity is that the economic burden of participating in a clinical trial is high, and payment often does not offset the burden.¹²² Ryan Huey reports that in a study of cancer patients undergoing a clinical trial, 48% of patients had “monthly total out-of-pocket costs of at least \$1,000.”¹²³ Courtney Williams argues that due to the high economic burden on participants, cost-related considerations impact participation in clinical trials,

115. *Id.*

116. *Id.*

117. Monica Chmielewski & Alexandra Maulden, *An Overview of FDA Diversity-Related Documents for Clinical Trials*, APPLIED CLINICAL TRIALS (May 30, 2024), <https://www.appliedclinicaltrials.com/view/an-overview-of-fda-diversity-related-documents-for-clinical-trials>.

118. NATIONAL ACADEMIES, *supra* note 107, at 12-14.

119. Don Tracy, *The Path Ahead to Improve DEI in Clinical Trials*, APPLIED CLINICAL TRIALS (Jan. 13, 2025), <https://www.appliedclinicaltrials.com/view/path-ahead-improve-dei-clinical-trials> (“Participants . . . should be representative of the patients who will use the medical products.” (quoting then-FDA Commissioner Robert M. Califf)).

120. Harpreet Singh, *FDA’s Vision for Multiregional Clinical Trials in Oncology*, PRECISION FOR MEDICINE (Sept. 12, 2024), <https://www.precisionformedicine.com/blog/fdas-vision-for-multiregional-clinical-trials-in-oncology> (highlighting diversity’s role in capturing “variability in drug metabolism and disease manifestation”).

121. Tracy, *supra* note 119 (noting diverse trials “enhance regulatory confidence and market acceptance”).

122. Ryan Huey et al., *Patient-Reported Out-of-Pocket Costs and Financial Toxicity During Early-Phase Oncology Clinical Trials*, 26 ONCOLOGIST 588, 590 (2021), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8265355/pdf/ONCO-26-588.pdf> [<https://perma.cc/FD53-PVCK>].

123. *Id.* at 590.

especially for people with lower incomes.¹²⁴ Moreover, in a clinical trial for participants with cancer, Huey found that the financial burden was higher for people with lower incomes, people who traveled further distances to receive care, and non-white and Hispanic participants.¹²⁵ As a result, he concluded that the high financial burden to participate in the clinical trial increased the opportunity for disparities in clinical trial recruitment and retention by income, race, and ethnicity.¹²⁶

Increasing compensation for clinical trial participation would likely improve diversity. The National Academies of Science, Engineering, and Medicine reported that “American women and underrepresented individuals make less money and are more likely to live below the federal poverty line compared with white men.”¹²⁷ With a high economic burden to participate in a clinical trial, “[r]educed economic resources can make elective participation in research a challenge.”¹²⁸

A lack of diversity is problematic because researchers gain a better understanding of the drug’s safety, effects, and benefits when the clinical trial uses a study population that represents the demographics of future users of the drug.¹²⁹ Greater diversity in a clinical trial improves the chances that the drug is safer for use in the target populations.¹³⁰ Therefore, current clinical trial participant payment practices that fail to gather a diverse population risk reducing drug safety and effectiveness in the end users.

II. CLINICAL TRIAL PAYMENTS MUST RESPOND TO THE EVOLVING DATA INTENSIVE LANDSCAPE

Clinical trial sponsors are using more patient data to inform and increase recruitment and retention, control for systemic disparities in recruitment, and

124. Williams et al., *supra* note 13, at 1203-04; Joseph M. Unger et al., *Patient Income Level and Cancer Clinical Trial Participation*, 31 J. CLINICAL ONCOLOGY 536 (2013), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3565180> [<https://perma.cc/4479-3QE6>]; Fumiko Chino & S. Yousuf Zafar, *Financial Toxicity and Equitable Access to Clinical Trials*, 39 AM. SOC’Y CLINICAL ONCOLOGY ANN. MEETING 11 (2019), <https://pubmed.ncbi.nlm.nih.gov/31099681> [<https://perma.cc/A3PN-MSYA>].

125. Huey, *supra* note 122, at 592.

126. *Id.*

127. NATIONAL ACADEMIES, *supra* note 107, at 80.

128. Ryan Huey et al., *Patient-Reported Out-of-Pocket Costs and Financial Toxicity During Early-Phase Oncology Clinical Trials*, 26 ONCOLOGIST 588, 590 (2021), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8265355/pdf/ONCO-26-588.pdf> [<https://perma.cc/FD53-PVCK>]; NATIONAL ACADEMIES, *supra* note 107, at 80.

129. ENHANCING THE DIVERSITY OF CLINICAL TRIAL POPULATIONS, *supra* note 112, at 14.

130. *Id.*

respond to the emerging marketplace for clinical data.¹³¹ Data-intensive methods include decentralized and remote methods, passive data collection, pragmatic clinical trials, data tokenization, and the use of real-world data (RWD).

Clinical trial participant payment innovation is necessary to respond to these emerging data-intensive methods. Limiting payment for participation in clinical trials to the four categories of “reimbursement, compensation, appreciation, and incentive” detailed in Part I also means that there is no standard mechanism to compensate participants specifically for the use and commercialization of their data. With more data-intensive methods used in clinical trials every day, researchers now run the risk of exploiting not only participants’ bodies but also their personal data.¹³²

A. Decentralized Methods are Data-Intensive

While participant compensation increases participation in clinical trials, overall study design also influences participation.¹³³ Decentralized methods have successfully improved participant recruitment and retention.¹³⁴ Decentralized methods “focus clinical study conduct around the patient.”¹³⁵ Accelerated by the onset of the COVID-19 pandemic, decentralized methods include using telemedicine, electronic consent forms, wearable biomarkers, home visits, and online advertisements through social media and email.¹³⁶ Decentralized methods may also involve operating a clinical trial from many local clinics rather than a

131. Brian L. Miyata, Barbara Tafuto & Nadina Jose, *Methods and Perceptions of Success for Patient Recruitment in Decentralized Clinical Trials*, 7 J. CLINICAL & TRANSLATIONAL SCI. e232 (2023), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10643920> [<https://perma.cc/MV8F-FFY2>]; Lampros C. Kourtis et al., *Digital Biomarkers for Alzheimer’s Disease: The Mobile/Wearable Devices Opportunity*, 9 NPJ DIGITAL MED. 2, 2 (2019), <https://www.nature.com/articles/s41746-019-0084-2> [<https://perma.cc/TGX5-DBFL>]; Ian Ford & John Norrie, *Pragmatic Trials*, 5 NEW ENG. J. MED. 375, 460 (2016).

132. See Marcel Salive, *Pragmatic Clinical Trials: Testing Treatments in the Real World*, NIH NAT’L INST. AGING (June 7, 2017), <https://www.nia.nih.gov/research/blog/2017/06/pragmatic-clinical-trials-testing-treatments-real-world> [<https://perma.cc/P3MD-4ERW>].

133. Beth Parkinson et al., *Designing and Using Incentives to Support Recruitment and Retention in Clinical Trials: A Scoping Review and a Checklist for Design*, 20 TRIALS 624 (2019), <https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3710-z#ref-CR1> [<https://perma.cc/9GP4-8ZED>].

134. Miyata et al., *supra* note 131, at 1.

135. *Id.*

136. *Id.*; see also Hélène L. Svahnquist & Anna Skabeev, *A Practical Overview of Patient-Centric Trials*, 26 APPLIED CLINICAL TRIALS 22 (2017), <https://www.appliedclinicaltrialsonline.com/view/practical-overview-patient-centric-trials> [<https://perma.cc/ZF4Z-99QJ>]; *Decentralized Clinical Trials: A Comprehensive Synopsis*, OBVIOHEALTH BLOG, <https://www.obviohealth.com/resources/decentralized-clinical-trials-a-comprehensive-synopsis> [<https://perma.cc/8H6T-HF57>].

single academic medical center to reduce participant travel barriers.¹³⁷ For example, during a clinical trial in a rural area, clinical trial managers recruited 130 participants by mail and telephone, completed consent over the telephone, delivered assessments through the mail with instructions to complete the assessments over the telephone, and used smartphone-based study instruments.¹³⁸ Using these virtual methods, the study retained over 90% of its participants over the four-month intervention phase.¹³⁹ It also gained a large amount of patient data that could potentially be resold to other parties, without any of the clinical patients receiving compensation for that purpose.

Decentralized methods are limited when the study requires access to specialized technology, equipment, or services.¹⁴⁰ However, decentralized methods can be used in conjunction with on-site methods in a hybrid design.¹⁴¹ A common hybrid design is to utilize remote data collection with periodic in-person assessments.¹⁴² For example, a study from Vanderbilt University Medical Center measured physical activity in patients with pulmonary arterial hypertension using remote sensor-based data collection during a twelve-week study period.¹⁴³ The study also involved in-person data collection at baseline and study completion.¹⁴⁴ Transitioning to using more digital health technologies through decentralized methods makes it essential to reconsider clinical trial payment.

B. Passive Data Collection

Trends toward decentralized study methods have accompanied increased data collection from participants, with the goal of reducing the burden on participants and addressing issues of low recruitment and retention. Passive data collection methods—those that allow for data collection without the participant's

137. Marc Leighton, *Overcoming the 7 Biggest Challenges in Decentralized Trials*, APPLIED CLINICAL TRIALS (Jan. 18, 2022), <https://www.appliedclinicaltrials.com/view/overcoming-the-7-biggest-challenges-in-launching-decentralized-trials>.

138. Jared W. Magnani et al., *Rurality and Atrial Fibrillation: A Pathway to Virtual Engagement and Clinical Trial Recruitment in Response to COVID-19*, 3 AM. HEART J. PLUS: CARDIOLOGY RSCH. & PRAC. 100017 at 3-4 (2021), <https://www.sciencedirect.com/science/article/pii/S266660222100015X?via%3Dihub> [<https://perma.cc/EF2K-SPQK>].

139. *Id.* at 5.

140. Ojasav Schrawat et al., *Data-Driven and Technology-Enabled Trial Innovations Toward Decentralization of Clinical Trials: Opportunities and Considerations*, 98 THEMATIC REV. ON FORWARD THINKING ON CLINICAL TRIALS IN CLINICAL PRACTICE 1404, 1405 (2023).

141. *Id.* at 1412.

142. *Id.*

143. Anna R. Hemnes, et. al, *A Mobile Health Intervention to Increase Physical Activity in Pulmonary Arterial Hypertension*, 160 CHEST 1042, 1043-44 (2021).

144. *Id.*

engagement or knowledge—allow for more intense collection.¹⁴⁵ Unlike active data collection, which requires action by the research participant, passive data collection does not require the participant's active engagement and therefore raises a host of new ethical issues.¹⁴⁶ Passive data collection increases the amount of data collection that is not influenced by participant input, reduces the burden on participants, and improves participant adherence.¹⁴⁷

Passive data collection is especially preferable to active data collection when addressing certain types of diseases where active data collection is more difficult. For example, researchers used phone usage and GPS data collected from mobile phones to detect symptoms of depression.¹⁴⁸ In addition, to predict and detect Alzheimer's disease, gait metrics, fine motor control, speech, eye movement, and heart rate variability have been measured using mobile or wearable devices.¹⁴⁹ These simple examples show that patient data is being used today to detect potential diseases and recommend treatments without participants receiving any compensation for their clinical role.

C. Pragmatic Clinical Trials, Data Tokenization, and Real-World Data

The rise of pragmatic clinical trials, data tokenization, and RWD usage in clinical trials has sparked more intense data collection and use. Pragmatic clinical trials provide evidence to inform the “adoption of the intervention into real-world clinical practice.”¹⁵⁰ Like decentralized methods and passive data collection, pragmatic clinical trials reduce participant burden by leveraging long-term follow-up through data gathered during routine clinical visits.¹⁵¹

With the increasing popularity of pragmatic clinical trials, researchers often pair together participant data from a variety of sources.¹⁵² To pair data, clinical trial data undergoes a process called data tokenization and is combined with RWD.¹⁵³ Data tokenization de-identifies data using a unique identifier.¹⁵⁴ The

145. Kourtis et al., *supra* note 131, at 2.

146. *Id.* at 1-2.

147. *Id.* at 2.

148. Sohrab Saeb et al., *Mobile Phone Sensor Correlates of Depressive Symptom Severity in Daily-Life Behavior: An Exploratory Study*, 17 J. MED. INTERNET RSCH. E175 at 9 (2015), <https://www.jmir.org/2015/7/e175/authors> [<https://perma.cc/MGP4-CB6B>].

149. Kourtis et al., *supra* note 131, at 2.

150. Ford & Norrie, *supra* note 131, at 454.

151. *Id.* at 460.

152. *See* Salive, *supra* note 132.

153. Dan Schell, *What is Clinical Trial Tokenization?*, CLINICAL LEADER (Jan. 30, 2024), <https://www.clinicalleader.com/doc/what-is-clinical-trial-tokenization-0001> [<https://perma.cc/R4Y6-B5Z5>]; Simon Dagenais et al., *Use of Real-World Evidence to Drive Drug*

data can then be sold to RWD vendors, who pair it with RWD.¹⁵⁵ RWD include a variety of sources generated from routine clinical care like electronic health record (EHR) data, medical claims data, medical registry data, and data collected from digital health technologies.¹⁵⁶ Pairing participant data from clinical trials with RWD allows researchers to receive data from clinical trial participants during clinical visits over the long term.¹⁵⁷

For example, the clinical trial ADAPTABLE (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-Term Effectiveness) tested the use of two common aspirin doses in a large population and used EHR and claims data to monitor long-term outcomes such as death, hospitalization, medical procedures, and other patient-reported outcomes.¹⁵⁸ Linking data from the clinical trial with participants' health-system data allowed for the recruitment of over 15,000 patients across forty study sites in the United States and improved long-term retention.¹⁵⁹

In addition, the IMPACT-AFib (Implementation of a Randomized Controlled Trial to Improve Treatment with Oral AntiCoagulants in Patients with Atrial Fibrillation) clinical trial tested whether education on stroke prevention could encourage the use of oral anticoagulants in participants with atrial fibrillation through the use of RWD.¹⁶⁰ The study enrolled over 47,000 participants and researchers obtained data from the FDA's Sentinel system, which captured RWD from patients enrolled in several health plans, to monitor

Development Strategy and Inform Clinical Trial Design, 111 *CLINICAL PHARMACOLOGY & THERAPEUTICS* 77, 83 (2022).

154. Schell, *supra* note 153; Dagenais et al., *supra* note 153, at 83.

155. Schell, *supra* note 153; Dagenais et al., *supra* note 153, at 83.

156. Dagenais et al., *supra* note 153, at 77; U.S. FOOD & DRUG ADMIN., SUBMITTING DOCUMENTS USING REAL-WORLD DATA AND REAL-WORLD EVIDENCE TO FDA FOR DRUG AND BIOLOGICAL PRODUCTS (2022), <https://www.fda.gov/media/124795/download> [<https://perma.cc/KMW9-NAJA>].

157. Schell, *supra* note 153.

158. See U.S. FOOD & DRUG ADMIN., FRAMEWORK FOR FDA'S REAL-WORLD EVIDENCE PROGRAM 10 (2018) <https://www.fda.gov/media/120060/download> [<https://perma.cc/QBE3-LBAY>]; *Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-term (ADAPTABLE)*, CLINICALTRIALS.GOV (July 1, 2021), <https://clinicaltrials.gov/study/NCT02697916> [<https://perma.cc/NNH2-MCTC>].

159. W. Schuyler Jones, *Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease*, 384 *NEW ENG. J. MED.* 1981, 1988 (2021).

160. Sean D. Pokorney et al., *Effect of Mailing Educational Material to Patients with Atrial Fibrillation and Their Clinicians on Use of Oral Anticoagulants*, 5 *JAMA NETWORK OPEN* e2214321, 1-3 (2022), <https://pubmed.ncbi.nlm.nih.gov/35639381/> [<https://perma.cc/Q8EQ-LRV4>]; *Implementation of an RCT to imProve Treatment With Oral AntiCoagulanTs in Patients With Atrial Fibrillation (IMPACT-AFib)*, CLINICALTRIALS.GOV (Dec. 13, 2021), <https://clinicaltrials.gov/study/NCT03259373> [<https://perma.cc/UZU2-J585>].

the effectiveness of the intervention over the long term.¹⁶¹

While the pairing of clinical trial data and RWD is not new, the legal landscape has changed to promote the use of RWD.¹⁶² In 2016, the 21st Century Cures Act sought to increase drug development by requiring the FDA to issue guidance on the use of RWD in regulatory and business decision-making.¹⁶³ Consequently, in 2018, the FDA created a framework to evaluate the use of RWD in drug approval.¹⁶⁴ The framework highlighted the potential for RWD to support decision-making when it is used as part of pragmatic clinical trials.¹⁶⁵ According to the FDA's framework, RWD can be used to inform clinical trial decision-making at each stage, including recruitment, retention, intervention facilitation, and outcomes assessment.¹⁶⁶ When study sponsors assess outcomes pertinent to drug development, the FDA recommends that pragmatic clinical trials and RWD be used to inform decision-making when the intervention is well suited to the routine clinical care setting and to ensure quality data can be captured in those settings, enough patients can be accessed, and variations in clinical practice don't preclude the feasibility of the study.¹⁶⁷

Following the FDA guidance, the scientific research community has increased their support of RWD usage in clinical trials, including randomized controlled trials (RCTs).¹⁶⁸ Researchers advocate that "routinely integrating [novel real-world methods and traditional clinical trial methods] . . . will yield a comprehensive understanding of how to use medical products in practice."¹⁶⁹

In addition, trends towards relying solely on RWD to inform decision-making further highlight the shift towards data-intensive practices and the value of patient data in the drug development process. FDA guidance says that RWD "may in some cases provide similar information with comparable or even superior characteristics to information collected and analyzed through a traditional clinical trial."¹⁷⁰ In addition, researchers have proposed using RWD to

161. Pokorney et al., *supra* note 160, at 1-4.

162. See FRAMEWORK FOR FDA'S REAL-WORLD EVIDENCE PROGRAM, *supra* note 158, at 3, 11.

163. Dagenais et al., *supra* note 153, at 78.

164. FRAMEWORK FOR FDA'S REAL-WORLD EVIDENCE PROGRAM, *supra* note 158.

165. *Id.* at 19.

166. *Id.*

167. *Id.*

168. See generally David C. Klonoff, *The New FDA Real-World Evidence Program to Support Development of Drugs and Biologics*, 14 J. DIABETES SCI. TECH. 345 (2020), <https://pubmed.ncbi.nlm.nih.gov/30862182/> [<https://perma.cc/93ZS-MDTD>].

169. Rachel E. Sherman, *Accelerating Development of Scientific Evidence for Medical Products Within the Existing US Regulatory Framework*, 16 NATURE REV. DRUG DISCOVERY 297, 298 (2017), <https://www.nature.com/articles/nrd.2017.25> [<https://perma.cc/HU5P-ANXV>].

170. U.S. FOOD & DRUG ADMIN., USE OF REAL-WORLD EVIDENCE TO SUPPORT REGULATORY DECISION-MAKING FOR MEDICAL DEVICES: GUIDANCE FOR INDUSTRY AND FOOD AND DRUG

create a real-world study population, relying solely on patient clinical data.¹⁷¹ The trend raises new, important questions about the proper utilization, management, and compensation for participant data.

D. Artificial Intelligence (AI) Developments Impact Data Use

The rise of artificial intelligence (AI) makes paying participants for their data more important than ever. For example, Google has begun testing an AI chatbot called Med-PaLM 2 in clinical settings to help answer medical questions.¹⁷² In addition, AI assistants, like DAX copilot, can improve patient monitoring by automatically documenting clinical visits.¹⁷³ AI was also used to reliably detect left ventricular dysfunction in an electrocardiogram.¹⁷⁴ While the adoption of AI in healthcare is emerging slowly compared to other sectors,¹⁷⁵ these developments have implications for clinical trial payments.

AI presents concerns over clinical trial participant data privacy and security.¹⁷⁶ Inadequate protections can leave participant data vulnerable to data breaches and misuse.¹⁷⁷ Therefore, clinical trial payment should compensate for data privacy and security concerns in the current AI landscape.

Beyond privacy and security, using AI to analyze data in a clinical trial presents additional risks to consider when compensating participants and designing a clinical study. Because AI models have been found to be biased

ADMINISTRATION STAFF (2017), <https://www.fda.gov/media/99447/download> [<https://perma.cc/F33V-3T8F>].

171. Veeneta Khozin, *Real-World Evidence in Support of Precision Medicine: Clinico-Genomic Cancer Data as a Case Study*, 37 HEALTH AFF. 765 (2018), <https://pubmed.ncbi.nlm.nih.gov/29733723> [<https://perma.cc/TA8K-TD2F>].

172. Karan Singhal et al., *Large Language Models Encode Clinical Knowledge*, 620 NATURE 172, (2023); Miles Kruppa & Nidhi Subbaraman, *In Battle with Microsoft, Google Bets on Medical AI Program to Crack Healthcare Industry*, WALL ST. J. (July 8, 2023), <https://www.wsj.com/articles/in-battle-with-microsoft-google-bets-on-medical-ai-program-to-crack-healthcare-industry-bb7c2db8> [<https://perma.cc/MG9V-K9ZU>].

173. Peter Durlach, *DAX Copilot—AI-Powered Solution Wins AI Tech Sprint to Reduce Clinician Burnout*, MICROSOFT (June 17, 2024), <https://www.microsoft.com/en-us/industry/blog/healthcare/2024/06/17/dax-copilot-ai-powered-solution-wins-ai-tech-sprint-to-reduce-clinician-burnout> [<https://perma.cc/7S5E-7RQL>].

174. Zach I. Attia et al., *Screening for Cardiac Contractile Dysfunction Using an Artificial Intelligence-Enabled Electrocardiogram*, 25 NATURE MED. 70, 70-74 (2019).

175. Nikhil R. Sahni & Brandon Carrus, *Artificial Intelligence in U.S. Health Care Delivery*, 389 NEW ENG. J. MED. 348, 348 (2023).

176. See Yu-Hao Li et al., *Innovation and Challenges of Artificial Intelligence Technology in Personalized Healthcare*, 14 SCI. REP. 1, 5 (2024).

177. See *id.*

based on personal characteristics like race, socio-economic status, and gender,¹⁷⁸ algorithmic bias could creep into clinical trials. Also, difficulties of human-machine interaction could lead to incorrect results, poor participant experience, and an overreliance on AI.

E. There is a Significant Market for Clinical Data

Of course, the increased use and surveillance of patient data coincides with a large (and fast-growing) market for clinical data. The value of the global healthcare analytics market is projected to rise from \$11.6 billion in 2018 to \$365.8 billion by 2032.¹⁷⁹ In addition, the healthcare industry already generates 30% of the world's data volume, and this share is growing annually.¹⁸⁰ IQVIA, a major healthcare data company that provides medical data to the healthcare sector, had nearly \$15 billion in revenue in 2023 and grew by four percent compared to 2022.¹⁸¹

F. The “Data Broker Paradox”: Paying Corporations, Not Contributors

The market for patient data is lucrative for all participants, except the patients themselves. In 2023, 23andMe, a leading (at the time) provider of consumer genetic testing, extended their collaboration with GSK with a one-year, \$20 million non-exclusive license to de-identified patient data for research activities.¹⁸² In other cases, healthcare data brokers have charged up to \$50 per

178. Mirja Mittermaier et al., *Bias in AI-Based Models for Medical Applications: Challenges and Mitigation Strategies*, 6 NPJ DIGITAL MED. 113, 113 (2023).

179. *Healthcare Analytics Market Size, Share & Industry Analysis, By Product (Descriptive, Predictive, and Prescriptive), By Application (Financial Analytics, Population Health Analytics, Clinical Analytics, and Operations and Administrative Analytics), By End User (Payers, Providers, and Others) and Regional Forecast, 2019–2032*, FORTUNE BUS. INSIGHTS (July 15, 2024), <https://www.fortunebusinessinsights.com/healthcare-analytics-market-102641> [<https://perma.cc/7LDH-YBPH>].

180. See Greg Wiederrecht & Andrew Callaway, *The Healthcare Data Explosion*, RBC CAPITAL MARKETS, https://www.rbcm.com/en/gib/healthcare/episode/the_healthcare_data_explosion [<https://perma.cc/QHD2-KCFL>].

181. *IQVIA Reports Fourth-Quarter and Full-Year 2023 Results; Issues Full-Year 2024 Guidance*, IQVIA.COM (Feb. 14, 2024), <https://ir.iqvia.com/press-releases/press-release-details/2024/IQVIA-Reports-Fourth-Quarter-and-Full-Year-2023-Results-Issues-Full-Year-2024-Guidance/default.aspx> [<https://perma.cc/M5GP-F3VV>].

182. Press Release, 23andMe, 23andMe Announces Collaboration Extension with New Data Licensing Agreement with GSK (July 27, 2023), <https://investors.23andme.com/news-releases/news-release-details/23andme-announces-collaboration-extension-new-data-licensing>.

medical record and \$100,000 per year for access to medical data.¹⁸³ Pharmaceutical companies recognize the value of patient data, and third party data providers such as 23andMe are well compensated for the data they provide.

Too often, patients are left out of the value equation. Patients are told outright in their research consent, which allows their data to be shared with companies like GSK, “You will not receive any direct benefits by taking part in 23andMe Research . . . Sometime in the future, you or others, including people who share your ancestry or health characteristics, may benefit indirectly from 23andMe Research discoveries.”¹⁸⁴ Patient data is viewed as highly valuable by markets—but as nearly valueless to the very people who provide it.

III. FAIR MARKET VALUE IS STANDARD PRACTICE AND REDUCES LEGAL LIABILITY IN PAYING RESEARCH SITES TO CONDUCT CLINICAL TRIALS

A. Fair Market Value is Important for Avoiding Legal Liability for Paying Research Sites

Fair market value (FMV) is the sale price agreed upon between a seller and a buyer.¹⁸⁵ To avoid legal liability, determining FMV is essential during the negotiation process between clinical trial sponsors and research sites.¹⁸⁶ The sponsor and investigator negotiate over investigator fees, study coordinator salaries, ancillary services, patient recruitment costs, and facilities and equipment.¹⁸⁷

Through negotiations, the sponsor and research site arrive at FMV.¹⁸⁸ FMV is not only standard practice in the payment for research services¹⁸⁹ but also

183. Todd Zigrang & Jessica Bailey-Wheaton, *Valuing Healthcare Data*, VALUE EXAMINER July-Aug. 2023, at 34, 37, <https://www.healthcapital.com/researchmaterialdocuments/publishedarticles/Valuing%20Healthcare%20Data.pdf> [<https://perma.cc/AWS3-XGMC>]. On the dark web, an EHR database can be sold for up to \$500,000. Carol Gibbons, *What is the Price of a Medical Record?*, MED. ECON. (July 15, 2017), <https://www.medicaleconomics.com/view/what-price-medical-record> [<https://perma.cc/PBH3-AE6G>].

184. *Research Consent Document*, 23andMe, <https://www.23andme.com/about/consent> (last visited May 3, 2025).

185. *How Fair Market Value Impacts Clinical Trial Budgets at Research Sites*, WCG CLINICAL.COM (July 7, 2023), <https://www.wcgclinical.com/insights/how-fair-market-value-impacts-clinical-trial-budgets-at-research-sites/> [<https://perma.cc/X7KA-6EHR>].

186. *Id.*

187. *Id.*

188. *Id.*

189. OIG Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23731, 23735 (May 5, 2003), <https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/2006053221-hi-050503frcpgpharmac.pdf> [<https://perma.cc/7PTU-6MM9>].

usually required to find an exception against liability under the Physician Self-Referral Law (Stark Law).¹⁹⁰ To prevent fraud and abuse, the Stark Law provides that “if a physician (or an immediate family member of such physician) has a financial relationship with an entity . . . the physician may not make a referral to the entity for the furnishing of designated health services.”¹⁹¹ However, the law may allow such referrals if they are made as a FMV exchange.¹⁹²

In addition, according to the OIG, “[p]ayments for research services should be fair market value for legitimate, reasonable, and necessary services.”¹⁹³ As defined in the Stark Law, fair market value represents “the value [that would be paid] in an arm’s-length transaction, consistent with the general market value of the subject transaction.”¹⁹⁴ General market value is “the compensation that would be paid at the time the parties enter into the service arrangement as the result of *bona fide* bargaining between well-informed parties that are not otherwise in a position to generate business for each other.”¹⁹⁵ The definitions reflect those used in the business community, which defines fair market value as “the price for which property would exchange between a willing buyer and a willing seller, each having reasonable knowledge of all relevant facts.”¹⁹⁶

A variety of strategies may be used in negotiations to arrive at FMV. Medicare pricing is one such strategy, but it may be too low to represent FMV because it is a national standard set by the government with no negotiation opportunity.¹⁹⁷ Benchmark pricing provided by third parties who manage datasets of prior payments for similar transactions can be useful in estimating the FMV of the current transaction. Companies like Medidata provide data to help sponsors and research sites budget their research projects.¹⁹⁸ However, Andrew Snyder points out that benchmark pricing often fails to perfectly predict the current fair market value because it could rely on data that is too old and not location-specific

190. 42 C.F.R. § 411.357; 42 U.S.C. § 1395nn(e)(2).

191. 42 U.S.C. § 1395nn.

192. See *Fraud & Abuse Laws*, *supra* note 30. Charles Honart details the ways that FMV has also been used as a defense against illegal remuneration claims under the federal anti-kickback statute. Charles M. Honart, *Is Fair Market Value Dispositive in an Anti-Kickback Statute Case?*, STEVENS & LEE (June 22, 2023), <https://www.stevenslee.com/health-law-observer-blog/is-fair-market-value-dispositive-in-an-anti-kickback-statute-case> [<https://perma.cc/7SFH-9VB4>].

193. OIG Compliance Program Guidance, 68 Fed. Reg. at 23735.

194. 42 C.F.R. § 411.351 (with authority from 42 U.S.C. § 1395nn(h)(3)).

195. *Id.*

196. Snyder, *supra* note 17.

197. *Id.*

198. See Shelly Douras, *Better Data Better Decisions*, MEDIDATA (2023), <https://www.medidata.com/wp-content/uploads/2024/04/Rave-Grants-Manager-White-Paper-Nov-23.pdf> [<https://perma.cc/WF3H-JNEV>].

enough.¹⁹⁹ A hospital’s charge master may be used by research sites to develop a budget for use in negotiations, but this number represents the hospital’s starting point for contract negotiations with insurers and is not appropriate for FMV either.²⁰⁰

While these methods are commonly used, the prices arrived at through negotiations between healthcare institutions and insurers are likely the closest estimate of FMV.²⁰¹ As Snyder states, these negotiations are true “arm’s-length contracted values” and “represent the spirit of the fair market value requirements and a financial compromise between Medicare and charge master rates.”²⁰²

Although negotiations between healthcare institutions and insurers represent the best estimate of FMV for sponsors to pay research sites, additional challenges remain using current approaches. Most importantly, Norman Goldfarb describes how the characteristics of the study site and needs of the study sponsor influence the FMV in ways that CMS regulators may not recognize.²⁰³ For example, a research site known for completing a study protocol faster than other sites would provide significant value to a sponsor on a tight timeline, which would influence fair market value.²⁰⁴ However, a higher payment to this site versus a slower research site would be difficult to defend to CMS regulators.²⁰⁵ To demonstrate that the increased price represents FMV, the sponsor would need “to develop a valid, consistent, and well-documented process” for capturing the FMV nuances.²⁰⁶

B. FMV Is Used to Calculate Participant Payment

Participant payment is one part of the budget involved in negotiations between study sponsors and research sites. As a result, FMV should also be used to determine the proper payment to research participants to promote standardization, assist with budget development, streamline negotiations, and protect research sites and sponsors against liability for illegal remuneration or referral. For example, the National Health Council, an advocacy group for people living with chronic diseases, created an FMV calculator to compensate patients,

199. Snyder, *supra* note 17.

200. *Id.*

201. *Id.*

202. *Id.*

203. Norman Goldfarb, *When FMVs Collide: Coming to Terms with Fair Market Value*, APPLIED CLINICAL TRIALS (Jan. 19, 2024), <https://www.appliedclinicaltrials.com/view/when-fmvs-collide-coming-to-terms-with-fair-market-value> [<https://perma.cc/93K7-GEX7>].

204. *Id.*

205. *Id.*

206. *See id.*

caregivers, and patient groups for involvement in “patient engagement activities,” which could be extended to participation in clinical trials.²⁰⁷ This FMV calculator is based on a reimbursement and compensation approach, where participants are reimbursed for their expenses and compensated for their time and effort.²⁰⁸ The FMV calculator determines an hourly rate for patient compensation based on the type of activity they will perform for the clinical trial site, what expertise is needed, travel time, and other risks and considerations.²⁰⁹ To calculate this, the FMV uses “compensation data for positions that require similar experience, knowledge, skills, etc., as those needed to perform the activities for which patients are expected to be engaged.”²¹⁰

IV. FAIR MARKET VALUE CALCULATOR FOR PARTICIPANT DATA

Given that FMV is the standard way to budget for clinical trials and that FMV is used to value clinical data, payments to clinical trial participants should use FMV calculation methods. To avoid legal liability, compensation to participants for their data would require a rationale for the FMV of data. Like clinical trial sponsors must defend the rest of their budget as FMV, sponsors must also be able to defend their FMV calculations for participant payment. Paying participants for the FMV of their data is likely an effective approach, but certain considerations must be included.

A. Clinical Trial Data Valuation Approaches

Data valuation approaches are applied to clinical data.²¹¹ Under current data valuation approaches, “data can be valued based on its cost, its sale value, or its

207. See *Patient Compensation Tools*, NAT’L HEALTH COUNCIL, <https://nationalhealthcouncil.org/additional-resources/patient-compensation-tools> [https://perma.cc/59WU-ZQYL].

208. *Online Fair-Market Value (FMV) Calculator User Guide*, NAT’L HEALTH COUNCIL, https://nationalhealthcouncil.org/wp-content/uploads/2020/06/FMV-User_Guide.pdf [https://perma.cc/B2UZ-RABW]; NAT’L HEALTH COUNCIL, *PRINCIPLES FOR COMPENSATING PATIENTS FOR PATIENT ENGAGEMENT ACTIVITIES 2* (2021), https://nationalhealthcouncil.org/wp-content/uploads/2021/06/NHC-FMV_Patient-Engagement-Compensation_Principles-final_.pdf [https://perma.cc/5Y92-BDC9].

209. NAT’L HEALTH COUNCIL, *FAIR-MARKET VALUE HOURLY RATE METHODOLOGY 2*, https://nationalhealthcouncil.org/wp-content/uploads/2020/06/FMV_Hourly_Rate_Methodology.pdf [https://perma.cc/9BDS-VY8W].

210. *Id.*

211. *Fair Market Value of Clinical Data*, HEALTHCARE APPRAISERS (May 6, 2021), <https://healthcareappraisers.com/fair-market-value-of-clinical-data> [https://perma.cc/P8UB-NFJL].

income potential.”²¹² With enormous growth in recorded medical data and the increasing potential to fuel drug development, companies are placing significant economic value on clinical data.²¹³ When life sciences and software companies purchase and use clinical data to develop their products, FMV is used to calculate the value of the clinical data.²¹⁴ Current market-based approaches to valuation of clinical data lend insight into the calculation of FMV of clinical trial data. These methods are the market, cost, and income approaches.²¹⁵ Each method has pitfalls for use within the clinical trial context, so additional considerations are required to appropriately value participant data.

1. The Market Approach

Using the market approach, “the valuator uses prices paid for comparable data as reference points to estimate the value of patient data.”²¹⁶ When calculating FMV under the market approach, life science and software companies use data on comparable transactions from private or public databases.²¹⁷

In the context of paying participants for clinical trials, study sponsors would need to identify comparable sales of data to determine the amount to pay participants for their data. The rationale for using the market approach is an appeal to our desire for equity: transfer to participants some of the market value of their own data. If companies derive value from the use of participants’ data, then participants should rightly receive some of that profit. This approach would be most sensible when the study sponsor plans to sell access to the data. However, because comparable data is often lacking and difficult to locate in the clinical context,²¹⁸ it is likely more difficult to access in the clinical trial context. The purpose of clinical trials is to collect novel types of data, so there may be no comparable data at all.

212. Mike Fleckenstein et al., *A Review of Data Valuation and Building and Scoring a Data Valuation Model*, 5 HARV. DATA SCI. REV. (2023), <https://hdr.mitpress.mit.edu/pub/1qxkrnig/release/1> [<https://perma.cc/DS76-RLWT>].

213. LEK, *Tapping Into New Potential: Realizing the Value of Data in the Healthcare Sector*, <https://www.lek.com/insights/hea/eu/ei/tapping-new-potential-realising-value-data-healthcare-sector> [<https://perma.cc/BHF5-F7RE>].

214. *Fair Market Value of Clinical Data*, HEALTHCARE APPRAISERS (May 6, 2021), <https://healthcareappraisers.com/fair-market-value-of-clinical-data> [<https://perma.cc/P8UB-NFJL>].

215. Zigrang & Bailey-Wheaton, *supra* note 183, at 36.

216. *Id.* at 37.

217. *Fair Market Value of Clinical Data*, *supra* note 211.

218. *Id.*

2. *The Cost Approach*

Under the cost approach, the valuator “estimates value as the cost of reproducing or replacing the subject data.”²¹⁹ For clinical data, this can be accomplished by estimating costs based on outsourced clinical trials.²²⁰

In the context of clinical trials, this approach would require assuming a hypothetical sale of participant data between the study sponsor and a buyer. The amount that the seller would need to spend to recreate the data determines the minimum amount the buyer would pay the study sponsor in the hypothetical transaction for the seller to receive a profit. Using that figure, study sponsors could calculate the amount they would pay participants. Like the market approach, the rationale for the cost approach is to transfer to participants some profit from the sale of their data.

However, one difficulty in using the cost approach in the clinical context is that the valuation of clinical data under the cost approach is typically very high. The cost approach usually determines the price floor because a seller would not accept payment for less than the cost of recreating the data,²²¹ and the cost to recreate clinical data is typically very high.²²² While high valuation would result in higher participant compensation, it also would require researchers to dedicate significant funds towards participant payment. In addition, like the market approach, comparable data may be lacking.

3. *The Income Approach*

Under the income approach, “the valuator analyzes the future benefits that a buyer is expected to receive after its acquisition.”²²³ The income approach is also called the “Relief from Royalty” method.²²⁴ This method requires the company to estimate the cost of paying for a license to the data by calculating the net present value of their projected royalties.²²⁵ In the context of paying participants for clinical trials, study sponsors would pay participants the net present value of projected royalties for access to their data. The rationale is that companies used clinical trial participant data to develop their product and receive income and, therefore, participants should be entitled to receive royalties.

However, this method is of limited use to value clinical trial data because it

219. Zigrang & Bailey-Wheaton, *supra* note 183, at 37.

220. *Fair Market Value of Clinical Data*, *supra* note 211.

221. *Id.*

222. *Id.*

223. Zigrang & Bailey-Wheaton, *supra* note 183, at 36.

224. *Fair Market Value of Clinical Data*, *supra* note 211.

225. *Id.*

would be difficult to apply and implicate issues of undue influence and fairness. With long drug development timelines for most innovative drugs, forecasting effectiveness and future income revenue from the drug before a Phase I clinical trial took place would be exceedingly difficult. Further, determining the amount of “royalty” that the patient is entitled to would also be subjective and lack standardization. Calculating participant compensation based on expected “royalty” could also have major issues for undue influence and fairness. Expecting to share in the company’s profits, participants may be willing to take on more risk expecting high compensation and there would be a high variability in payment.

B. Considerations for the Valuation of Clinical Trial Data

Beyond the three market-based approaches discussed above, additional considerations impact the FMV of clinical trial participant data.

1. Clinical Trial Data are More Valuable than Clinical Data

Clinical trial data are more valuable than RWD primarily because clinical trial data come from a highly regulated and specialized population. While RWD can be useful, Vivek Rudrapatna notes that data quality issues, bias, and a lack of reliability often plague the analytical value of the data.²²⁶ In contrast, clinical trials have safeguards in place to ensure data quality,²²⁷ remove bias by randomizing the population, and limit variation by utilizing inclusion and exclusion criteria to limit the participant sample.²²⁸

In addition, data from two clinical trials may not hold identical values because methods to ensure data quality, lack of bias, and increased reliability may vary between clinical trials. To compensate clinical trial participants correctly based on the quality of the data, data quality, bias, and reliability would need to be determined from proposed methodology.

226. Vivek A. Rudrapatna & Atul J. Butte, *Opportunities and Challenges in Using Real-World Data for Health Care*, 130 J. CLINICAL INVESTIGATION 565 (2020), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6994109> [<https://perma.cc/U45X-2HKL>].

227. Colin Baigent et al., *Ensuring Trial Validity by Data Quality Assurance and Diversification of Monitoring Methods*, 5 CLINICAL TRIALS 49 (2008), <https://pubmed.ncbi.nlm.nih.gov/18283080> [<https://perma.cc/X4QD-2PJD>].

228. U.S. FOOD AND DRUG ADMINISTRATION, *EVALUATING INCLUSION AND EXCLUSION CRITERIA IN CLINICAL TRIALS 2* (2018). However, applying overly restrictive inclusion and exclusion criteria reduce generalizability. See Collins et al., *The Magic of Randomization Versus the Myth of Real-World Evidence*, 382 NEW ENG. J. MED. 674, 675 (2020).

2. Intensity and Risk of Data Collection from the Participant Impacts Value

The value of participant data may depend upon the invasiveness or burden of the data collection method to the participant. There are several types of data collection methods in clinical trials.²²⁹ Data collection methods that are more invasive, burdensome, or utilize more resources may warrant paying a higher FMV. Notably, FMV may vary by participant because different participants or population groups may experience different risks based on the procedures used.

In patient-reported data collection, patients either complete questionnaires on their own or with the help of an interviewer in person, by phone, through the mail, or on the internet.²³⁰ Questionnaires often collect data on “socio-demographic characteristics, lifestyle practices, medical history, and use of prescribed and/or over the counter medications” and the “participant’s knowledge and attitudes toward various lifestyle and disease predisposing factors.”²³¹

Proxy or informant data involves someone other than the patient responding to survey questions on their behalf.²³² Informant perspectives may be useful for certain situations, like determining the amount of assistance a patient requires with daily activities, and may also be useful when the informant is a caregiver.²³³

Researchers may review ambulatory or hospital medical records to help document a patient’s medical history.²³⁴ However, potentially important patient reported information might be lacking, especially if information is stigmatized or difficult to assess in the clinical setting.²³⁵ Researchers may also collect biologic materials, which involves more invasive methods to the participant than other methods.²³⁶ Methods range from collecting biologic samples like hair, saliva, urine, or serum to taking images to obtain deeper insights.²³⁷

In contrast to active data collection methods, where participants report their own data, passive data collection methods collect data automatically from participants through mobile or wearable devices and involve less effort by the

229. See Jane S. Saczynski et al., *Commonly Utilized Data Collection Approaches in Clinical Research*, 126 AM. J. MED. 10.1016 at 2 (2013), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3827694/pdf/nihms525481.pdf> [<https://perma.cc/G9L3-6A7Y>].

230. *Id.*

231. *Id.*

232. *Id.* at 3.

233. *See id.*

234. *Id.*

235. *Id.* at 4.

236. *Id.* at 4-5.

237. *Id.*

participant to collect data.²³⁸ While passive data collection methods place less burden on the participant than active data collection methods, these methods are more invasive because they collect more personal data.

The FMV of data retrieved from the participant may also depend on the study design: data, resource use, and time burden by participants vary across studies. First, a cross-sectional study requires the investigator to observe the exposure to a risk factor and cases of disease within a pre-selected period and location.²³⁹ Cross-sectional studies are often used with publicly administered national-level surveys, but data gathered from specialized surveys may also be used.²⁴⁰

Second, case-control studies involve “the initial selection of a sample of individuals with the disease or health outcome of interest (cases) and a comparison group (controls) of those without the disease under study or a related clinical condition.”²⁴¹ The researchers then determine whether the participants were exposed to the risk factor of interest.²⁴² Case-control studies are not very intensive to participants and are less costly than other study designs because they are retrospective, looking backward in time.²⁴³

In longitudinal studies, “healthy subjects free from disease are selected and are non-randomly categorized as to whether they were, or were not, exposed to a risk factor(s) of interest” and “[b]oth groups are followed over time for purposes of examining differences in the incidence rates of the study outcome(s) in persons exposed to the risk factor of interest as compared to those without this risk factor.”²⁴⁴ These studies require a large cohort and involve significant time investment for participant follow-up, increasing the burden on participants.²⁴⁵

Randomized controlled trials (RCTs), are the “gold standard” study design. RCTs follow participants over time like longitudinal studies, but an RCT randomizes the participants into treatment and control groups.²⁴⁶ Staff and patients may be blinded to their status of treatment or control to prevent both intentional and unintentional bias from influencing resulting data.²⁴⁷ Both RCTs

238. Kourtis et al., *supra* note 131, at 2.

239. Robert J. Goldberg et al., *Greater Knowledge and Appreciation of Commonly Used Research Study Designs*, 126 AM. J. MED. 169.e1 at 2 (2013) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3553494/pdf/nihms429602.pdf> [<https://perma.cc/F9PN-7P7N>].

240. *Id.*

241. Goldberg et al., *supra* note 239, at 3.

242. *Id.*

243. *Id.*

244. *Id.* at 4.

245. *Id.*

246. *Id.* at 5.

247. *Id.*

and longitudinal studies will likely place a greater burden on and have more invasive procedures for participants than cross-sectional or case-control studies.

3. *Data Management and Sharing Plans Impacts Patient Data Value*

As the market for clinical trial data has expanded and data sharing has increased, data management and sharing (DMS) plans have become necessary to reduce the risks to participants and sponsors that result from data sharing.²⁴⁸ DMS plans also help to ensure that the data from clinical trials is used properly to identify the efficacy of interventions and benefit society with new therapies.²⁴⁹ As a result, the National Institutes of Health (NIH) now requires researchers to include a DMS plan in their grant applications for NIH funding.²⁵⁰

With different approaches, DMS plans may influence the FMV of the data collected from clinical trial participants. While placing restrictions on the secondary use of data could reduce the FMV by making it more difficult for secondary users to use the data, restrictions may increase the FMV because the restrictions reduce the risk of sharing data. A typical DMS plan includes information about the type of data being shared, the length of data access for secondary users, the data storage location, and safeguards implemented, which each affect the risk borne by participants and sponsors by sharing the data.²⁵¹

The FMV would likely reflect this risk. For example, sharing participant data that is easily identifiable, allows for more widespread sharing over a longer period, is stored in a less protected location, and has fewer safeguards preventing unwarranted use is riskier to both the participant and sponsor and may therefore carry a higher FMV. Payment could be used not only to compensate participants and sponsors for riskier data sharing plans but also disincentivize the development of riskier DMS plans.

248. *See generally* INST. OF MED. OF THE NAT'L ACADEMIES, SHARING CLINICAL TRIAL DATA: MAXIMIZING BENEFITS, MINIMIZING RISK (2015), <https://www.ncbi.nlm.nih.gov/books/NBK269030> [<https://perma.cc/63HZ-DNLC>].

249. Jeffrey M. Drazen, *Sharing Individual Patient Data from Clinical Trials*, 372 NEW ENG. J. MED. 201 (2015).

250. *Final NIH Policy for Data Management and Sharing*, NAT'L INST. OF HEALTH, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-013.html> [<https://perma.cc/6Z7G-6J22>].

251. *See Supplemental Information to the NIH Policy for Data Management and Sharing*, NAT'L INST. OF HEALTH, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-014.html> [<https://perma.cc/4KE5-D7Y7>]; *see also* SHARING CLINICAL TRIAL DATA: MAXIMIZING BENEFITS, MINIMIZING RISK, *supra* note 248. Examples of DMS plans can be found at Writing a Data Management & Sharing Plan: Sample Plans, NAT'L INST. OF HEALTH, <https://sharing.nih.gov/data-management-and-sharing-policy/planning-and-budgeting-for-data-management-and-sharing/writing-a-data-management-and-sharing-plan#sample-plans> [<https://perma.cc/CP5S-MMR8>].

The type of data being shared likely affects the FMV of the data. Two data types, raw data and analyzable data sets, require specific attention. Raw data include “observations about individual participants used by the investigators.”²⁵² Raw data is sometimes shared because it “most closely reflects the study observations” and allows secondary data users to accurately observe the limitations of the dataset.²⁵³ Raw data also may contain sensitive or identifiable data, which increases the risk that participant privacy rights will be infringed.²⁵⁴

An analyzable data set is created from the raw data after an editing and cleaning process.²⁵⁵ Like raw data, however, an analyzable data set may include sensitive or identifiable data on participants.²⁵⁶ Further, since some information from the raw dataset has been edited, secondary data users may miss important information about the data critical to their results.²⁵⁷ Accurate secondary data analysis is important to the development of useful interventions.

Data management and sharing plans consider the timeline that the data is available for sharing, which likely affects the FMV of the data.²⁵⁸ Allowing secondary users to access data over a longer timeline is likely to increase the risk to participants and sponsors, thereby increasing the FMV of the data. The data storage location affects FMV because storing data in less secure locations likely increases the risk of unauthorized data sharing. The NIH recommends that data gathered by NIH-funded clinical trials are stored in repositories that balance easy access and broad and measured reuse with security measures that preserve the integrity and confidentiality of the data so that only authorized individuals can access the data.²⁵⁹

The number of safeguards protecting the sharing of clinical trial participant data also likely affects the FMV of the data. With fewer safeguards, there is more risk to the participant, study sponsor, and society. Safeguards protect participant privacy and prevent unfair use of data for commercial purposes.²⁶⁰ For example, companies that can obtain regulatory approval for therapies based off of shared clinical trial data have fewer incentives to obtain their own data to develop novel

252. *The Clinical Trial Life Cycle and When to Share Data*, in SHARING CLINICAL TRIAL DATA: MAXIMIZING BENEFITS, MINIMIZING RISK, *supra* note 248, at 97.

253. *Id.* at 97-98.

254. *Id.* at 98.

255. *Id.* at 98-99.

256. *Id.*

257. *Id.* at 99-100.

258. *Final NIH Policy*, *supra* note 250.

259. *Supplemental Information to the NIH Policy for Data Management and Sharing*, NAT'L INST. OF HEALTH, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-016.html> [<https://perma.cc/Z7MW-Z3WG>].

260. *See Access to Clinical Trial Data: Governance*, in SHARING CLINICAL TRIAL DATA: MAXIMIZING BENEFITS, MINIMIZING RISK, *supra* note 248, at 143.

therapies.²⁶¹ Safeguards also protect against invalid secondary analyses because users of the secondary data could misunderstand the circumstances around which the data was gathered.²⁶² The risk of misinterpretation of clinical trial data to sponsors and to society is large. Misinterpretation of clinical trial data can fuel inaccurate results, which potentially creates liability for sponsors and harms patients.²⁶³ Finally, safeguards mitigate the risk that sponsors who acquire data from clinical trials are given appropriate credit for their work.²⁶⁴ If data is shared before the team who has gathered the data are able to publish study results, then other researchers can publish first and destroy the value to the team that did the work first.

Several common safeguards likely enhance the FMV of the data by protecting participant privacy. One safeguard is the de-identification of study results. De-identification serves to protect participant privacy when study results are shared by removing any personal identifiers from the data.²⁶⁵ In addition, sponsors may elect to make data available for online use only without the option to download the data. Through this mechanism, sponsors can limit data analysis to certain parameters and, by prohibiting download, limit the dissemination of data.²⁶⁶ Data use agreements (DUAs), “agreements executed between the party sharing the data and the data recipient that bind the recipient to certain conditions related to the data,” are also an important safeguard.²⁶⁷ DUAs commonly prohibit attempts at re-identification, further data sharing, supporting unfair commercial use, publication of results from the use of the data without acknowledgement, and assigning “intellectual property rights for discoveries from the shared data.”²⁶⁸

Another safeguard protecting participant privacy is to require expert review of data requests.²⁶⁹ In reviewing data requests, access is controlled based on qualifications or study protocols.²⁷⁰ Reviewers commonly look to see whether the research team has relevant expertise for their protocol and whether the protocol is likely to meet the scientific objectives of the study.²⁷¹ However, due to issues of conflict of interest in the data request review process, data sharing plans may

261. *Id.* at Box 5-2.

262. *Id.* at 143-44.

263. *See id.*

264. *Id.* at 144.

265. *Id.*

266. *Id.* at 147.

267. *Id.*

268. *Id.* at 148.

269. *Id.* at 149.

270. *Id.* at 150-52.

271. *Id.*

create independent review panels, such that those reviewing the data request are free from bias.²⁷² In addition to independent review panels, implementing further transparent methods will likely reduce bias in the review process and data sharing process generally.²⁷³ Transparent methods can include publishing review criteria, the number of requests, and reasons for denial.²⁷⁴ As data sharing evolves, new insights on safeguards and standards will help determine the value of clinical trial participant data.²⁷⁵

4. Value of the Data to the Participant

Research shows that Americans deeply value their medical privacy.²⁷⁶ This priority is codified in federal privacy laws and regulations like the Health Insurance Portability and Accountability Act (HIPAA),²⁷⁷ which seeks “to assure that individuals’ health information is properly protected.”²⁷⁸ Patient data and privacy protection is a clear goal of this law.

However, the value of patient health data is not well understood.²⁷⁹ Alessandro Acquisti has shown that the value of data to individuals is difficult to measure because the value of data varies between people, varies between data types, and changes over time.²⁸⁰ In addition, without an open market for personal data in which consumers participate as willing sellers and buyers, it is difficult to

272. *Id.* at 154.

273. *Id.* at 156.

274. *Id.*

275. The Clinical Data Interchange Standards Consortium is a non-profit organization developing standards for the exchange of digital clinical study data among associations. See W. Kuchinke et al., *Extended Cooperation in Clinical Studies Through Exchange of CDISC Metadata Between Different Study Software Solutions*, 45 *METHODS INFO. MED.* 441 (2006); S.M. Meystre et al., *Clinical Data Reuse or Secondary Use: Current Status and Potential Future Progress*, 26 *Y.B. MED. INFORMATICS* 38 (2017). In addition, data banks are used to share data relating to a single disease or set of diseases. For example, ARAMIS is a consortium of North American rheumatic disease data banks used for multiple clinical trials. James F. Fries & Dennis J. McShane, *ARAMIS (The American Rheumatism Association Medical Information System): A Prototypical National Chronic-Disease Data Bank*, 145 *W.J. Med.* 798 (1986).

276. See Inst. of Med. of the Nat’l Academies, *The Value and Importance of Health Information Privacy*, in *BEYOND THE HIPAA PRIVACY RULE: ENHANCING PRIVACY, IMPROVING HEALTH THROUGH RESEARCH* (2009).

277. See *id.*

278. *Summary of the HIPAA Privacy Rule*, U.S. DEP’T OF HEALTH AND HUM. SERV. (Mar. 14, 2025), <https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html> [<https://perma.cc/AM4B-3TR6>].

279. Nelson Shen, *Understanding the Patient Privacy Perspective on Health Information Exchange: A Systematic Review*, 125 *INT’L J. MED. INFORMATICS* 1 (2019).

280. Alessandro Acquisti et al., *The Economics of Privacy*, 54 *J. ECON. LITERATURE* 446 (2016).

determine the value of personal data.²⁸¹

V. PAYING PARTICIPANTS THE FAIR MARKET VALUE OF THEIR DATA
COULD CONFORM TO THE UNITED STATES' LEGISLATIVE AND REGULATORY
FRAMEWORK

Paying clinical trial participants the FMV of their data could conform to our nation's legislative and regulatory framework with reform. Currently, while participants are paid for their time spent engaged in clinical trial procedures, they are not paid for the data they contribute. This practice infringes on the justice and fairness component of the FDA guidelines for participant payment. By providing their data, participants take on risks of privacy violations for which they are not currently compensated. As a result, paying participants for their data and educating participants about the risks of providing their data would improve justice, transparency, and fairness without increasing the risk of undue influence.

Policy reform is necessary to encourage clinical trial sponsors to implement (and IRBs to approve) this payment innovation. While this paper provides a rationale for determining the FMV of participant data, there are currently no standards for the value of participant data recognized by the FDA and IRBs, making IRBs unlikely to approve payment for participant data contributions. The FDA, SACHRP, OHRP, and IRBs should work together to develop guidance and standards for clinical trial sponsors to pay participants for their data contributions.

*A. Paying Clinical Trial Participants for Their Data Increases Justice,
Fairness, Ethics, and Diversity in Clinical Trials*

Paying participants for the FMV of their data will enhance diversity, because data from a diverse and representative sample is more valuable than data from a uniform sample. Current payment mechanisms can work against our diversity goals by paying wealthier individuals more for participation in clinical trials. For example, the compensation method, which pays participants for lost economic opportunities, favors higher payment to people who have higher incomes because the opportunity cost for them to skip work to participate in a clinical trial is greater than that for people with lower incomes.²⁸² Indeed, SACHRP's calls for equal payment under the compensation method²⁸³ have been met with concerns of undue influence for people with lower incomes.²⁸⁴

281. *Id.*

282. *Id.*

283. *Id.*

284. Grady, *supra* note 46, at 1149.

Paying participants for the FMV of their data will offset concerns of inequity and undue influence under the compensation model because data from participants who add diversity to a clinical trial is more valuable than that of participants who do not add diversity. Greater participant diversity in a clinical trial adds to the generalizability of the results, ensures more representative science, increases a drug's safety and effectiveness, and increases the drug's value to society.²⁸⁵ Because participant diversity adds value to the clinical study, clinical trial sponsors would be required to increase the pay of participants who add more diversity to the sample. A safer drug is better for consumers and reduces costs for drug companies. It costs a staggering amount to develop a drug, so it is critical for companies to create a drug that is safe and effective. In addition, a safer drug will protect consumers and could reduce mass tort lawsuits, which cost pharmaceutical companies billions of dollars annually.²⁸⁶ Also, intuitively, safer drugs are likely to be used more often by consumers, which increases revenues for pharmaceutical companies. Therefore, a more diverse sample of clinical trial participants is more valuable to clinical trial sponsors, and sponsors should be willing to compensate participants who add diversity accordingly.

B. Paying Participants Increases Trial Costs, but Costs Could be Offset by Efficiencies Gained and Risks Averted

On the other hand, paying clinical trial participants the FMV of their data could increase costs for clinical trials, especially those that use data-intensive methods. Higher costs of clinical trials could disincentivize pharmaceutical manufacturers from sponsoring clinical trials and, as a result, chill drug development. The costs of clinical trials are already high, which is a major concern for pharmaceutical companies.

Paying participants the FMV of their data would increase costs in several ways. First, with the rise of more data-intensive clinical trial methods, such as pragmatic methods and passive data collection, the time and effort burden of clinical trials is low, but the data collection intensity is high. In these clinical trials, paying participants for the FMV of their data would likely be more costly than paying participants for their time and effort.

Second, paying participants for their data could impose additional costs on obtaining informed consent. Obtaining informed consent is burdensome and

285. See NATIONAL ACADEMIES, *supra* note 107, at 24–30.

286. STEVEN GARBER, RAND INST. FOR CIV. JUST., ECONOMIC EFFECTS OF PRODUCT LIABILITY AND OTHER LITIGATION INVOLVING THE SAFETY AND EFFECTIVENESS OF PHARMACEUTICALS, at xv (2013).

time-consuming for participants and researchers. Instead of time and effort, from which it is easier to rationalize a value, it could be more difficult for participants to rationalize the value of their own clinical data, increasing the burden for researchers to explain the risks and benefits of the study.

Third, when RWD is used in a clinical trial, the payment of participants based on their data would also raise questions about compensation for participant RWD. Clinical trial sponsors would then be not only paying medical institutions for access to RWD but also paying participants for the use of RWD. Paying participants, in addition to medical institutions, for the use of RWD is appropriate because medical institutions perform the effort of collecting this data as part of clinical care. Paying participants for the use of their RWD would ensure that they are being compensated for imposing increased risk of privacy violations and data utilization on participants. With massive expansion of the healthcare analytics market,²⁸⁷ RWD is expensive and highly valued. Clinical trial sponsors who pay participants for using their RWD would likely have to pay participants high additional costs under a FMV approach, thereby increasing the cost of clinical trials.

However, efficiencies gained and risks averted could offset these additional expenses. Operational efficiency represents a large portion of the costs in a clinical trial. For example, in one study measuring costs across 726 studies (including Phase I, II, and III clinical trials) administered by seven major pharmaceutical companies, “the disparity in operational efficiency . . . between companies in the data set equate[d] to a roughly \$700 million annual difference in overall clinical trial costs for the average-sized company.”²⁸⁸ With efficiency differentials representing such a large portion of clinical trial costs, efficiency gains could offset additional expenses.

Several efficiencies offset costs. First, paying clinical trial participants the FMV of their data could speed up the timeline for drug development by improving recruitment and retention without increasing the risk of undue influence. Participants may be more attracted to payment rationales that account for the value of extracting data from them and the risks of using their data after their participation is complete. In addition, IRBs may more easily accept higher payment to participants when clinical trial sponsors have a strong rationale for the value of patient data, drawing on standardized FMV approaches.

Paying clinical trial participants the FMV of their data also promotes standardization among payments from sponsors to research sites to satisfy the FMV exception to the Stark Law and reduce the likelihood of liability under the

287. *Healthcare Analytics Market Size*, *supra* note 179.

288. Linda Martin et al., *How Much Do Clinical Trials Cost?*, 16 NATURE REVIEWS DRUG DISCOVERY 381 (2017).

AKS. Because the Stark Law is designed to prevent fraud and abuse, a FMV exchange operates as an exception against liability.²⁸⁹ FMV also has been used as a defense against illegal remuneration under the federal anti-kickback statute.²⁹⁰

Additionally, this approach would incentivize companies to formulate a better data management plan, including plans for how collected data will be used. According to researchers, “studies have shown that it is possible to reduce clinical procedure costs by simplifying clinical trial protocols and planning carefully to avoid costly protocol amendments, whenever possible.”²⁹¹ For example, reducing the amount of data collection through better planning can reduce costs as a large portion of data collected ultimately is unused, which “add[s] \$20–\$35 million in direct drug development costs for the average drug.”²⁹² However, this also could discourage the collection of data that may end up being necessary, thereby imposing additional costs if the data ends up being necessary.²⁹³ Despite a change in payment mechanisms, the risk of collecting too little data may drive clinical trial sponsors to continue the status quo.

C. Legislative and Regulatory Changes Are Required to Encourage Payment to Trial Participants for Their Data

While payment for participants of clinical trials based on the FMV of their data theoretically fits within the current legislative and regulatory structure, IRBs will unlikely approve the payment mechanism without additional policy changes. The FDA should issue guidance that identifies payment for the FMV of data as a possible payment mechanism. Currently, the FDA does not comment on the use of the value of data as the baseline for clinical trial participant compensation. With no guidance, the industry and IRBs are likely hesitant to offer this type of payment to clinical trial participants. FDA guidance has been helpful in clarifying payment mechanisms in the past. For example, the FDA’s January 2018 guidance on payment and reimbursement to research subjects clarified that “reimbursement for travel expenses to and from the clinical trial site and associated costs such as airfare, parking, and lodging [does not] raise issues regarding undue influence.”²⁹⁴ Similar guidance on payment for participant data

289. 42 C.F.R. § 411.357; 42 U.S.C. § 1395nn(e)(2).

290. Honart, *supra* note 192.

291. Sertkaya et al., *Key Cost Drivers of Pharmaceutical Clinical Trials in the United States*, 13 CLINICAL TRIALS 117 (2016).

292. *Id.*

293. *Id.*

294. *Payment and Reimbursement to Research Subjects: Guidance for Institutional Review Boards and Clinical Investigators*, U.S. FOOD & DRUG ADMIN. (Jan. 25, 2018), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/payment-and-reimbursement-research-subjects> [<https://perma.cc/83L7-T5VF>].

would also allow sponsors to start using and IRBs to start approving the payment mechanism.

In addition, the FDA, SACHRP, and OHRP should collaborate with IRB representatives to determine appropriate standards for payment for clinical trial participants based on the FMV of their data. While this paper has outlined several options for determining standards to guide clinical trial participant data valuation, there are currently a lack of standards to help IRBs determine the appropriate mechanism for paying for participant data without causing undue influence. The agencies' innovations in payment standards could be tested for feasibility and effectiveness within pilot programs that measure recruitment, retention, and undue influence. Until standards are developed, IRBs may be hesitant to approve this type of payment.

As a further step, Congress, in partnership with the FDA, SACHRP, and OHRP, might consider whether compensation for clinical trial participants based on the FMV of their data should be mandated by law. This step would be relatively extreme given that neither Congress nor regulatory agencies currently mandate any payment for clinical trials. However, it would push clinical trial sponsors to overcome short-term cost concerns in favor of enhanced recruitment potential.

Finally, to enhance diversity and access in clinical trials, tax changes must happen simultaneously with innovation in payment mechanisms. Congress should pass a law removing clinical trial compensation from taxable income to enhance the diversity of and access to clinical trials. Currently, compensation is treated as taxable income and must be reported to the IRS.²⁹⁵ In response to this issue, Representatives Mike Kelly and Chrissy Houlahan have introduced a bill that “aims to exempt all payments received by participants in clinical trials from being counted towards their gross income.”²⁹⁶ These proposed changes are important for improving diversity of and access to clinical trials.

D. Participant Payment Reform Should Be Used in Concert with Non-Market Based Solutions

Because a market-based solution may not entirely solve the market failures present in clinical trials, participant payment reform should also be used in concert with other strategies to increase recruitment. In addition to participant

295. *About Form 1099-MISC*, *supra* note 28; Largent et al., *supra* note 29.

296. Press Release, Rep. Mike Kelly, Kelly, Houlahan introduce “Harley Jacobsen Clinical Trial Participant Income Exemption Act” (Jan. 29, 2024), <https://kelly.house.gov/media/press-releases/kelly-houlahan-introduce-harley-jacobsen-clinical-trial-participant-income> [<https://perma.cc/TVV3-L66C>].

compensation, major barriers to participating in clinical trials include mistrust, time and resource constraints, and awareness of clinical trials.²⁹⁷ To address these barriers, community-based, patient-centered, and technological methods are useful.

One community-based method to improve recruitment and retention could include training community clinicians to become involved in clinical trials.²⁹⁸ Community clinicians understand the populations they serve, have trusting relationships with their patients, and are located close to their patients.²⁹⁹ In addition, clinical trial sponsors can build a connection with community organizations to enhance recruitment efforts and combat mistrust of clinical research.³⁰⁰

Technological tools, including electronic medical records, social media, registries, email or text messaging, mobile applications, and AI, can improve outreach to boost recruitment.³⁰¹ For example, one resource barrier to recruitment is the high burden of manually matching patients to an appropriate clinical trial. Initial tests of AI methods to automate the matching process have shown promising results, achieving an accuracy comparable to human expert judgment.³⁰²

CONCLUSION

Failure to recruit and retain a large and diverse sample of clinical trial participants reduces pharmaceutical safety and innovation, imposes major financial costs to biotech and pharmaceutical companies, and limits access to novel drug therapies for society and for patients who need them. Paying clinical trial participants directly for the value of their data would combat this failure while reinforcing fundamental principles of equity and fairness. However, current legislative and regulatory rules, as well as industry standards, limit the innovation necessary to increase recruitment and retention. Moreover, current payment mechanisms fail to enhance the diversity of clinical trial participation, leading to drugs that are not sufficiently tested on the target populations that they

297. Luther T. Clark et al., *Increasing Diversity in Clinical Trials: Overcoming Critical Barriers*, CURRENT PROBS. IN CARDIOLOGY 148, 152-53 (2019).

298. Janet Woodcock et al., *Integrating Research into Community Practice—Toward Increased Diversity in Clinical Trials*, 385 NEW ENG. J MED 1351 (2021).

299. *Id.*

300. Clark et al., *supra* note 297, at 165.

301. Geoff K. Frampton et al., *Digital Tools for the Recruitment and Retention of Participants in Randomised Controlled Trials: A Systematic Map*, 21 TRIALS 478 (2020); Qiao Jin et al., *Matching Patients to Clinical Trials with Large Language Models*, 15 NATURE COMMUNICATIONS 9074 (2024).

302. Jin et al., *supra* note 301.

aim to treat.

In addition to failures to recruit and retain participants, the evolution of data-intensive clinical trial methods and an increasing market for clinical data have created new considerations for payment of clinical trial participants. These new methods of gathering and utilizing patient data challenge the current FDA guidance on payment to clinical trial participants. Most crucially, by not paying patients for their own data, even though that data is already being sold by other actors, we are failing to meet the FDA guidance that compensation to trial participants must be “just and fair.” Clinical trial participants undergo significant risk in offering up their bodies, time, effort, and data to clinical trial sponsors to develop new drug therapies for the benefit of society. Nearly everyone in the system benefits from this data—except the rightful owners.

We evaluate and propose several standards to engage in that trial data valuation effort. First, current valuation approaches used for non-trial patient data can be helpful at providing a baseline. However, clinical trial data is more valuable than clinical patient data alone, because trials consist of a well-regulated sample of participants created through rigorous inclusion and exclusion criteria. In addition, the intensity and invasiveness of the procedures used in the clinical trial, the robustness of a clinical trial data sharing plan, and the value of the data to the clinical trial participants themselves should be considered when valuing clinical trial participant data.

Accomplishing this goal of direct payment to trial participants based on the value of their data requires legislative and regulatory reform. The FDA should issue guidance that identifies payment for the FMV of clinical trial patient data as a legal mechanism, regulatory agencies should collaborate with Institutional Review Boards to determine appropriate standards for payment, and Congress should consider whether compensation for clinical trial participants should be mandated by law. Doing so will fairly account for participants’ essential and risky data contributions.

In sum, paying clinical trial participants for their data will improve the recruitment, retention, diversity, and fairness of clinical trials. A new payment regime might even help accelerate pharmaceutical development.