Paying Research Subjects: An Analysis of Current Policies

Neal Dickert, BA; Ezekiel Emanuel, MD, PhD; and Christine Grady, PhD

Background: **Few data are available on guidelines used by research organizations to make decisions about paying subjects.**

Objective: **To analyze existing guidance regarding payment of research subjects and to identify common characteristics and areas for further research.**

Design: **Descriptive content analysis of policies.**

Measurements: **Written policies and rules of thumb about paying subjects from 32 U.S. research organizations.**

Results: **Of 32 organizations, 37.5% had written guidelines about paying subjects; all but 1 reported having rules of thumb. Few (18.8%) were able to provide a confident estimate of the proportion of studies that pay subjects. Organizations reported that investigators and institutional review boards make payment decisions and that both healthy and ill subjects in some studies are paid for their time (87%), for inconvenience (84%), for travel (68%), as incentive (58%), or for incurring risk (32%). Most organizations require that payment be prorated (84%) and described in the consent document (94%).**

Conclusions: **Most organizations pay some research subjects, but few have written policies on payment. Because investigators and institutional review boards make payment decisions with little specific guidance, standards vary.**

Ann Intern Med. 2002;136:368-373. www.annals.org
For author affiliations, current addresses, and contributions, see end of text.

Clinical research would be impossible without the participation of willing human subjects. Research institutions are recruiting more participants more quickly than ever before (1). Some researchers consider payment crucial to recruitment, as evidenced by the sheer number of advertisements for paid studies in newspapers, on the radio, and on the Internet. Although paying research subjects is a common and long-standing practice in the United States (2), it remains contentious. Decisions about when, why, and how much to pay research subjects continue to spark disagreement within the research community.

Some have argued that paying subjects is unethical (3, 4), but most agree that it is acceptable in some cases. The prominent ethical concern is that money may unduly induce subjects to participate in research by compromising the voluntary nature of their decisions or their willingness to explore the risks and benefits of the study (5–7). Others worry that payment may target economically vulnerable persons or compromise scientific integrity by altering the makeup of the subject population. No empirical data exist on the validity of these concerns.

Federal regulations and guidelines provide minimal guidance on payment of research subjects. The U.S. Code of Federal Regulations never specifically mentions payment (8). *The Official IRB Guidebook* simply advises that the local institutional review board (IRB) should determine "whether the rewards offered for participation in research constitute undue inducement" (9). Information sheets from the U.S. Food and Drug Administration state that payment is not a "benefit, [but] a recruitment incentive" and advise IRBs to "review both the amount of payment and the method and timing of disbursement to assure that neither are coercive or present undue influence" (10). It is unknown how investigators or IRBs use these guidelines in designing and evaluating payment in research proposals.

Given the pervasiveness of the practice of paying research subjects, the disparate views on its appropriateness, and the sparseness of regulations, we examined and describe guidance that research organizations actively engaged in clinical research use to decide about payment of research subjects. Although alternate forms of "payment" raise similar ethical concerns (11), we focused on guidance regarding monetary payment of research subjects.

METHODS

The study included 32 geographically diverse organizations involved in the development, conduct, and review of biomedical research. We selected 12 academic research centers, 3 in each of the 4 census regions, from the 50 centers that receive the most funding from the U.S. Public Health Service; of these 12 centers, 9 agreed to participate. We contacted 20 of the largest pharmaceutical companies in the United States, and 7 agreed to participate; the others refused, citing the proprietary nature of the information. Eight of 12 contract research organizations (CROs) identified from the Centerwatch

Web site agreed to participate (12). Nine independent IRBs (freestanding, for-profit IRBs that review commercially funded as well as federally funded and community research) were identified from the Web site of the Health Industry Manufacturers Association (now called AdvaMed) (13), and 8 agreed to participate.

The project was explained over the telephone to the chair of the IRB, the vice president for research, or the equivalent person at each organization. Participation was requested, and a follow-up letter was sent. Data were collected in 1998 and 1999. We asked organizations to provide 1) the total number of clinical research studies initially approved in 1997; 2) the total number of studies that paid subjects in the same year; and 3) all organizational policies, guidelines, or rules of thumb regarding paying research subjects. Respondents were asked to send official copies of policies and guidelines (defined as written rules formally authorized by the organization) and to describe rules of thumb (defined as unwritten "rules" that had become standard practice at the organization) in a return letter. We clarified written submissions through follow-up telephone calls.

Responses were analyzed to determine the type of guidance used by the organization; descriptions of the purpose of payment; and specific requirements regarding advertising, informed consent, and determination of how much to pay subjects. We had previously identified these categories as important for analysis through literature review and discussion with IRB members, ethicists, and clinical researchers.

This study received IRB exemption from the Office of Human Subjects Research at the U.S. National Institutes of Health. Data are aggregated to protect the confidentiality of participating organizations. The Department of Clinical Bioethics, W.G. Magnuson Clinical Center, National Institutes of Health, funded the study, and members of the department were responsible for the collection, analysis, and interpretation of the data and the decision to submit the results for publication.

Context

Many investigators pay research subjects. Paying research subjects could inappropriately influence them to participate in studies. We know little about how research organizations handle payment of research subjects.

Contribution

This survey of 9 academic centers, 7 pharmaceutical companies, 8 contract research organizations, and 8 independent institutional review boards showed that most paid subjects but few had formal policies to guide the amount or circumstances of payment.

Policy Implications

Without standard policies for paying research subjects, there are uncertain safeguards against unfair or coercive payment.

It is uncertain whether the organizations that participated are representative of all research organizations in the United States.

—The Editors

Results

Thirty of 32 organizations paid subjects in at least some clinical studies that were initially approved during 1997. One organization reported no paid studies, and 1 could not determine whether any subjects had been paid. Few organizations (18.8%) were able to provide a confident estimate of the proportion of studies that paid subjects. Six of 9 academic research centers provided the total number of studies approved in 1997. Of these, only 4 had an electronic method of identifying paying studies; for the other 2 centers, we collected information from the cover page of the study description or from IRB minutes. At these 6 academic research centers, 23% of studies approved in 1997 offered payment to subjects.

Most pharmaceutical companies and CROs could not provide the total number of studies approved in 1997 or provided it only for units that do phase I studies and pay almost all participants. Of 8 independent IRBs, 4 did not release the total number of studies approved because of proprietary reasons and none could determine the precise number of studies that paid subjects. However, 2 independent IRBs described the proportion of paid studies as "most" and 1 described it as "close to 80%."

Existence of Guidance on Payment

Only 37.5% of organizations (12 of 32) reported having written policies or guidelines about payment of research subjects. Three pharmaceutical companies reported having written guidance that applies only to phase I units and not to other studies that the companies support. In contrast, 31 of 32 organizations reported having unwritten rules of thumb. One pharma-

Table 1. **Content of Guidance on Payment to Research Subjects***

Specific Requirements for Payment Found in Policies or Rules of Thumb	Academic Research Centers (*n* = 9)	Pharmaceutical Companies (*n* = 6)	CROs (*n* = 8)	Independent IRBs (*n* = 8)
	← *n* →			
What to pay for				
Incentive	4	4	5	5
Time	7	6	6	8
Travel	6	5	5	5
Inconvenience	8	6	6	6
Risk	3	0	1	6
How to pay				
Specific formula	2	3	3	0
Prorating	8	5	5	8
Restrictions				
Completion bonus	5	4	4	5
Payment of patient-subjects	1	2	0	0

* CRO = contract research organization; IRB = institutional review board. Seven academic institutions, 3 pharmaceutical and biotechnology organizations, 0 CROs, and 2 independent IRBs had written policies or guidelines.

ceutical company with no written guidelines or rules of thumb reported that it leaves decisions about payment of subjects entirely to the site investigators and the IRB.

Participating pharmaceutical companies and CROs reported having little involvement with decisions about paying subjects in off-site studies. Study budgets are generally negotiated among sponsors, CROs, and study sites. Site investigators and staff typically determine the details of subject recruitment and payment, and the IRB is the ultimate arbiter in deciding whether a particular payment strategy is appropriate.

Content of Guidance

Guidance reflected wide variation in reasons for offering payment (**Table 1**). Slightly more than half of the organizations with payment guidelines or rules of thumb (58%) described payment as an incentive. Academic institutions, compared with the other three types of organizations, were least likely to do so (44% vs. 62.5% to 66%, respectively). Overall, most organizations said that subjects were paid for the time (87%), inconvenience (84%), or travel (68%) associated with research participation. Thirty-two percent reported that subjects were paid for incurring risk. Independent IRBs were more likely than other organizations to report that risk level affected payment decisions (75% vs. 0% to 33%, respectively). Notably, written guidance described payment almost exclusively as compensation for time and inconvenience. Half of the written guidelines explicitly stated that subjects should not be paid for risk, and only 4 of 12 written guidelines (33%) described payment as incentive for participation.

Only 8 of 32 organizations (2 academic institutions, 3 pharmaceutical companies, and 3 CROs) reported using a particular formula to calculate amount of payment (**Table 1**). For the 3 pharmaceutical companies and 3 CROs, the payment formula applies only to on-site phase I studies. Seven organizations with written guidance but no specific formula for calculating payment advise against excessive payment to avoid undue inducement; however, they do not specify what should be considered "excessive."

The eight formulas varied both in level of specificity and basis for calculating payment. Four organizations calculate payment for time by the hour, ranging from $4 to $10; the other four calculate payment per inpatient day or outpatient visit. Three of the organizations pay a flat rate per day or visit (range, $25 to $125) that is not altered for procedures performed during the study. Five organizations provide supplemental payment for procedures; of these, two specifically determine the supplemental amount according to the "inconvenience" of the procedure. No formula explicitly incorporates risk into determination of payment amounts. Only two pharmaceutical companies include formulas for calculating completion bonuses, which are predetermined lump-sum payments designed as incentives to finish a study.

Additional Requirements for How To Pay Subjects

Ninety percent of organizations reported paying healthy subjects and patient-subjects (persons who have

the disease or condition under study) similarly when participation for each group involves similar procedures and no apparent difference in the likelihood of direct benefit. Only three organizations reported explicit restrictions on paying patient-subjects.

Most organizations (84%) require prorated payment (partial payment based on the amount of time or procedures actually finished) rather than payment that is contingent on completion of the study (**Table 1**). However, few organizations provide details on how to prorate. Three organizations consider the reason for subject withdrawal and pay the full amount of money to those who withdraw for medical reasons but a prorated amount to those who withdraw for nonmedical reasons.

Eighteen organizations (58%) reported rules on the use of completion bonuses (**Table 1**). Four prohibit completion bonuses, 2 use set completion bonuses for certain procedures or amounts of time, and 5 require that completion bonuses not exceed a certain percentage (25% to 50%) of the total. The other 7 organizations advise against excessive completion bonuses or allow them only for low-risk follow-up visits.

Specific Requirements for Informing Subjects about Payment

Twenty-nine organizations require IRB review of study advertisements (**Table 2**), which is consistent with the guidelines of the U.S. Food and Drug Administration (10); the other 2 organizations leave advertising decision to the study site. No organization completely prohibits mentioning payment in an advertisement, although 14 (48%) restrict the way in which such a mention can appear. Four organizations allow mention of payment but prohibit inclusion of the specific amount, 1 organization prohibits payment in advertisements for pediatric studies, and 1 organization prohibits listing a "theoretical maximum." Other organizations simply require that advertisements not "overemphasize" payment.

Most organizations require informed consent documents to contain the amount of payment subjects can expect (94%) and terms of payment (84%) (**Table 2**). Most (81%) also require that payment be described in a specific section of the document, usually a discrete section titled "payment for participation," "financial," "remuneration," or "compensation." Five organizations recommend including payment in the "benefits" section, and two specifically stipulate that it not be included in the "benefits" section.

Discussion

These data suggest that standards for payment of subjects vary widely and that investigators and IRBs make decisions about payment with minimal guidance. We studied four major types of organizations that conduct and review human subjects research. Our data probably represent current practices across the country. Six findings are especially relevant.

First, many research organizations, surprisingly, have no systematic method of tracking how many of their studies pay subjects for participation. This makes it impossible to obtain an accurate count of paid studies. Information about payment to subjects, which would be relatively simple to add to existing databases, would not only help in analyzing the costs of subject recruitment

Table 2. **Requirements for Advertising and Informed Consent***

Specific Requirements for Informing Potential Subjects about Payment	Academic Research Centers (n = 9)	Pharmaceutical Companies (n = 6)	CROs (n = 8)	Independent IRBs (n = 8)
	←	n		→
Advertising				
Not addressed	0	1	1	0
IRB review required	9	5	7	8
Mention of payment prohibited	0	0	0	0
Mention of payment restricted	5	2	2	5
Informed consent document				
Not addressed	0	0	1	0
Mention of payment required	9	6	7	8
Specification of total amount of payment required	9	6	7	7
Specific terms of payment (for example, prorating) required	9	5	5	7
Specific section for payment required	6	5	6	8

* CRO = contract research organization; IRB = institutional review board.

but would also help gauge the pervasiveness of payment and the range of paying studies.

Second, IRBs seem to judge the acceptability and appropriateness of plans for paying subjects with little substantive guidance from sponsors, institutions, or federal regulations. Only 9 of the 17 IRBs sampled (7 academic and 2 independent) have written policies or guidelines with varied content. Most written guidelines simply caution against "undue inducement," but none describe how investigators or IRBs should determine when money is "undue." Little is known about the circumstances in which or the extent to which money inappropriately induces subjects to participate in research that is contrary to their interests. As Lemmens and Elliot observed, "it is no wonder that IRBs are baffled" (14).

Written guidance can contribute to standardization in an institution and assist persons involved in planning, conducting, and reviewing research (15). At the least, written guidance can articulate an organization's view of the purpose and nature of payment so that practices adhere to those values. This seems especially important given the demonstrated disagreement in the field over whether the purpose of payment is compensation for time, inconvenience, incentive, or risk. Written guidance can also provide a structure for calculating payment.

Third, few organizations, except pharmaceutical phase I units, have specific formulas for calculating payment. Rather, decisions tend to be made on the basis of each individual study. With no formula or statement detailing the purpose of payment, significant variation in payment among studies seems likely. Some may argue that there are too many types of studies to use a single formula. We recommend a model combining standardized payments for time with increases for inconvenient procedures and important follow-up visits (15). Amounts calculated with this model are generally moderate or low, minimizing the potential for undue inducement while simultaneously discouraging inadequate compensation. Such a model promotes standardization when studies are similar but allows flexibility when relevant differences exist, thereby minimizing competition between studies and adhering to a principle of fairness. While a specific dollar amount may be unworkable for some organizations, a structure for determining amounts (relationship to local wages, for example) would help to standardize payments in reasonable ways.

Fourth, most organizations require investigators to include detailed information about payment in a specific section of the informed consent document, separate from the risks and benefits of the study. Separating the description of payment from possible direct medical benefits of participation presents information to participants in an appropriately clear manner, thus facilitating informed choice.

Fifth, almost all respondents reported paying patient subjects and healthy subjects similar amounts when their participation involves similar procedures and no apparent difference in the likelihood of direct medical benefit. Although some have argued that patients and healthy subjects should be treated differently with respect to payment (16, 17), most organizations do not make an inherent distinction. We believe that treating subjects similarly when they play similar roles makes good ethical sense (15). Some argue against paying patients because patients derive medical benefit from research participation or may be especially vulnerable. Although many studies offer patients the prospect of direct benefit, others are conducted for purely research purposes and require a similar contribution of time and effort from both patient and healthy groups (for example, magnetic resonance imaging done solely to examine structural joint differences between patients with rheumatoid arthritis and healthy persons). While patients may be vulnerable in the context of clinical research, it is not clear that payment aggravates that vulnerability. In fact, payment may help patients distinguish procedures that are done purely for research purposes from those done for their benefit, thus minimizing vulnerability due to "therapeutic misconception" (15, 18).

Finally, although most respondents require prorated payment for subjects who do not complete a study, few have rules about prorating or about whether to consider subjects' reasons for withdrawal. Prorated payment recognizes the actual time and effort a subject contributes to research and is less likely to pressure a subject into completing a study or concealing information in order to receive money. This simultaneously guards the integrity of scientific data and the safety of human subjects.

Our study has limitations. First, our sample of 32 organizations is small. Second, our findings are limited in their application to pharmaceutical companies because of low participation from this group. However, academic institutions and independent IRBs seem to make most of the decisions about paying subjects, and

both responded at a very high rate and make up a geographically diverse sample.

Our data illustrate several common practices regarding payment of human subjects that may represent benchmarks in the field. Of course, mere convergence does not make standards ethical, nor does variation imply a problem. However, knowing how conscientious organizations approach a difficult issue can aid in developing one's own approach. Our data also highlight several areas of variation that deserve further attention. Organizations should develop mechanisms for tracking studies that pay subjects, as well as written guidance about subject payment to guide their investigators and IRBs. Lack of a clear statement of the purpose of payment and a standardized way to determine acceptable amounts seems likely to lead to wide variations in practice and inconsistent judgments, even within an institution. Finally, most existing guidance discusses the need to minimize undue inducement. Further study and discussion are needed to understand when money is an undue influence, as well as the impact of payment on subject selection and scientific integrity.

Disagreement remains about the acceptable circumstances and manner in which to pay subjects for research participation. We hope that these data will stimulate discussion about appropriate practices within the research community and help organizations continue to evaluate and refine their own policies and practices.

From W.G. Magnuson Clinical Center, National Institutes of Health, Bethesda, Maryland.

Acknowledgments: The authors are grateful for the help and involvement of the representatives of participating organizations. They also thank persons who reviewed the manuscript. Names of these persons are not included to protect the confidentiality of participating organizations.

Grant Support: By W.G. Magnuson Clinical Center, National Institutes of Health.

Requests for Single Reprints: Christine Grady, PhD, Department of Clinical Bioethics, W.G. Magnuson Clinical Center, Building 10/1C118, National Institutes of Health, Bethesda, MD 20892-1156; e-mail, cgrady@nih.gov.

Current Author Addresses: Mr. Dickert: 2626 East Baltimore Street, Baltimore, MD 21224.
Drs. Emanuel and Grady: Department of Clinical Bioethics, W.G. Magnuson Clinical Center, Building 10/1C118, National Institutes of Health, Bethesda, MD 20892-1156.

Author Contributions: Conception and design: E. Emanuel, C. Grady.
Analysis and interpretation of the data: N. Dickert, E. Emanuel, C. Grady.
Drafting of the article: N. Dickert, E. Emanuel, C. Grady.
Critical revision of the article for important intellectual content: N. Dickert, E. Emanuel, C. Grady.
Obtaining of funding: C. Grady.
Collection and assembly of data: N. Dickert, C. Grady.

References

1. Recruiting human subjects: pressures in industry-sponsored clinical research. Office of Inspector General, Department of Health and Human Services. June 2000:13.2. Available at http://oig.hhs.gov/oei/reports/a459.pdf.

2. **Levine R.** What should consent forms say about cash payment? IRB. 1979;1:7-8.

3. **Wartofsky M.** On doing it for money. In: Research Involving Prisoners: Report and Recommendations. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Washington, DC: U.S. Dept. of Health, Education, and Welfare; 1976.

4. **McNeil P.** Paying people to participate in research: why not? Bioethics. 1997;11:390-6.

5. **Ackerman TF.** An ethical framework for the practice of paying research subjects. IRB. 1989;11:1-4.

6. **McGee G.** A piece of my mind. Subject to payment? JAMA. 1997;278:199-200. [PMID: 9218656]

7. **Macklin R.** "Due" and "undue" inducements: on paying money to research subjects. IRB. 1981;3:1-6.

8. Title 45, U.S. Code of Federal Regulations (CFR), part 46. Protection of Human Subjects. 45CFR46.116. Available at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm.

9. The Official IRB Guidebook. Washington, DC: Office of Protection from Research Risks; 1993:3-44.

10. Guidance for investigational review boards and clinical investigators. 1998 update. Available at www.fda.gov/oc/ohrt/irbs/default.htm.

11. **Grady C.** Money for research participation: does it jeopardize informed consent? American Journal of Bioethics. 2001;1:40-4

12. www.centerwatch.com/professional/proflist.html. Accessed 3 March 2001

13. www.himanet.com/solutions/reviewboards.shtml. Accessed 3 March 2001.

14. **Lemmens T, Elliott C.** Justice for the professional guinea pig. American Journal of Bioethics. 2001;1:51-3.

15. **Dickert N, Grady C.** What's the price of a research subject? Approaches to payment for research participation. N Engl J Med. 1999;341:198-203. [PMID: 10403861]

16. **Lemmens T, Elliott C.** Guinea pigs on the payroll: the ethics of paying research subjects. Accountability in Research. 1999;7:3-20.

17. **Yaes RJ.** What's the price of a research subject? [Letter] N Engl J Med. 1999;341:1551; discussion 1552. [PMID: 10577117]

18. **Appelbaum PS, Roth LH, Lidz CW, Benson P, Winslade W.** False hopes and best data: consent to research and the therapeutic misconception. Hastings Cent Rep. 1987;17:20-4. [PMID: 3294743]

© 2002 American College of Physicians–American Society of Internal Medicine