



## **Paying Research Participants: Ethical Guidance for IRBs and Investigators**

Harvard Catalyst Regulatory Foundations, Ethics, & Law Program

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## INTRODUCTION

Paying people who participate in research is a common and widely accepted practice.<sup>1</sup> Nonetheless, evaluating offers of payment can be challenging from an ethical and regulatory perspective. From the standpoint of regulatory guidance, the main concern is that offers of payment could compromise understanding or otherwise distort an individual's decision to participate in research, undermining or even invalidating informed consent.<sup>2</sup> At the same time, United States regulatory guidance stops short of saying when or at what point payment distorts judgment and indeed recognizes that drawing clear borders or bright lines is not feasible.<sup>3</sup> Moreover, there is little empirical work on this topic to inform evaluation of payment offers. This can lead to uncertainty over how to set reasonable payment limits. In addition, while avoiding undue influence is important, there are reasons favoring payment that warrant deliberation within and among IRBs. These reasons stem from considerations of fairness and appropriate recognition of the expenses, time, and burdens borne by research participants, as well as the importance of facilitating recruitment in IRB-approved studies.

This guidance document makes recommendations on several key ethical and regulatory issues associated with paying research participants, in three parts. The first part addresses foundational regulatory and conceptual issues involved with evaluating offers of payment, including the definition of key but ill-defined regulatory terms (i.e., 'coercion' and 'undue influence'), the distinction between payment appropriately and inappropriately (or 'unduly') motivating research participation, and general strategies for reducing the risks of excessive payment.

The second part of the document sets out a practical framework for proposing and evaluating offers of payment that categorizes payments into one of three categories, depending on their rationale and justification: (1) reimbursement for out-of-pocket expenses incurred by participants, (2) compensation for participant time and burdens, and (3) recruitment incentives.

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<sup>1</sup> This guidance document is based in part on Gelinias L, Largent EA, Cohen IG, et al. "A Framework for Ethical Payment to Research Participants." *The New England Journal of Medicine* 378/8 (2018). The ideas in that article were in turn informed and sharpened by a half-day working group on payment held at Harvard Law School in December of 2016, in conjunction with a public conference titled "Payment to Research Participants: Ethical and Regulatory Parameters." We are very grateful to the members of the working group, listed here in Appendix C. Full citations for all works cited in the notes are available in Appendix D.

<sup>2</sup> OHRP, [Informed Consent FAQs](#), "When does compensating subjects undermine informed consent or parental permission?"

<sup>3</sup> "Because of their relative nature and lack of clear-cut standards on the boundaries of inappropriate and appropriate forms of influence, investigators and IRBs must be vigilant about minimizing the possibility for coercion and undue influence" (OHRP, [Informed Consent FAQ](#), "When does compensating subjects undermine informed consent or parental permission?").

This framework provides an intuitive template for breaking down payment sums and understanding their rationale in many cases.

The third part of the document addresses issues associated with the timing of payment as well as whether, or how, the fact that a study holds the prospect of direct health benefit should influence payment offers.

Throughout, the document makes several assumptions.

- First, the document’s scope is limited to providing recommendations on how researchers and IRBs should evaluate cash and cash-equivalent offers of payment (e.g., gift cards, coupons, prize lotteries) made prospectively to adults who are considering enrolling in research. Our analysis does not include, for example, tokens of appreciation (e.g., gift cards not disclosed up front) offered after research is complete, or non-monetary goods (e.g., ancillary medical care), although such offers may raise some of the same issues.
- Second, the document assumes that the participant protections afforded by IRB review are in place. In particular, the guidance that follows assumes that a well-functioning IRB has discharged its regulatory obligation to ensure appropriate study design, including a favorable risk-benefit determination that minimizes overall risks to participants and does not count payment as a benefit of participation.
- Third, importantly, this framework was developed with a specific focus on the United States and participants in developed countries. We acknowledge important and potentially distinct ethical issues with payment to vulnerable and underrepresented populations, in low and middle-income countries or elsewhere. These deserve their own ethical and process analyses, which we plan to address at a later time.

## EXECUTIVE SUMMARY

The main recommendations of this document are as follows (see also [Appendix A](#) and [B](#)).

1. In the context of research, the key regulatory terms ‘coercion’ and ‘undue influence’ are often used in imprecise ways such that IRB members risk miscommunicating with each other. To avoid this problem, and in line with the Belmont Report and regulatory guidance, we posit that these terms should be understood as follows:
  - a. **Coercion** occurs when a *threat of harm* is used to influence decision-making, undermining the possibility of voluntary informed consent.
  - b. **Undue influence** occurs when an *offer of an excessive or inappropriate reward* distorts decision-making, compromising a prospective participant’s evaluation of

risks or voluntary choice to participate, thereby undermining the possibility of voluntary informed consent.<sup>4</sup>

2. The main concern raised by payment is the risk of undue influence, not coercion, as payment involves an offer and never a threat.
3. Being motivated by payment to participate in research, even when someone would not otherwise have made the choice to participate, is not by itself concerning; payment only raises concerns when it threatens to distort decision-making.
4. IRBs concerned about undue influence should consider placing increased safeguards around informed consent (such as methods to ensure comprehension) as payment amounts increase.
5. The IRB's risk-benefit determination, made independently of payment considerations, ensures that the risks of research are reasonable compared to the benefits and acts as a significant safeguard against payment influencing people to make a bad or unreasonably risky choice to participate in research, thereby lowering the stakes around payment offers.
6. Offers of payment can be categorized into one of three categories: (1) reimbursement for-out-of-pocket expenses, (2) compensation for time and burdens, and (3) recruitment incentive. Reimbursement and compensation are service-based reasons for offering payment; recruitment incentives, by contrast, aim simply to improve participation rates.
7. Reimbursing participants for reasonable expenses they incur is fair, appropriate, and desirable, and there is a rebuttable presumption in favor of reimbursement that can be overturned in particular cases.
8. Compensating participants for their time and assumption of research-related burdens is fair and desirable. When evaluating compensation rates, IRBs should consider what would be fair compensation for similar time-commitments and burdens in contexts outside of research.
9. There is nothing inherently wrong with offering recruitment incentives that go beyond what is demanded by fair reimbursement and compensation. IRBs have ethical reasons to consider the positive role that payment might play in facilitating recruitment.
10. When considering the timing of payment, the risk of undue influence should be weighed against the importance of incentivizing study completion, taking into account safeguards that exist for identifying participants who should not continue in the study (e.g., ongoing monitoring by study staff).
11. The prospect of direct medical benefit can justify paying less than would otherwise be considered fair, but should not typically be grounds for withholding reimbursement.

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<sup>4</sup> National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, [The Belmont Report](#), Part C; United States Office for Human Research Protections (OHRP), [Informed Consent FAQs](#), “What does it mean to minimize the possibility of coercion or undue influence?”

## PART 1: KEY REGULATORY AND CONCEPTUAL ISSUES

### 1. *Coercion and undue influence*

Discussions of paying research participants often focus on the risk that payment will undermine voluntary informed consent to participate in research. Both the U.S. “Common Rule” and Food and Drug Administration (FDA) regulations instruct researchers to minimize the possibility of ‘coercion’ and ‘undue influence’ during the consent process but do not connect payment to these concepts or explicitly mention payment at all.<sup>5</sup> Regulatory guidance on payment does, however, connect payment and consent. The existing regulatory guidance on payment comes primarily from an Office of Human Research Protections (OHRP) FAQ and an FDA Information Sheet.<sup>6</sup> OHRP acknowledges that payment is “a common and, in general, acceptable practice” before going on to say that “IRBs should be cautious that payments are not so high that they create an ‘undue influence’ or offer undue inducement to participate in research” (OHRP).<sup>7</sup> The FDA Information Sheet echoes this warning, saying that “the IRB should review both the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive or present undue influence” (FDA Information Sheet).<sup>8</sup>

**Point 1a:** Regulatory guidance does not specify whether the ethical concern with payment is the risk of ‘coercion,’ the risk of ‘undue influence,’ or both. This raises the possibility that these terms will be used in vague or inaccurate ways—as “catchalls”—to describe a variety of concerns about payment or in ways that inhibit more nuanced discussion of key questions. Adopting shared definitions may help IRB members and researchers engage in more productive discussion of the underlying ethical issues.

**Recommendation 1a:** While there is a debate in research ethics over the correct definitions of ‘coercion’ and ‘undue influence,’ and while different definitions have costs and benefits, for the purpose of this document we will understand these terms in accordance with OHRP guidance, as follows:

Coercion occurs when an *intentional threat of harm* is used to influence decision-making, undermining the possibility of valid informed consent.

Undue influence occurs when an *offer of an excessive reward* distorts decision-making, compromising a prospective participant’s evaluation of risks or affecting the

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<sup>5</sup> [45 CFR 46.116](#); [45 CFR 50.20](#).

<sup>6</sup> OHRP, [Informed Consent FAQs](#), “When does compensating subjects undermine informed consent or parental permission?” FDA, “[Payment and Reimbursement to Research Subjects— Information Sheet](#).”

<sup>7</sup> OHRP, [Informed Consent FAQs](#), “When does compensating subjects undermine informed consent or parental permission?”

<sup>8</sup> FDA, “[Payment and Reimbursement to Research Subjects— Information Sheet](#).”

voluntariness of their choice, thereby undermining the possibility of valid informed consent.<sup>9</sup>

**Point 1b:** These definitions draw a sharp line between ‘coercion’ and ‘undue influence.’ The key difference is that coercion always involves a **threat** of something undesirable while undue influence involves an **offer** of something desirable that distorts decision-making. Because of this, a genuine offer of payment will never be coercive.

**Recommendation 1b:** The main ethical and regulatory concern with payment is the risk of undue influence, not coercion. The research community should not conceptualize the risk posed by payment in terms of ‘coercion’ or worry about ‘coercive’ offers of payment.

**Point 1c:** Money is often an acceptable influence on decision-making and source of motivation, such as when individuals rationally (and without distortion) weigh the benefits of money when deciding on employment options. The same holds for research participation. Indeed, OHRP explicitly recognizes that “compensation may be an acceptable motive for agreeing to participate in research.”<sup>10</sup> Given this, being motivated by money to participate in research does not on its own raise concerns about *undue* influence. IRBs and researchers should be mindful of the distinction between *mere* influence, which is typical and not problematic, and undue influence, which is or may be problematic.

**Recommendation 1c:** Being motivated by payment to participate in research, even if someone would not have made the choice to participate in the absence of payment, is not by itself ethically concerning. The problem arises when payment leads to a distortion of decision-making that puts the validity and voluntariness of consent in doubt.

**Example 1a:** Patient A—who is sick—goes to see their primary care physician, Dr. B. Dr. B, tells Patient A that Patient A will not receive care until she agrees to participate in a research study that Dr. B is conducting, and subsequently offers Patient A \$200 to participate. Having no other option to receive the medical care that she needs, Patient A enrolls in the study.

**Analysis 1a:** Since this case involves a threat to withhold treatment when doing so would wrongfully harm Patient A, it is a case of coercion. Such coercion invalidates informed consent and is ethically wrong, and offering payment on top of the threat does not change this.

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<sup>9</sup> OHRP, [Informed Consent FAQs](#), “What does it mean to minimize the possibility of coercion and undue influence?” See also Wertheimer and Miller 2008; Largent et al. 2013; and Largent and Lynch 2017.

<sup>10</sup> OHRP, [Informed Consent FAQs](#), Note to “When does compensating subjects undermine informed consent or parental permission?”

**Example 1b:** Rather than threatening to withhold care, Dr. B offers Patient A what Patient A perceives to be a large sum of money, over \$5,000, to enroll in the research study that Dr. B is conducting. Patient A is currently in need of cash and the offer of payment is a strong motivator for Patient A to enroll. In subsequent conversations with Patient A, research staff begin to suspect that Patient A does not fully appreciate the burdens and risks of the study, being single-mindedly focused on the payment. The research coordinator assigned to obtain Patient A's consent suspects that the offer of payment may be clouding her judgment and placing the validity of Patient A's consent to enroll in the study in doubt.

**Analysis 1b:** Since this case involves an offer of something desirable (i.e., money), it is not a case of coercion. It may, however, be a case of undue influence, if as the offer of payment causes Patient A to ignore or under-estimate the risks of research, thereby casting doubt on informed consent. Had Patient A *rationaly* weighed the benefits of the payment against the risks and burdens of participation and decided that study participation was "worth it," all things considered, this would be a case of *mere* rather than *undue* influence and would not raise ethical concerns. That said, it may difficult and even impossible in practice to know if a subject is rationally or unduly influenced by an offer of payment (see below, Section 2).

## SECTION 1 SUMMARY

- **Coercion** involves an intentional **threat of harm** that influences decision-making and undermines informed consent, while **undue influence** involves an **offer of something desirable** that distorts decision-making and undermines informed consent.
  - Given this, the main ethical and regulatory concern with offers of payment is undue influence, not coercion.
  - Payment can be an acceptable motivation to participate in research, when individuals rationally weigh the payment offered against the risks and burdens of participation. This is 'mere' influence.
  - Undue influence, by contrast, occurs when an offer of payment compromises comprehension or otherwise distorts subjective decision-making in a way that puts the validity of consent in doubt.
2. *Minimizing the risks of excessive payment*

From a regulatory perspective, the main concern with payment is that it may influence individuals to make ill-advised decisions to participate in research. However, there are other worries that deserve mention.

- First, there is evidence that offers of payment may induce individuals to lie or deceive investigators about their eligibility for a study that may jeopardize their safety as well as undermine the scientific integrity of the research.<sup>11</sup>
- Second, offering payment may result in an unfair societal distribution of the burdens and risks of research, by disproportionately attracting people of lower socio-economic standing.

Both these issues involve empirical questions that have not been sufficiently explored; it is not clear how frequently payment motivates deception, or whether studies with higher payment rates disproportionately attract people of lower socio-economic standing. The importance of these considerations is likely to vary with context, depending on the details of the study. While these concerns do not by themselves justify imposing limits on payment in all cases, they should be kept in mind by investigators and IRBs.

Regulatory guidance enjoins IRBs to ‘minimize’ the risk of undue influence posed by excessive payment, understood as the risk that payment will undermine the ability to give voluntary informed consent and lead to an ill-advised decision to participate in research. However, regulatory guidance does not specify how to accomplish this. Given that money may merely, not unduly, influence prospective participants' decision-making, IRBs need to know at what point payment tends to distort decision-making rather than influencing it in acceptable ways. This is challenging for two reasons.

First, individuals experience payment in different ways: what may be unduly influential to one person may be merely influential to another. That is, there is no bright line that divides ethically acceptable payments from those that are ‘excessive.’ Second, it is not clear that offers of payment *actually* distort decision-making in practice. The available data suggests that payment may actually *increase* caution and perception of risks among prospective participants, rather than distorting understanding.<sup>12</sup> To the extent that undue influence is more of a theoretical than an actual concern, protecting against undue influence may not deserve as prominent a place in IRB deliberation as it currently receives.

**Point 2a:** The main regulatory concern with offers of payment is the possibility that payment may distort decision-making and undermine informed consent. This is a concern with protecting the ability of individuals to make an autonomous choice about whether to participate in research. Thus, the risk of excessive payment might be addressed by placing greater emphasis on the informed consent process and taking steps to ensure adequate comprehension, such as quizzes aimed at testing participant understanding, as payment amounts increase. If it is clear that an individual adequately understands the risks and what is being asked of him or her,

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<sup>11</sup> See Elliott 2011, Devine et al. 2015, and Walker et al. 2018, cited in Appendix C.

<sup>12</sup> See Cryder et al. 2010 and Halpern et al. 2004, cited in Appendix C.



concern that payment may compromise evaluation of risks or otherwise distort judgment should be abated even in cases of relatively high payment.

**Recommendation 2a:** As payment amounts increase, investigators and IRBs should consider increased safeguards around informed consent (e.g. methods for testing comprehension of a study's purpose, procedures, risks, and benefits; including “teach-back” methodologies) as a first line of defense against undue influence. Such measures, which are generally a good idea even when payment is not involved, may allay concerns about higher payment and be preferable to disallowing payment amounts as ‘excessive.’

**Point 2b:** A distinct but related concern is not that payment will undermine informed consent *per se* but rather that it may influence individuals to participate in research when doing so is bad or unreasonably risky for them. This concern is grounded in beneficence and the duty to avoid harms in the research context. Indeed, one of the main ethical reasons for avoiding distorted decision-making is to ensure that individuals do not make choices that significantly conflict with their interests.

However, the IRB’s determination that the risks of research are reasonable in light of the benefits, which should not, per OHRP,<sup>13</sup> consider payment as a benefit and is needed for study approval, is evidence that the risks of the study are generally acceptable for the study population. This lowers the stakes around the potentially negative effects of payment. If the risks of a study are independently reasonable, offering payment for participation (in any amount) will not change this.

**Recommendation 2b(i):** The IRB’s independent risk-benefit determination itself acts as a safeguard against payment influencing people to make an unreasonably risky choice to participate in research. IRB approval thereby minimizes the potential impact of distorted decision-making and lowers the stakes around offers of payment.

**Recommendation 2b(ii):** IRBs concerned about excessive payment in particular cases should consider whether their concern is tied to discomfort with the risk-benefit balance; IRBs should ensure that the risks are reasonable and that the negative impact of any potential distortion is minimized.

**Point 2c:** A favorable risk-benefit determination by the IRB diminishes the potential impact of payment distorting decision-making but does not eliminate it entirely, since there may be individuals with unusual situations who are not captured by the IRB’s risk-benefit analysis in the abstract (e.g., a concert pianist in a study with a risk of hand joint damage, or someone whose

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<sup>13</sup> OHRP, [Informed Consent FAQs](#), “When does compensating subjects undermine informed consent or parental permission?”

personal religious beliefs conflict with a study requirement for reliable birth control measures other than abstinence). However, such individuals will not be typical or the norm, nor can IRBs predict their potential participation.

**Recommendation 2c:** In typical cases, IRBs should not use the possibility of individuals who fall outside the IRB’s risk-benefit analysis as a sufficient basis for restricting payment amounts or providing less payment than would be considered fair and appropriate for the average or majority of participants in the study. That said, if the IRB has good evidence that a specific population may be difficult to account for in its risk-benefit assessment, it may consider a different approach.

**Example 2:** Investigator C is conducting a study on an experimental medication for seizures. The study involves 15 visits and multiple intrusive and uncomfortable interventions, including lumbar punctures, MRIs, and multiple blood draws. Investigator C proposes to reimburse participants for out-of-pocket expenses as well as compensate them for the time and burden of visits. Some members of the IRB feel the compensation rate proposed by C is excessive and there are doubts about whether to allow it.

**Analysis 2:** In this situation, the IRB should begin by considering whether the reimbursement and compensation are ‘excessive.’ If the IRB does have concerns that payment is excessive, they should (1) clearly describe why it is excessive, (2) reexamine the risk and benefits of the research to ensure that the balance is appropriate, and (3) consider placing greater safeguards around informed consent would allay concerns about undue influence. The IRB may also wish to reconsider the risk-benefit balance of the study, to assure itself that the risks are generally reasonable for the study population and thus that the impact of possible distorted judgment is minimized. Either or both of these strategies in combination may suffice to allay concerns about undue influence and be preferable to disallowing the proposed payment amount as excessive, for reasons emphasized below.

## SECTION 2 SUMMARY

- Per regulatory guidance, the main ethical concern with payment is that offers of excessive payment might distort judgment and undermine voluntary informed consent to participate in research.
- However, empirical evidence on whether and at what point payment distorts judgment is lacking, making it difficult for IRBs to set justified limits on payment amounts.
- A favorable risk-benefit determination by the IRB minimizes the potential negative impacts of payment distorting decision-making by ensuring that study participation is generally reasonable for the study population.

- As a first line of defense against undue influence, IRBs should consider placing increased safeguards around informed consent (such as the use of comprehension tests) as payment amounts increase. This may often suffice to allay concerns over higher payment offers.

### 3. *Reasons in favor of payment*

Regulatory and bioethical discussions of paying research participants tend to focus on the risks of excessive payment, but it is also important to recognize the positive ethical reasons in favor of payment, which often weigh against setting payment rates too low. These reasons stem primarily from the importance of respecting participants, recognizing them fully as engaged participants in the process, and ensuring that they are not exploited but treated fairly from a financial perspective, which typically involves reimbursing them for out of pocket expenses and compensating them for their time and burdens. Additionally, there are often ethical reasons in favor of facilitating recruitment for IRB approved studies that support offering payment.

**Point 3a:** According to OHRP, “remuneration for participation in research should be just and fair.”<sup>14</sup> The language of fairness suggests a concern with payment being *too low*, in addition to more familiar concerns about excessive payment. In this regard, it is critical to keep in mind that in non-research spheres, such as employment, it would be considered unfair and exploitative not to compensate individuals for their time and burdens, or to compensate them at a rate less than their time and burdens are worth.

**Recommendation 3a:** When evaluating reimbursement and compensation amounts for particular studies, IRBs should consider what would be fair compensation for the time-commitment and burdens involved (see below, Section 5). Considerations of fairness may favor higher payment amounts.

**Point 3b:** IRB approval is based on the assumption that the study will answer the research question and deliver socially valuable knowledge, but many studies do not meet recruitment targets and as a result are under-powered or terminate early, exposing participants to burdens and risk for absent or limited social benefits. IRBs thus have ethical reasons to facilitate recruitment for the studies they approve. While there is a need for more empirical work on the correlation between payment and recruitment rates, and while higher payment is unlikely to solve all recruitment challenges, it is reasonable to assume that higher payment facilitates recruitment, just as it incentivizes behavior in other contexts. Indeed, payment’s ability to motivate participation is part of the reason there is concern about high payment, though the distinction between ‘mere’ and ‘undue’ influence must be kept in mind.

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<sup>14</sup> OHRP, [Informed Consent FAQ](#), “When does compensating subjects undermine informed consent or parental permission?”

**Recommendation 3b:** IRBs should consider the positive role that payment might play in facilitating recruitment and study completion that may weigh in favor of higher payment amounts (see below, Sec. 6).

**Example 3:** Investigator D is conducting a Phase 1 study involving an experimental cancer drug. The study involves a five-day inpatient hospital stay with multiple planned burdensome interventions, including MRIs, endoscopy, and blood draws. Investigator D is proposing to reimburse participants for out-of-pocket expenses and compensate them for their time spent in the hospital undergoing burdensome procedures. Based on prior experiences with similar studies, Investigator D knows that recruitment can be challenging for this type of research. Thus, in addition to reimbursement and compensation for time and burdens, Investigator D wishes to offer an additional payment sum as an incentive to motivate people to enroll. The IRB is concerned that the total payment amount offered may unduly influence some people to enroll in the study.

**Analysis 3:** In this study, considerations of fairness support compensating participants in proportion to their time-commitment and the burdens of the research, similarly to how a fair wage would be determined in employment contexts. Additionally, insofar as this study is deemed to be valuable and meets other regulatory criteria for IRB approval, the IRB has reasons to facilitate recruitment, which are grounded in the importance of avoiding situations where enrolled participants are exposed to burdens and risks in under-powered studies. The IRB should weigh both considerations of fairness as well as the importance of facilitating study completion against the risk of undue influence when deciding whether to approve the proposed amount. The IRB should also consider whether placing increased safeguards around informed consent (see above, Sec. 2a) would alleviate concerns with undue influence in this case, and should also keep in mind the role of its risk-benefit analysis in ensuring that the research is a reasonable option for the study population and lowering the stakes around offers of payment.

## SECTION 3 SUMMARY

- There are ethical reasons in favor of payment, based in fairness to participants and facilitating recruitment that should be balanced against concerns about undue influence.
- Considerations of fairness and avoiding exploitation are relevant for evaluating offers of payment and may count in favor of higher payment rates.
- IRBs have ethical reasons to facilitate recruitment for the studies they approve, based on preventing situations where participants are exposed to risks in under-powered studies, that may argue in favor of higher payment rates.

## **PART 2: A PRACTICAL FRAMEWORK FOR DESIGNING AND EVALUATING OFFERS OF PAYMENT**

Payment might be offered to research participants for a variety of reasons. Payment is sometimes offered to acknowledge services provided, such as when it is offered to reimburse subjects for out-of-pocket expenses related to participation or to compensate them for their time and assumption of research-related burdens. Offers of payment may also in many cases function to incentivize participation, so that the research has a better chance of being completed and delivering useful knowledge.

We suggest that appropriate offers of payment fall into the following categories: reimbursement, compensation, and recruitment incentives. Reimbursement and compensation are service-based reasons for offering payment; recruitment incentives, by contrast, aim simply to improve participation rates. The relevant considerations and best process for reviewing offers of payment may depend in part upon the category of payment, as will be illustrated below. Because of this, when developing an offer of payment, investigators should begin by thinking through their reasons for offering payment and the rationale for the amount offered, and then communicate this clearly to the IRB. Although we acknowledge that these categories proposed may not have pristine boundaries and that research participants might not make the same distinctions concerning different types and rationales for payment as do IRBs or investigators, it is a useful heuristic and helpful to the IRB to delineate and itemize payment sums into component parts, providing clear rationales for offers of payment when evaluating whether the total payment amount offered is justified and not ‘excessive.’

### *4. Reimbursement for out-of-pocket expenses*

Reimbursement for reasonable expenses incurred during research is generally acknowledged to be an ethically acceptable way of restoring subjects financially to their baseline. The CIOMS guidelines, for example, state that “participants should not have to pay for making a contribution to the social good of research ... in the form of direct expenses (for example, transportation costs), and must therefore be reasonably reimbursed for such expenses” ([CIOMS 2016](#), Guideline 13). Examples of expenses for which reimbursement is appropriate may include reasonable costs of travel, meals, accommodation, child care, and research procedures not covered by insurance. IRBs should not mandate reimbursement as a condition of approval, as it is acceptable for participants to altruistically choose to shoulder the costs of research out of pocket. Nonetheless, reimbursing participants for reasonable out-of-pocket expenses is a desirable default and should not raise concerns about undue inducement, given that it does not provide a net benefit to participants.

**Point 4a:** Particular institutions and IRBs may differ over what types of expenses are eligible for reimbursement as well as over the price range considered ‘reasonable’ for different expenses. IRBs should consider developing standard operating procedures addressing this issue.

**Recommendation 4a(i):** So long as expenses are reasonable, reimbursement does not constitute a net benefit to participants and thus does not raise concerns about undue influence.

**Recommendation 4a(ii):** Investigators should consult with the IRB on what types of expenses and amounts the IRB considers reasonable. IRBs may wish to develop policies in this sphere.

**Recommendation 4a(iii):** To the extent that investigators are categorizing payment as reimbursement (rather than compensation for time or burdens or incentive payments), they should not “pad the numbers” by offering to reimburse participants an amount in excess of what is reasonable. Fair estimates of out-of-pocket expenses paid up front to subjects may be acceptable, given the added administrative burden with requiring subjects to submit documentation for all expenses.

**Point 4b:** Research-related expenses may vary between geographical locales (e.g., public transit may or may not be available) and depend on the details of particular individuals and situations (e.g., how far particular participants must travel for research appointments).

**Recommendation 4b:** The precise amount reimbursed may differ between subjects and/or across sites without necessarily raising concerns about fairness, when there are legitimate reasons for variation.

- For example, individuals could be compensated for mileage according to a set formula, so that, while some participants would be paid more than others because they drove further, the methodology for determining payment would be equivalent and fair.

**Point 4c:** In some cases, there may be reasons that mitigate or defeat the need to offer reimbursement, such as extremely limited study budget or the fact that research visits overlap with a participant’s routine medical visits and care.

**Recommendation 4c(i):** While there is a strong presumption in favor of reimbursement, it is not always strictly obligatory. The assumption in favor of reimbursement can be overridden in certain cases by study-specific considerations.

**Recommendation 4c(ii):** While some participants may be altruistically willing to pay out of pocket for research related-expenses, investigators should not assume such altruism. Rather, they should offer reimbursement to participants and only withhold the payment when participants actively and of their own accord decline the offer.

## SECTION 4 SUMMARY

- Offers of reimbursement should be clearly communicated to participants, including the types of expenses and amounts that will be eligible.
- So long as out-of-pocket expenses are reasonable and stay within the parameters of the specified offer, reimbursement is not a net benefit and does not raise concerns about undue influence.
- Investigators should consult with the IRB over what the IRB considers ‘reasonable.’
- The amount reimbursed may vary between participants without raising concerns about fairness.
- Reimbursement for reasonable expenses is always fair and should be the default.
- Reimbursement is not strictly obligatory when there are study-specific reasons that defeat the presumption in favor of reimbursement, such as extremely limited study budget, or situations where research in the course of clinical care.

### 5. *Compensation for time and burdens*

Payment may also be offered as a way of compensating participants for the time they spend in the study and the research-related burdens they undertake. In typical cases, offers of compensation are made *in addition to* reimbursement and have a different rationale and aim. Whereas reimbursement simply functions to restore participants financially to their pre-research baseline, compensation aims to provide a fair recognition of the participant’s time and discomfort. As with reimbursement, IRBs should not mandate compensation as a condition of approval but fair compensation is a desirable default.

One foundational issue when evaluating participant compensation rates, important for IRBs to consider, is whether research meaningfully differs from other areas of life, such as employment, where treating people fairly involves compensating them for time and burdens. Even if the analogy between research and employment is rejected, however, the goal of compensation should be to treat subjects fairly by adequately acknowledging their time and burdens.

**Point 5a:** Concerns about undue influence or excessive payment typically do not arise for people in risky professions, such as firefighters, police officers, and the like. Analogous to people in these professions, research participants give of their time, undertake burdens and risks, and make personal sacrifices for the social good.

**Recommendation 5a:** The analogy between research participation and employment in certain professions creates a presumption in favor of compensating research participants for their time and acceptance of burdens, though (similar to reimbursement) this presumption can be overturned in particular cases.

**Point 5b:** Some compensation rates may be reasonable and fair, while others may be excessive, by offering more payment than what the participant's time and burden are worth (for example, a very large sum of payment to participate in a one-time blood draw study).

**Recommendation 5b:** Investigators and IRBs should strive to determine fair compensation rates, by asking what similarly time-consuming and burdensome unskilled labor is worth. When participant compensation rates resemble fair compensation rates in analogous non-research endeavors, they will not be 'excessive' and concerns about undue influence do not arise.

**Point 5c:** There is no regulatory guidance on acceptable or fair compensation rates, and rates vary in actual practice. However, one reasonable strategy for determining compensation rates involves applying typical payment rates for analogously time-consuming and burdensome endeavors in contexts outside of research, such as employment.

**Recommendation 5c(i):** It is appropriate to compensate subjects at an hourly rate for time-consuming study visits or procedures. Such rates should be sensitive to local norms and standards for hourly wages for similarly burdensome activities, to the extent that those local standards are themselves just.

**Recommendation 5c(ii):** Investigators should provide justification for why the compensation rate they are proposing is fair, drawing comparisons to people who undertake similar time-commitments and burdens in employment or non-research endeavors in the particular locale. IRBs should evaluate whether the rationale for the compensation rate is sound and document the methodology used in their determination of fairness.

**Recommendation 5c(iii):** Compensation rates should reflect the time and burdens of the study rather than being tied to individual participants' actual earning potential or what they would have earned in the course of their normal employment.

- Basing compensation rates on actual earning potential would, for example, result in an investment banker being paid more to participate in research than a grocery store clerk, even though both undertook the same time-commitment and burdens of research, which would be unfair.

**Point 5d:** In addition to time-commitment and burdens, participants also accept the risks of research, understood as negative outcomes that may or may not occur and that are not part of the study design (e.g., the risk of side effects from an experimental drug as opposed to the certain



burden of, say, a planned blood draw). Regulatory guidance and ethics guidelines differ on whether risk level is an appropriate basis for determining compensation rates.<sup>15</sup>

**Recommendation 5d(i):** It is important to distinguish compensating participants for the mere possibility of harms before they come to pass from compensating participants for risks if and when they actually result in harms. The latter is always fair and can be accomplished by offering insurance or other mechanisms, analogous to worker compensation programs.

**Recommendation 5d(ii):** If or when IRBs wish to permit compensating participants on the basis of risks that have not materialized, they should ensure that payment is not considered a benefit that offsets risks when deciding whether to approve the study.<sup>16</sup> As a routine practice, IRBs should complete the risk-benefit determination of a study in advance of any analysis of appropriate compensation for risks that have not materialized, or otherwise separate these processes to avoid any tainting of judgment.

## SECTION 5 SUMMARY

- There is a presumption in favor of compensating participants for their time and burdens, which is widely considered to be fair and the norm outside of research contexts.
- Participant compensation rates that resemble rates for similarly burdensome and time-consuming non-research endeavors should not raise concerns about undue influence.
- It is appropriate to compensate research participants at an hourly wage, which should be sensitive to local norms.
- Investigators should provide justification for why the compensation rate they are proposing is fair and the IRB should evaluate what would be considered fair compensation for analogous time-commitment and burdens in employment or non-research endeavors.
- Compensation rates should reflect the actual burdens of the study rather than being tied to the individual's actual earning potential.
- Compensating for risks that materialize in actual harms is desirable and fair and may be accomplished through systems of participant insurance or other similar mechanisms. h

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<sup>15</sup> OHRP states that “IRBs should not consider remuneration as a way of offsetting risks” but nonetheless explicitly condones compensation for risks: “Remuneration to subjects may include compensation for risks associated with their participation in research” (OHRP, [Informed Consent FAQ](#), “When does compensating participants undermine informed consent or parental permission?”). [CIOMS](#) Guideline 13, by contrast, state that compensation should not be based on risks.

<sup>16</sup> OHRP, [Informed Consent FAQs](#), “When does compensating subjects undermine informed consent or parental permission?”

## 6. Recruitment Incentives

In addition to reimbursing for out of pocket expenses and compensating subjects for time and burdens payment may also be offered to incentivize enrollment and improve participation rates. While more empirical work measuring correlations between payment and recruitment rates is needed, it is reasonable to assume that higher offers of payment increases willingness to participate in research, similarly to how payment incentivizes behavior in ordinary life.

**Point 6a:** Recruitment incentives are payment amounts beyond what would be justified for reimbursement and compensation, offered to further motivate participation. While the aim of reimbursement and compensation is fairness and acknowledging services provided by participants, the aim of recruitment incentives is simply to improve participation rates. It is only payment sums offered in addition to reasonable reimbursement and compensation that merit their own attention as recruitment incentives.

**Recommendation 6a:** When developing payment offers, investigators should first focus on reimbursement and fair compensation, proposing payment as a recruitment incentive only when they wish to offer more than would be justified for reimbursement and compensation.

**Point 6b:** Regulatory guidance does not prohibit and indeed assumes that payment may be offered as a recruitment incentive (cf. [FDA Information Sheet](#)). When evaluating the acceptability of recruitment incentives, there are, as discussed above (Sec. 3), other ethical reasons in favor of facilitating recruitment that should be weighed against the risk of undue influence. These reasons stem from the importance of avoiding situations where participants are subjected to burdens in studies that, due to poor recruitment and/or retention, do not answer the research question(s).

**Recommendation 6b(i):** There is nothing inherently wrong with recruitment incentives. As with other types of payment, they may provide acceptable motivation, rather than unduly influence (see above, Sec 2).

**Recommendation 6b(ii)** Researchers and IRBs have ethical reasons to facilitate recruitment for approved studies. These reasons count in favor of allowing higher recruitment incentives and should be balanced against the risk that recruitment incentives may be a source of undue influence.

### SECTION 6 SUMMARY

- When developing payment offers, investigators should begin by focusing on reimbursement and fair compensation, proposing recruitment incentives only when they wish to offer more payment than would be justified under these categories.

- There is nothing inherently problematic with recruitment incentives. They become problematic only when they unduly influence participation, the risk of which may be addressed in the ways outlined above (Sec. 2).
- There are ethical reasons in favor of facilitating recruitment for IRB-approved studies that count in favor of higher recruitment incentives and that should be balanced against concerns about undue influence.

### **PART THREE: OTHER CONSIDERATIONS**

In this third and final part, two additional issues are addressed: (i) the timing of payment disbursements to participants and (ii) whether offers of payment should be evaluated differently for research that holds the prospect of direct therapeutic benefit than for research that does not.

#### *7. Timing of payment*

It is possible to incentivize research participation, particularly completion, not just by offering certain payment amounts but also by timing payment in certain ways, i.e., by making disbursement of some or all payment contingent on completion of the study or key parts of it, such as by offering ‘completion bonuses.’ Regulatory guidance permits such practices within limits but warns against situations where the timing of payments may unduly influence enrolled participants to remain in research or compromise their right to withdraw (e.g. withholding all payment until the end or offering excessive completion bonuses).<sup>17</sup>

**Point 7a:** Even for studies that enroll enough participants, the ability to produce valuable knowledge depends on retaining participants and collecting the necessary data. This provides reason to encourage study completion, which must be weighed against the risk of unduly influencing participants to remain in research by delaying payment. Identifying undue influence in the retention of participants is no less challenging than identifying undue influence in the enrollment of participants. Similarly to how increased emphasis on the consent process and other elements of IRB review mitigate the risks of excessive payment in enrollment decisions (Sec. 2), ongoing monitoring by study staff aimed at identifying participants who would be put at excessive risk by remaining in the study lowers the stakes around participants being unduly influenced to remain in research via the timing of payment.

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<sup>17</sup> OHRP recommends that “payment be prorated for the time of participation in the study rather than delayed until study completion, because the latter could unduly influence” a subject to remain in research ([FAQ](#), ‘When does compensating subjects undermine informed consent or parental permission?’). FDA guidance, by contrast, explicitly permits “payment of a small proportion as an incentive for completion of the study” ([Payment to Research Subjects—Information Sheet](#)).

**Recommendation 7a(i):** There are ethical reasons in favor of facilitating participant retention through the timing of payment, which should be balanced against the risk for undue influence.

**Recommendation 7a(ii):** Ongoing monitoring by study staff aimed at identifying participants who may be put at increased risk by continuing in the study should mitigate concerns about the timing of payment unduly influencing participants to remain in research.

**Point 7b:** Determining an acceptable and fair payment schedule may depend upon which category payment falls (reimbursement, compensation, or recruitment incentive). For reimbursement and compensation, considerations of fairness are relevant and count in favor of regular payment disbursements, just as treating workers fairly in employment contexts requires paying them regularly for the ongoing work they complete (e.g., on a weekly or bi-weekly basis). For recruitment incentives that go beyond compensating participants, delaying payment does not raise the same concerns about fairness.

**Recommendation 7b(i):** Payments intended for reimbursement and compensation should be disbursed regularly and not be delayed for the purpose of incentivizing retention.

**Recommendation 7b(ii):** Recruitment incentives may be delayed for the purpose of incentivizing retention, within reasonable bounds.

## SECTION 7 SUMMARY

- There are ethical reasons in favor of facilitating retention that should be weighed against the risk of undue influence.
- Payment offered as compensation for participant time and burdens should be disbursed on a regular schedule and not be delayed in order to incentivize retention.
- Payment offered as a recruitment incentive may be delayed in order to incentivize retention so long as concerns about undue influence are addressed.

### 8. *Payment and the prospect of direct medical benefit*

Payment for research participation may be offered in studies that hold no prospect of direct medical benefit, such as in Phase 1 clinical research with healthy volunteers, as well as in studies that do hold a prospect of direct benefit, such as Phase 3 cancer research. The category of payment influences the relevance of direct health benefits for evaluating offers of payment. Further, in all cases, it is important to keep in mind that, given the uncertainty that characterizes research, what is at issue is the *prospect* or *chance* of health benefits, which may or may not materialize.

**Point 8a:** With respect to payment, the main question with studies that offer the prospect of direct health benefit is whether this justifies offering less payment than would otherwise be considered reasonable and fair, or no payment at all.

It is plausible that the prospect of direct benefit can serve a compensatory function and contribute to fairness for participants, which may bear some weight when determining fair payment amounts. At the same time, typically, the prospect of direct benefit does not by itself adequately compensate participants for the expenses and burdens of research participation or make payment unnecessary. Placing too much weight on the prospect of direct benefit may perpetuate a problematic ‘therapeutic misconception,’ by assuming that health benefits *will* rather than merely *might* materialize, which researchers and IRBs should avoid. In addition, even if health benefits do result for the participant, participants may still reasonably expect to be reimbursed and fairly compensated, similarly to how people who enjoy non-monetary benefits from their employment still expect to be paid. A similar dynamic may apply for ancillary health and other benefits, which can bear some weight—but not all—when determining fair payment.

**Recommendation 8a(i):** The prospect of direct health benefit is relevant for determining fair payment and can justify lower reimbursement and compensation rates than would otherwise be appropriate, but does not typically justify foregoing reimbursement or compensation completely, particularly when the expenses and burdens of research are high.

**Recommendation 8a(ii):** With respect to recruitment incentives, it may often take less payment to incentivize participation in studies with a prospect of direct benefit, since people may be more willing to enroll for the potential health benefits without payment as a motivating factor. There are no ethical concerns with offering lower recruitment incentives in these cases.

## SECTION 8 SUMMARY

- The prospect of direct benefit is relevant for determining fair payment and may justify less payment than would otherwise be appropriate.
- However, the prospect of direct benefit should not by itself be used to justify foregoing reimbursement or compensation altogether, particularly when the burdens of a study are high.
- It may take less to incentivize participation in research with a prospect of direct benefit; there is no ethical concern with offering lower recruitment incentives on this basis.

## CONCLUSION

The ethical issues involved with evaluating offers of payment are challenging. Regulatory guidance emphasizes the importance of avoiding undue influence due to excessive offers of payment, but there is uncertainty around setting reasonable limits on payment amounts, given the lack of empirical data on whether or at what point payment distorts judgment and undermines informed consent. At the same time, while avoiding undue influence is important, there are also ethical reasons in favor of payment that should be acknowledged in IRB deliberations. These stem from the importance of treating participants fairly from an economic perspective, which supports reimbursement for expenses and compensation for time and burdens, as well as from the importance of facilitating recruitment in IRB approved studies.

This document has suggested strategies for balancing these considerations and proposed a practical framework for proposing and evaluating offers of payment. Its goal has not been to resolve all the ethical or regulatory issues surrounding payment but rather to provide a structure for IRB deliberation and to offer guidance that might facilitate proposal and review of payment offers. The Appendices that follow further contribute to this goal, containing a checklist for investigators proposing payment amounts and a checklist for IRBs reviewing payment offers, and further suggested readings on this topic.

## **APPENDIX A: CHECKLIST FOR INVESTIGATOR DESIGNING PAYMENT OFFERS.<sup>18</sup>**

- Investigators proposing payment amounts should consider increasing safeguards around participant comprehension and informed consent, particularly as payment amounts increase.
- Investigators should clearly communicate the rationale for payment amounts to the IRB by itemizing payment into the following categories: (1) reimbursement for out-of-pocket expenses, (2) compensation for time and burdens, and (3) recruitment incentive.
- Investigators should offer to reimburse participants for out-of-pocket expenses unless there are circumstances that defeat this presumption.
- With respect to reimbursement, investigators should consult with the IRB on what types of expenses and amounts the IRB considers reasonable, and should not ‘pad the numbers’ by offering to reimburse for amounts in excess of what is reasonable.
- Investigators should plan to compensate participants for their time-commitment and the burdens they assume, unless there are countervailing considerations that defeat this presumption.
- It is acceptable for investigators to offer participants an hourly wage. Investigators should provide justification for why the compensation rate they propose should be considered fair, drawing analogies to non-research contexts such as employment.
- Investigators should first focus on treating participants fairly by reimbursing and compensating them for participation, proposing payment as a recruitment incentive only when they wish to offer more than would be justified for reimbursement and compensation.
- While reimbursement and compensation should not be delayed or withheld to incentivize participant retention, investigators may propose to delay recruitment incentives to encourage retention and study completion.
- Investigators who wish to delay recruitment incentives should clearly communicate to the IRB their plan for ensuring that withholding payment will not influence participants who should not finish the study to remain enrolled.
- Investigators may take the prospect of direct medical benefit to mitigate, but not eliminate, the reasons in favor of reimbursing and compensating participants.

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<sup>18</sup> These checklists are based on those found in Gelinas et al. 2017.

## **APPENDIX B: CHECKLIST FOR IRBS REVIEWING PAYMENT OFFERS.**

- IRBs should keep in mind the distinction between ‘mere’ and ‘undue’ influence and recognize that payment can be an acceptable motivation to participate in research.
- IRBs concerned about payment distorting judgment and undermining informed consent in particular cases should consider whether additional emphasis on the consent process, such as mechanisms for ensuring comprehension, would adequately address the concern.
- IRBs concerned about excessive payment in particular cases should recognize the positive role that their risk-benefit determination plays in protecting participants and consider whether their concern is tied to discomfort with the risk-benefit ratio. IRBs should ensure that the risks are reasonable and that the negative impact of any potential distortion is minimized.
- IRBs should recognize the positive ethical reasons in favor of payment, stemming from fairness to participants and the importance of preventing under-powered studies, which may balance concerns about undue influence.
- IRBs should encourage investigators to itemize payment into the following categories: (1) reimbursement for out-of-pocket expenses, (2) compensation for time, burdens, and risks, and (3) recruitment incentive.
- IRBs should permit and encourage investigators to reimburse participants for reasonable out-of-pocket expenses and may wish to develop standard operating procedures on the types of expenses and amounts they consider reasonable.
- When evaluating compensation rates, IRBs should focus on what would be considered a fair wage in the particular locale, given the time-commitment, burdens, and risks involved in the research. If a compensation rate is fair, it should not raise concerns about undue influence.
- IRBs should consider whether rates of payment from similarly burdensome and risky non-research endeavors, such as employment, should serve as a benchmark for participant compensation in their deliberations.
- IRBs should encourage, or require, investigators to offer payment as a recruitment incentive only when they wish to offer more than would be reasonable and fair for reimbursement and compensation.
- IRBs should recognize the positive ethical reasons in favor of facilitating recruitment through the use of recruitment incentives, which may balance concerns about undue influence.
- IRBs should require reimbursement and compensation to be disbursed on a regular basis and not withheld for the purpose of facilitating retention.
- IRBs may permit recruitment incentives to be withheld as a way of encouraging retention and study completion, so long as concerns about undue influence are addressed.



- IRBs should discourage investigators from using the prospect of direct therapeutic benefit as sufficient grounds for withholding reimbursement and compensation altogether, although the prospect of benefit may bear some weight when determining fair payment.

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