

- the informed consent process in cancer clinical trials. *Journal of Clinical Oncology* 14(3):984–986.
- Anonymous. 1976. Patient consent given—but forgotten. *Medical World News* 17(4):26.
- Appelbaum, P. S., L. H. Roth, and C. Lidz. 1982. The therapeutic misconception: Informed consent in psychiatric research. *International Journal of Law and Psychiatry* 5:319–329.
- Braddock, C. H. III, S. D. Finn, W. Levinson et al. 1997. How doctors and patients discuss routine clinical decisions: Informed decision making in the outpatient setting. *Journal of General Internal Medicine* 12(6):339–345.
- Byock, I. 1997. *Dying well: Peace and possibilities at the end of life*. New York: Riverhead Books.
- Christakis, N. 1999. *Death foretold: Prophecy and prognosis in medical care*. Chicago: University of Chicago Press.
- Daugherty, C., M. J. Ratain, E. Grochowski et al. 1995. Perceptions of cancer patients and their physicians involved in Phase I clinical trials. *Journal of Clinical Oncology* 13(5):1062–1072.
- Eichenwald, K., and G. Kolata. 1999. Drug trials hide conflicts for doctors. *New York Times*, 16 May.
- Grady, C. 2001. Money for research participation: Does it jeopardize informed consent? *American Journal of Bioethics* 1(2):40–44.
- Jonsen, A. R., and J. Stryker, eds. 1993. *The social impact of AIDS in the United States*. Washington: National Academy Press.
- Minogue, B., G. Palmer-Fernandez et al. 1995. Individual autonomy and the double-blind controlled experiment: The case of desperate volunteers. *Journal of Medicine and Philosophy* 20:43–55.
- Pellegrino, E. D., and D. C. Thomasma. 1981. *A philosophical basis of medical practice: Toward a philosophy and ethic of the healing professions*. New York: Oxford University Press.
- U.S. Department of Health and Human Services. Office of the Inspector General. 2000. *Recruiting human subjects: Pressures in industry-sponsored clinical research*. Washington: GPO.
- Yukimasa, A., K. Nakagawa, K. Hasezawa et al. 1997. Significance of informed consent and truth-telling for quality of life in terminal cancer patients. *Radiation Medicine* 15(2):133–135.

## Justice for the Professional Guinea Pig

Trudo Lemmens, University of Toronto

Carl Elliott, University of Minnesota

Six news items:

In a Scottish study healthy volunteers are paid £600 pounds to drink orange juice laced with pesticides (Dobson 1998).

In the United States the Environmental Protection Agency (EPA) announces that it will be considering guidelines to allow pesticide testing in humans. In accordance with the Food Quality Protection Act of 1996, the EPA must review 9,000 pesticides currently on the market to ensure that they meet new safety standards (Spotts 1999).

Researchers at the National Institutes of Mental Health (NIMH) and elsewhere pay healthy subjects \$100 to take a hallucinogenic drug called ketamine. Ketamine is ordinarily used as an animal tranquilizer, but it has also gained notoriety as a street drug. Because of the alleged use of ketamine for date rape, several states have made possession of it a felony. The purpose of the NIMH studies is to induce a temporary psychotic state. Researchers argue that the studies may offer new insights into the treatment of schizophrenia (Kong 1998).

Opposition parties in Canadian Parliament raise questions about the collaboration of the army in vaccination trials to protect soldiers against chemical agents during the Gulf War. A contract is revealed showing that a private contract research organization (CRO) has conducted these trials on healthy volunteers, offering Can\$1400 for participation. The consent form raises the spectrum of a host of potential side

effects, “including death” (Commons 1990, 15762–15764; study protocol on file with authors).

VanTx, a CRO operating in Basel, Switzerland, and with subsidiaries in many different countries, recruited research subjects from Estonia, Poland, Macedonia, Slovakia, Peru, and Ecuador to participate in Phase I and II drug trials. All subjects are paid for their participation. Some are flown in from outside Switzerland. Others are asylum seekers (Hirtle, Lemmens, and Sprumont 2000; see also Lafraniere, Flaherty, and Stephens 2001).

A Philadelphia 'zine for human research subjects called *Guinea Pig Zero* publishes “report cards” on a number of research laboratories. Bob Helms, its publisher, gives high marks to several laboratories but criticizes others severely. He writes of incompetent venipuncturists, surly doctors and nurses, last-minute cancellations, and a patient in one study who “emerged with \$7,000 in his pocket and his mind on planet Zork.” *Harper's Magazine* reprints several of *Guinea Pig Zero's* report cards. Both *Harper's* and *Guinea Pig Zero* are promptly sued by one of the criticized institutions. *Harper's* prints an apology and a retraction (Weiss 1997; see also *Guinea Pig Zero* 1996).

Should we be worried that healthy people are being paid to enroll in research studies? Bioethicists cannot decide and so the issue has dropped into a regulatory vacuum. U.S. and Canadian regulations and guidelines frown

on paying research subjects, but they do not prohibit it. They allow researchers to pay subjects, but discourage them from paying very much, lest subjects be “unduly influenced” or “coerced” into enrolling in a study against their better judgment (this basic approach can be seen in Royal College of Physicians 1986; Medical Research Council 1998; National Health and Medical Research Council of Australia 1992; Department of Health and Human Services 1993). Some guidelines or statutes suggest that “compensation for loss and inconvenience is acceptable,” but other payment is not (for example, see the Quebec Civil Code Article 25 (2)). Given this sort of waffling, it is no wonder that Institutional Review Boards (IRBs) are baffled. How much are researchers allowed to pay a research subject undergoing a bronchoscopy? How much for a simple blood drawing? What is it worth to go without sleep for 36 hours, or to be exposed to malaria, or to try an experimental antipsychotic drug?

In the world that regulatory bodies have created, healthy subjects take part in studies because of the money, yet researchers have to pretend that the subjects are motivated by something other than money. Research subjects cannot negotiate payment, since payment is not supposed to be the focus of the transaction. Local research ethics boards are expected not to determine what is fair, but what is “undue inducement.” Even worse, they must determine this on a case-by-case basis. Thus, if the research population is very poor, IRBs can plausibly conclude that payment must be kept very low, so as not to unduly induce subjects into enrolling. But if the research population is wealthy, subjects can be paid much more.

If you are a hammer everything looks like a nail; and if you are a North American bioethicist, everything looks like a problem of informed consent. But the matter of paying healthy subjects to enroll in research studies is not merely a problem of informed consent. It is a problem of exploitation. Like it or not, research on healthy subjects has become a commercial transaction. Volunteers generally take part in research studies not for humanitarian motives, but for the money. The studies they take part in are often funded or conducted by pharmaceutical companies or other large corporate bodies. In many cities these protocols take place in CROs—for-profit bodies often set up solely for the purpose of conducting research, mostly on healthy volunteers. Unlike patients, healthy volunteers have no personal stake in the illnesses to which the research might be applied. They typically volunteer in response to advertisements in the newspapers or on the Internet.

It is time to stop pretending that the relationship between for-profit, multibillion-dollar corporate entities and healthy volunteers is the same as the relationship between an academic physician-investigator and sick patients. We

have argued that research studies on healthy subjects—unlike research on sick patients—are best characterized as a kind of labor relation (Lemmens and Elliott 1999). If regulatory bodies realized this, they would be in a far better position to protect these subjects from exploitation. Labor-type legislation could give research agencies the clout of occupational health and safety agencies by giving them the power to conduct inspections and ensure that “working” conditions are safe. Collective negotiations and unionization could give research participants a stronger voice in arguing for good working conditions. Research participants could negotiate standards of payment based on the level of discomfort they are asked to undergo, the number and types of procedures, the duration of the studies, and other factors. As with worker compensation schemes, research sponsors could offer appropriate compensation schemes to provide some form of financial security in case participants are harmed in research studies.

Are there dangers to this kind of shift? Yes, absolutely. The most serious danger is that the payment argument could be hijacked to defend even more commercialization of the research enterprise and even more exploitation of vulnerable subjects. Research participants could be placed at even greater risk of exploitation if limitations on payment are simply lifted without significant regulatory overhaul. *Guinea Pig Zero* notwithstanding, research participants are not yet organized sufficiently to obtain better working relations through negotiations and labor pressure tactics. And since participating in research studies currently does not count as “employment,” research participants do not even qualify for the resources and protection provided by labor legislation. When research subjects from Eastern Europe and South America were brought to Switzerland, their only goal was to make money. Yet their work did not fall under any category of labor. Immigration and labor authorities did not deal with the issue as a matter of immigration law. Occupational health and safety regulations did not protect the research participants, nor did employment regulations. Thus the issue was left in the hands of Swiss health authorities, who acted only after the media became involved in the case.

It would also be a mistake to force all research participants, sick and healthy, into the same regulatory box. Dickert and Grady have argued in the *New England Journal of Medicine* that “(t)here is no inherent reason to treat patients and healthy subjects differently with respect to payment” (1999). But patients are in situations fundamentally different from those of healthy volunteers. Often they are vulnerable because of their illnesses. They are frequently asked to accept significant risks by foregoing standard treatment and accepting experimental treatment. They may have a sense of obligation toward the physician-investigator or to an institution that has provided them

with care in the past. To import commercial considerations into this already fragile relationship would be to court the risk of serious exploitation.

There are other dangers in introducing payment without significant regulatory changes. First, if market mechanisms are introduced without well-constructed limitations, noncommercial research sponsors could find themselves facing problems recruiting study participants. Second, efforts to compensate participants fairly according to local market standards may be undermined as research moves beyond national borders. Third, payment could create problems with subject selection and the generalizability of research findings by attracting a limited, unrepresentative population of participants. However, this risk may be minimal in many clinical trials involving healthy volunteers, which are often of little scientific value and are conducted simply to fulfill regulatory testing requirements for “me-too” drugs.

The current regulatory system is even more dangerous. Ethical guidelines and regulations ought to protect healthy research subjects from exploitation. But instead, the current regulatory scheme prohibits subjects from receiving a fair wage and denies them the legal resources available to other high-risk workers. As the lawsuit against *Guinea Pig Zero* showed, research participants are virtually powerless in their dealings with the multi-billion dollar biomedical research industry. Labor legislation, in contrast, would reflect the recognition that healthy research subjects volunteer because they are in financial need, and that financial need is the locus of their vulnerability. ■

#### References

- Canada. House of Commons. *Debates*, 22 Nov. 1990–18 Dec. 1990.
- Dickert, N., and C. Grady. 1999. What's the price of a research subject? Approaches to payment for research participation. *New England Journal of Medicine* 341(3):198–203.
- Dobson, R. 1998. Boom in drug tests on humans. *The Independent*, 2 August.
- Guinea Pig Zero: A Journal for Human Research Subjects*. 1996. 2 August.
- Hirtle, M., T. Lemmens, and D. Sprumont. 2000. A comparative analysis of research ethics review mechanisms and the ICH GCP Good Clinical Practice Guideline. *European Journal of Health Law* 7:75–102.
- Kong, D. 1998. Drug studies are questioned. *The Boston Globe*, 31 December.
- Lafraniere, S., M. P. Flaherty, and J. Stephens. 2000. The body hunters part 3: Submit or suffer: “Uninformed consent” is raising ethic of drug test boom. *Washington Post*, 19 December.
- Lemmens, T., and C. Elliott. 1999. Guinea pigs on the payroll: The ethics of paying research subjects. *Accountability in Research* 7(1): 3–20.
- Medical Research Council. Natural Sciences and Engineering Council and Social Sciences and Humanities Research Council of Canada. 1998. *Tri-council policy statement on ethical conduct for research involving humans*.
- National Health and Medical Research Council of Australia. 1992. *Statement on human experimentation*.
- Royal College of Physicians. 1986. Research on healthy volunteers. A report of the Royal College of Physicians. *Journal of the Royal College of Physicians of London* 20(4):243–257.
- Spotts, P. 1999. How ethical is testing pesticides on people, EPA asks. *The Christian Science Monitor*, 14 January.
- U.S. Department of Health and Human Services. Office of Protection from Research Risks. 1993. *Protecting human research subjects: IRB guidebook*. Washington: GPO.
- Weiss, R. 1997. Hospital demands *Harper's* halt distribution of July issue. *Washington Post*, 18 June.

## Treating Research Subjects as Unskilled Wage Earners: A Risky Business

Nancy King Reame, University of Michigan

As a women's health researcher, I routinely compensate volunteers who participate in my clinical studies (Reame 2001). Like Christine Grady (2001), I think it would be wrong to not do otherwise, given the time demands, level of inconvenience, and potential risks. Our protocols involve an overnight stay in the university hospital's clinical research center, during which time blood is sampled every ten minutes through an IV line for 24 hours. Sometimes

subjects undergo treatment with hormones or drugs, EEG monitoring for sleep assessment, and other invasive or potentially embarrassing procedures such as pelvic exams. Sometimes they must return three or four times at weekly intervals to repeat the protocol. Most contribute approximately 36 hours of their time. Depending on the goal of the experiment, volunteers for these tedious, labor-intensive studies include college students, patients, hospital