What’s New in GCP? SACHRP Provides Questions to Ask Regarding Pay-to-Participate Research

Acknowledging that full pay-to-participate research might not be regulated by federal human subject protection rules, the Secretary’s Advisory Committee on Human Research Protections (SACHRP) provided recommendations for institutional review boards (IRBs), researchers, sponsors and potential subjects to consider.

“SACHRP is aware that IRBs are increasingly asked to review pay-to-participate trials, but lack clear guidance about their ethical and regulatory acceptability, as well as how best to systematically examine the ethical and regulatory issues,” the committee said, adding “prospective subjects considering pay-to-participate trials are also in need of guidance.”

“Investigators and sponsors conducting pay-to-participate trials may also face conflicts between optimal study design and conduct and the expectations of those subjects who, because they are bearing the financial costs of the research, consequently expect individual benefit,” SACHRP said.

SACHRP noted “the ethical acceptability of pay-to-participate trials is highly fact-specific. Therefore, SACHRP does not recommend a default presumption against pay-to-participate trials, even though in general, research subjects should not be expected to pay to contribute to socially valuable research. Instead we recommend a careful review of each trial” based on five questions and the satisfaction of all regulatory criteria for approval. The questions are:

Does the study meet relevant thresholds of scientific quality?

“The question of a study’s scientific validity is integral to the IRB’s assessment of whether a study’s benefits justify its risks and burdens,” SACHRP said. “Because pay-to-participate studies typically lack the well-established peer review processes that generally precede IRB review, the IRB’s responsibility to evaluate the evidence of scientific validity of such proposals is heightened. The IRB should be prepared to confirm the scientific validity and value of the proposed study and its design, either directly when they have the expertise to do so, or through reliance on expert consultants or other institutional committees. An IRB that lacks access to sufficient expertise to conduct the necessary review of scientific quality may, of course, decline to review any study, including a pay-to-participate trial,” the recommendation said.

Is the risk-benefit balance justifiable?

Assuming the threshold of scientific quality has been confirmed, SACHRP said the IRB must continue to evaluate the study’s risks in relation to its benefits to subjects and society. “Just as payment to subjects is not to be considered as a benefit that could balance research risks, payment to participate should not be considered as a harm in the risk-benefit assessment.” Instead, the IRB should evaluate a study’s risks and benefits without considering payment. “If the balance is unacceptable on that account, the study should not be approved. If, however, the balance appears to be acceptable independent of any payment to participate, the IRB should next consider whether payment raises other concerns that need to be addressed to satisfy ethical and regulatory criteria for approval,” the recommendation said.
Why are traditional research funding sources not being used? Could the study potentially be funded by means other than charging subjects?

SACHRP said IRBs should require investigators to “specifically explain and justify the rationale for charging subjects, including whether traditional funding was sought and why other funding sources are not available or appropriate. Although it should not be necessary for investigators to demonstrate that all other funding options have been exhausted, they should demonstrate an adequate and reasonable justification for charging subjects. In particular, IRBs should examine each trial’s potential to exploit subjects for profitseeking motives,” the recommendation said.

SACHRP said investigators should provide a detailed breakdown of the amount charged and a description of what exactly subjects will pay for. They also should explain whether the payment is expected as a lump sum or in installments, as well as the conditions under which a subject would receive a partial or complete refund, if any. For example, what happens if a subject withdraws part way through the research or the investigator removes a subject from the study for medical or noncompliance reasons? This information should be included in the consent form.

IRBs also should review sufficient information to promote confidence that the payment required is minimized and reflects the actual costs of making possible the development of a potentially valuable intervention or the gathering of important information. SACHRP noted FDA regulations covering charging for investigational products (21 C.F.R. Parts 312 and 316) “may provide IRBs with useful guidance in this regard. If the justification for charging subjects is not compelling, then IRBs should not approve the trial,” the recommendation said.

Will requiring payment for participation influence equitable subject selection?

In cases where the justification for charging is deemed acceptable, the IRB should then consider "whether and how study results may be affected by an expectation of payment by subjects,” SACHRP said. “Investigators should be expected to make efforts to mitigate concerns regarding generalizability and inequitable subject selection, potentially considering efforts to include some subjects who are unable to pay their own way (e.g., a sliding payment scale or an approach where economically disadvantaged subjects are subsidized by those who are able to pay).”

Is requiring payment from subjects likely to exacerbate the possibility of therapeutic misconception? If so, how can that concern be mitigated?

If a pay-to-participate study has appropriate scientific validity, an acceptable harm-benefit ratio, a strong rationale for charging subjects, and a plan for equitable subject selection, the next question is how to minimize the potential for a payment requirement to interfere with subjects’ informed decision-making process.

“When subjects are charged for participation, they may be more likely to expect direct benefit, or to regard trial participation as a means of gaining early access to a promising new treatment. This raises concerns about their adequate consideration of and reflection about important study features, such as risks, burdens, discomforts and uncertainty,” SACHRP said.

Therefore, IRBs, investigators and sponsors should “pay special attention to whether the informed consent process will provide clear and complete information about the study and support adequate consideration and comprehension of that information. Similar consideration should be given to any recruitment materials,” the recommendation said.
Although individuals are free to make decisions outside of research that reflect misunderstanding or insufficient consideration of key information. However, “IRBs and investigators fail to fulfill their responsibilities for subject protection if they do not strive to assist potential subjects in reasoned decisionmaking. IRBs need not monitor the enrollment process of each individual subject but rather should encourage investigators to adopt approaches that will support high quality decision-making.” These may include:

- Setting aside sufficient time for knowledgeable study staff to review the entire consent form with potential subjects and answer any questions, rather than permitting a passive consent process in which potential subjects are expected to review materials on their own.
- Including tests of comprehension or “teach back” methods that will provide an indication that potential subjects are aware of and understand key information about the study, such as the difference between research and clinical care, the uncertainty of benefit, and the amount they will be required to pay.
- Incorporating a waiting period for potential subjects to reflect on their desire to participate and potentially discuss the study with trusted others.
- Facilitating prospective subjects’ explicit consideration of their interests (for example, asking for reflection about the possibility that the intervention may have no beneficial effects or may be harmful).
- Providing further support for any individual who expresses that he or she “has no choice” but to enroll, because of his or her medical circumstances.

Questions for Potential Subjects To Consider

While the informed consent form and process “offer an important source of information for prospective research subjects, individuals considering enrollment in pay-to-participate trials may also seek more specific information.”

SACHPR provided a list of questions to help potential subjects in pay-to-participate trials focus on the research’s key attributes. “Many of the questions apply to all research, but should be addressed so that questions specific to payment-to-participate can be understood in the context of the whole trial. This list is not exhaustive and is offered only as a starting point for IRBs, investigators, and sponsors to develop best practices for communicating effectively with potential subjects in the consent form and process for pay-to-participate trials,” the committee said.

The questions are:

- Who has reviewed this research and said it is OK to do?
- Why do the researchers think that what is being tested might help people like me? What do they think it might do, if it works?
- Has it been tested before? If so, how many people has it been tested on?
- Why am I being asked to pay to join this research?
- How much will the researchers charge me to be in this research?
- What exactly will I be paying for?
- What are some reasons I might be willing to pay to join this research? What are some reasons I might not be willing to pay to join this research?
- Besides the people like me who join this research, are any other people or groups also paying for this research? If so, what exactly are they paying for?
- If I am injured, who will pay for the treatment of that injury?
- When will I be expected to pay?
If I quit the research, will I get any of my money back?
If the researchers make me leave the research, will I get any of my money back?
What other costs might I have to pay if I join this research?
Will being in this research affect my health insurance coverage? Will my health insurance cover any part of what I am being charged for this research?

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