Sheet 20: GUIDELINES FOR REMUNERATION OF RESEARCH SUBJECTS IN THE INTRAMURAL RESEARCH PROGRAM AND REGISTRATION IN THE CLINICAL RESEARCH VOLUNTEER PROGRAM DATABASE

This information and guidance was developed by the Clinical Bioethics Department, Warren Grant Magnuson Clinical Center, NIH.

This information on remuneration of research subjects will assist investigators in writing/designing studies and consent documents that involve remuneration and assist IRBs in reviewing/approving them. This information will help to guide judgments about the appropriateness of remuneration. Such a judgment takes into consideration the recruitment needs, the expected benefits to individuals, and the vulnerabilities of the potential subjects for each clinical protocol. In addition, guidance provided here may promote standardization and consistency in the practice of remunerating subjects, while permitting flexibility and the consideration of practicalities.

The registration and tracking of research volunteers through the Clinical Research Volunteer Program allows for a centralized database through which all research volunteers who are registered and remunerated are tracked. Such a centralized database provides a central repository of information about volunteers that can be used to enhance safety, as well as demographic information about prospective volunteers that can be used to enhance recruitment.

BACKGROUND

Virtually ever since its opening the NIH has been paying subjects for participation in research. In the early years, compensation often went to churches and other organizations whose members served as 'normal' volunteers for research. In 1973, after requesting a recommendation from the Normal Controls Committee about remuneration for patient subjects (defined as those that have the condition under study), the Medical Board decided that patients could also be remunerated for participation in research when their reason for admission was "a study neither diagnostic nor therapeutic in intent, or when the patient was admitted as a control in research directed towards another disease or condition."

A survey of Clinical Directors in 1996 and a review by the Department of Clinical Bioethics of intramural protocols approved in 1997 revealed that a large number of healthy and patient subjects are paid each year for their participation in intramural studies across most institutes. Clinical Directors reported that the decision to pay subjects was usually made by the Principal Investigator on the basis of lack of direct benefit to the subject and/or predicted or actual difficulty recruiting subjects. Approximately 30% of intramural protocols approved in 1997, representing 9/13 institutes, offered payment to subjects for a wide range of studies; and in half of these studies, patient subjects were paid. Guidelines

available from the Clinical Research Volunteer Program (CRVP) for paid studies with healthy clinical research volunteers describe payment for time (inpatient per diem or an outpatient hourly amount) as “mandatory” and payment for inconvenience units as optional. There is great variation in how protocols discuss payment. For example, a 5 fold or greater variation was noted in inconvenience units assigned for certain procedures, such as venipuncture and PET scan. Although a mechanism for registering, tracking, and paying healthy subjects was created by CRVP in 1995, only subjects who are paid through the CRVP are in this database. An unknown number of healthy and patient subjects are paid independently of this mechanism.

ETHICAL CONSIDERATIONS REGARDING REMUNERATION OF RESEARCH SUBJECTS

Remuneration to research subjects may be justified on at least four distinct grounds, 1) as reimbursement for expenses, 2) a means to reduce financial sacrifice on the part of the subjects, 3) compensation for their time and effort, or 4) an incentive to facilitate adequate and timely recruitment for and/or completion of a study.

Although paying subjects is common and pervasive and has been done for many years, there remains some discomfort with the practice. Moral concerns include: 1) the possibility that paying subjects may be an ‘undue inducement’, that is, inducing people to participate in research against their interests; 2) the potential that an offer of money may obscure the risks of research and/or provide an incentive to conceal relevant information, and 3) the possibility that payment preferentially attracts poorer populations as research participants. These concerns relate to paying any research subject, whether they are patient or healthy volunteers. A successful approach would balance these concerns with the reasons for offering remuneration.

To what extent should patient-subjects be treated differently from healthy subjects, especially with respect to the above concerns? Some argue that since patient-subjects are more likely to receive benefit from participating in research, they should not be paid. However, many studies offer no direct benefit to patient subjects. While payment may be *unnecessary* as a recruitment incentive for studies that do offer possible therapeutic benefit, there is nothing inherently wrong with offering payment to patient-subjects in these studies. Some people object to paying patients because they see patients as more vulnerable than healthy subjects and therefore in need of greater protections. Vulnerability is based, presumably at least in part, on a patient’s dependency on their physician and on the possibility that patients will perceive participation in research as treatment designed to benefit them (‘therapeutic misconception’). Offering remuneration to patient subjects may, in fact, reduce the therapeutic misconception by clarifying for them what is done for their benefit and what is done for research purposes only.

PROCEDURES/SPECIFIC GUIDELINES

I. Investigator Responsibilities:

- The Principal Investigator (PI) shall decide whether or not to offer remuneration to potential subjects in accordance with IC procedures and approvals.

- PIs shall follow the recommended NIH guidelines for determining the amount of remuneration to be offered to subjects in a particular protocol. Deviations from the guidelines are permissible, but should be justified. Investigators at non-Clinical Center intramural sites may use site-appropriate guidelines.

- In the protocol submitted to the IRB, the PI shall include a section on remuneration containing justification for remuneration, and details about the amount and conditions of remuneration.

- Details about remuneration shall be disclosed to subjects in the consent document under a separate section entitled “Remuneration.”

- PIs shall ensure that subjects to be remunerated are registered in the CRVP database before participating in protocols. Off-site research programs may use their own mechanisms for remunerating and tracking subjects.

- PIs or their designees are responsible for evaluating prospective subjects’ current and previous protocol participation as part of past medical history. MIS retrieval screens can be used for subjects who have participated in prior studies at the Clinical Center.

- PIs or their designees are responsible for documenting protocol and procedure information and including a copy of the signed informed consent in the medical record. All medical orders and procedures such as blood draws, pharmaceuticals including investigational agents, radiation and radionuclide procedures, shall be ordered and/or recorded in MIS.

- PIs or their designees are responsible for completing an inpatient or outpatient payment form in MIS that corresponds to documented procedures and approved remuneration schemes.

- PIs who decide that a research subject is inappropriate or unacceptable for research participation (e.g. because of falsifying information, presenting a danger to themselves or others, or exhibiting threatening behavior) will notify the Director, CRVP and file an incident report detailing the date and circumstances that led to this decision. The files of these subjects will be flagged and they may lose the privilege of participating in other studies.

II. IRB Review and Responsibilities:

- The IRB shall review the justification for remuneration to ensure it is appropriate given the particular protocol and the population to be recruited. In making this decision, the IRB should consider potential vulnerabilities of the targeted subject population and the proposed methods for assessing subjects' knowledge of risks and benefits and ability to make voluntary autonomous decisions. Although subjects may consider remuneration in their decision about research participation, it should not substitute for nor bias careful attention to the risks, benefits, and alternatives of the study.

- The IRB should not view remuneration as a benefit to offset research risks in deciding whether a protocol should be approved. As in all cases, the IRB is charged with determining whether research risks are justified by the potential benefits of doing the research. Risks that are otherwise unacceptable cannot be made acceptable by offering increasing amounts of money to subjects.

- The IRB shall be satisfied that the guidelines for calculating amounts have been followed, or that justification provided for any deviation is appropriate.

- The IRB shall review and approve the remuneration section of the consent document and other methods of communication about remuneration to subjects, including advertisements, information sheets, and other documents.

III. Informed consent document

- Remuneration shall **not** be listed as a benefit, but detailed under a separate section labeled 'Remuneration'.

- The informed consent document shall specify what is being paid for, when and in what manner the subject will be paid, including the total amount the subject will potentially receive and how amounts will be prorated. For example, "This study requires 4 clinic visits, each lasting 2 hours. The remuneration will be $30 per visit. The total remuneration for completing the protocol will be $120. A check will be mailed to you at the end of each completed visit."

IV. CRVP Responsibilities:

- All research subjects, both healthy and patient, to receive remuneration for research participation will be registered in the CRVP database. Registration can be done either in person at the CRVP office, or through the completion of a form which is sent to CRVP. Research volunteers only need to be registered once provided they participated in a protocol with remuneration at least once in three years. Information obtained at registration includes

demographic information and verification. CRVP shall process payments for the research subjects.

- CRVP shall provide a monthly report to Institute Clinical Directors and Administrative Officers, as well as to the Chief Operating Officer, Clinical Center. The monthly report will include subject names, protocols, and amount of remuneration, as well as compensation charged to Institute CAN numbers.

- Off-site clinical programs that maintain their own databases shall download selected variables to the CRVP database monthly.

SUMMARY

- Adult research subjects participating in intramural research at the NIH **may** receive remuneration for participating in research. This may be in addition to reimbursement for travel, meals, lodging, parking, or other expenses. Remuneration will come through the Clinical Research Volunteer Program (CRVP) for studies conducted in the Clinical Center.

- Remuneration is offered for the inconvenience, time, and effort it takes to participate in research. The amount of remuneration offered in a particular protocol shall be calculated according to NIH guidelines, reviewed and approved by the Institute Clinical Director (or other Institute/Center [IC] procedures) and by the Institutional Review Board, and disclosed to the subject. In this way, remuneration recognizes the contribution research subjects make without being so large as to serve as the sole or predominant reason for participating in research. Paid subjects are not considered employees of the NIH and shall not be treated as such.

- Remuneration may be offered to healthy subjects or patient subjects participating in studies. Although remuneration is usually offered to participants in studies or procedures offering little or no prospect of direct benefit to the subjects themselves, it is not necessarily restricted to those studies. For fairness reasons, all subjects in a given protocol should receive the same amount of remuneration for the same type of contribution.

- Subjects to receive remuneration for participation in a protocol should be registered in the CRVP database. Principal Investigators (PIs) should authorize a subject's participation in each protocol in MIS, and document procedures and interventions in the Medical Information System (MIS) and the medical record according to Clinical Center documentation standards.