Penn
University of Pennsylvania
Human Research Protections Program

Payments in Human Research Subjects: Guidance and Requirements

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Payment to Subjects Participating in Research

The Penn IRB is responsible for reviewing the rates, forms and schedules of remunerations to subjects participating in research at the university. It is the IRB's charge to ensure that the amount of remuneration and the proposed method and timing of disbursement do not present undue influence to subjects.

Definitions

Compensation: Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research.

Remuneration: Payment for participation in research. (NOTE: It is wise to confine use of the term "compensation" to payment or provision of care for research-related injuries.)

This guidance refers to remuneration as defined above. Determinations of forms and rates of payment to subjects for participation in research present some of the more challenging ethical issues in human subjects' research design. It is accepted that, under many circumstances, subjects should receive payment for research participation, as a way to reciprocate for time, effort and inconvenience and demonstrate gratitude to subjects as well as help researchers fulfill study objectives. While subject remuneration has its merits and benefits, paying subjects for their participation can also present negative ethical consequences, as payments have the potential to impinge upon the free choice and autonomy of subjects.

Current regulations do not provide guidance on appropriate methods or rates of subject payment. Department of Health and Human Services (DHHS) [45 CFR 46.116] regulations state that "an investigator shall seek consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence" (emphasis added).

Food and Drug Administration (FDA) regulations state that IRBs have the responsibility to "review both the amount of payment and the proposed method and timing of disbursement to assure that either are coercive or present undue influence [21 CFR 50.20]." As such, neither regulatory source endorses, prohibits or provides direction on acceptable practices regarding payment to subjects.

Given the lack of direct guidance on the matter, the charge within DHHS and FDA regulations for IRBs to review payment practices, and the challenging nature of establishing these practices in protocol design, the purpose of this document is to outline guidance and factors that the IRB will consider when reviewing payment to subjects participating in research.

Reasonable Remuneration and Avoiding Undue Influence

The main ethical concern with remunerating subjects for participation in clinical research is that payment has the potential to constitute undue inducement, distorting the judgment of subjects and affecting the voluntary nature of their informed consent.

Commonly the concern is stated that payment has the potential to represent "coercion." Coercion, in its simplest definition, involves a threat that makes a certain choice irresistible. The concept of coercion identifies situations where the intentional threat of harm is used to compel someone to do something, i.e., the classic "your money or your life" scenario.

Considering this definition and today's regulatory systems, coercion is not the chief concern when considering remuneration to subjects. The potential for "undue inducement," therefore, is the main concern when considering the effects of payment to subjects. In order to prevent the undue inducement of subject, the IRB offers the following guidance:

- The IRB considers remuneration as an undue inducement if the nature of the payment is such that it has the potential to alter a subject's decision-making process such that she or he may not appropriately consider the risks of participating in the research.
- It is the IRB's position that remuneration to subjects participating in research should be reasonable, equitable and comparable to other studies involving equivalent time, effort and inconvenience.
- Remuneration should not be contingent upon the subject completing the entire study. Payment of a small proportion as an incentive for completion of the study

has been stated as acceptable to FDA, providing that such incentive is not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn. For short studies involving one visit, depending on the nature of the study, it may be acceptable to provide payment contingent upon completion, provided that if subjects are disqualified through no fault of their own they receive appropriate payment for their time and effort prior to their exclusion.

- Payment to subjects who withdraw from the study may be made at the time they would have completed the study (or completed a phase of the study) had they not withdrawn, unless this may create undue inconvenience or a coercive practice. Payment to subjects who withdraw should be prorated to reflect the time, effort and inconvenience to the subjects participation to the point of withdrawal.
- Payment should be prompt.
- The amount, method, schedule, form and prorating of remuneration should be described clearly in the informed consent form.
- Non-monetary forms of remuneration such as gift cards/certificates are acceptable forms of payment. The monetary value of these forms should be considered as equal to cash payment. The form of payment should be clearly described in the consent form.
- All information regarding remuneration to subjects should be detailed in the appropriate field of the IRB application for each submitted protocol.

Payment for Referral/Recruitment of Subjects in Human Research (Finder's Fees and Bonus Payments)

Background

Bonus payments for subject recruitment and finder's fees for subject referral may compromise the integrity of a research study by giving an appearance of affecting the judgment of the investigator/research team and in some cases may violate federal law. Ethical conduct of research requires that the participation of all human volunteers be completely voluntary.

Particularly in a health care setting where relationships are hierarchical, it is important that there be no suggestion of subtle encouragement for any person's participation in a research study by someone who will receive a finder's fee or bonus payment if that person is enrolled as a subject.

The American Medical Association, and RhPHARMA have issued guidelines suggesting that finder's fees and bonus payments may represent real or perceived cases of fee-splitting a well-recognized and unethical behavior. Individuals participating in the conduct of research should be reimbursed only for activities directly related to performance of the research and at a rate not exceeding the fair-market value for the level of activity performed. Federal Medicare anti-kickback laws may also prohibit finder's fees and bonus payments if there is real or apparent billing of standard of care costs as part of the research activity.

In addition, the University of Pennsylvania IRB believes that finder's fees and bonus payments to investigators and study staff create a potential conflict of interest. Specifically, the investigator may be motivated by financial interest to refer a patient when such referral might not be of any benefit to, or in the best interest of the subject. Finder's fees to physicians or nurses may diminish the patient's free choice in deciding whether to volunteer for a clinical study. Specifically, the patient may rely unduly on the physician's or nurse's recommendation to enroll, against his/her own better judgment.

Finally, the IRB believes that there does need to be guidance for investigators who wish to recruit subjects for research activity and where outside third parties need to be reimbursed for their activities in such manner as to avoid the appearance of fee splitting.

Payment of Finder's Fees and Bonus Payments to University of Pennsylvania Physicians, Investigators or Study Staff by External Sponsors

The Institutional Review Boards do not approve of finder's fees being paid to University of Pennsylvania or UPHS investigators, physicians, nurses, and others who have a treating and/or counseling relationship to a subject being referred for enrollment in a clinical trial. The Institutional Review Boards do not approve of finder's fees being paid to any, house staff or University of Pennsylvania Health System (UPHS), or University of Pennsylvania employee for referring or recruiting prospective subjects. The IRB may review and approve small, nominal value gifts to staff organizations as long as such gifts are not based on any indicator of trial enrollment.

All payments for the conduct of a research project must be negotiated at the beginning of the study and not provide for additional payments based on either number or rate of subject enrollment. Payments tied to the number or rate of subject enrollment are considered to be bonus payments and are not permissible. Supplemental payments, or additional compensation, payments, or other incentives beyond nominal (less than $100 in value) must be negotiated as part of an addendum to the clinical agreement and reported to the IRB. The investigator, physicians and staff must be aware of the existing reporting requirements under the University Policy on Conflicts of Interest should there be any change in their financial relationship with any sponsor during the performance of a research study.

Payment of Finder's Fees to Referring Physicians or Others Outside the University of Pennsylvania or University of Pennsylvania Health System

Finder's fees include any payment or gift to an individual who identifies or assists in the recruitment of prospective subjects.

The use of finder's fees to elicit recruitment of research subjects from outside the University of Pennsylvania or University of Pennsylvania Health System is discouraged.

In some cases, it may be acceptable for investigators to offer a nominal incentive if the IRB can be assured that the person who receives that incentive will in no way encourage subjects to enroll in a study and that applicable laws are not violated. Each case must be considered individually. The use of any compensation (payment, gift, etc.) must be reviewed and approved by the IRB prior to being initiated. Payment to physicians outside of the University of Pennsylvania Health System (UPHS) should be structured as a contract with the referring physician(s) and provide reimbursement for actual services rendered by the physician or their staff for the recruitment purposes.

If an investigator wishes to consult the IRB regarding this issue, the following questions must be answered as part of the protocol submission:

- What compensation will be offered (for example, money, textbook, dinner, movie pass)?
- Who will obtain consent or HIPAA authorization (if applicable) from the subject?
- To whom is the compensation being offered and what is the person being asked to do?
- Could the compensation provided be coercive or appear to be linked to successful enrollment in the study?
- Will the subject or their insurance be charged for any study-related activity?
- If a person is enrolled in the study, will there be a change in the responsibility for patient care? For example, will the study investigators now provide primary treatment for a problem?

The IRB requires that the role of a person not directly involved in the study who is identifying potential subjects be limited to asking the potential subject if he/she would be willing to talk to a researcher about a relevant study. If the potential subject is not interested, no further encouragement should occur.

Compensation to the person assisting in identifying potential subjects should be made whether or not the potential subject enrolls in the study.