MEDICAL HUMANITIES REPORT

Undue Inducement in Internationally Sponsored Research

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In terms of their potential for research, developing countries appear to be especially attractive places for scientists. Yet scientific research in developing countries brings with it many challenges for the application of the standard ethical principles involving respect for persons, beneficence, nonmalificence, and justice. What is now emerging is the fact that there are different issues both about the societies and about related ethical questions and dilemmas that people conducting research in developing countries must understand. The goal of this paper is to highlight some of the problems ethics committees in developing countries face in trying to operationalize the use of incentives in human research in a fair and non-coercive way. The subject of incentives has received a lot of attention from bioethicists because of fear that if not handled appropriately, incentives may degenerate into other problems. I approach this topic from an African perspective and, in the end, recommend operationalizing incentives as a way of mitigating some of the ethical dilemmas of international research.

I begin by acknowledging that incentives are not inherently bad. In fact, since research participation can be considered a form of sacrifice, incentives can often be seen as an appropriate gesture of appreciation. More than being dichotomously good or bad, incentives are necessary as a way of encouraging individuals to agree to participate in a trial and to remain in it until the end. The phrases—"money enables participation" and "time is money"—accurately reflect the necessity of paying research participants in order to secure their participation. The need to pay research participants raises the following question: What is the value of time for the person in the study? Incentives become problematic if this question is not appropriately addressed. Specifically, incentives become bad when they sway decisionmaking capacities of individuals by forcing them to ignore risks involved in the trial and to instead only consider the attractive cash amount or gift being offered.

Before continuing my discussion of incentives, it is important to distinguish incentives from compensation and reimbursements. Compensation in research is simply reimbursement for costs incurred while participating in a study. Some types of compensation are more straightforward and thus easier to address than others, including reimbursements for meals, babysitting, and bus fare to and from the research site. Compensation for time spent at the research facility, in contrast, is more difficult to calculate since it has to do with the individual value of one's time. The value of a person's time depends on a variety of factors such as local economic conditions as well as individual personalities. In similar circumstances, due inducement varies among people: for example, the circumstances may be due inducement for one person, but not another. Two other types of compensation that are difficult to calculate for similar reasons are payments for pain and inconvenience. Such payments are typically based on a participant's cooperation in a scientific program, but may also be based on the sale price of the participant's blood sample, bodily tissues, or bodily fluid. Much literature already exists on these two additional subjects, and so I do not pursue them here. Importantly, incentives also need to be differentiated from

reimbursements which give back to trial participants any of their own money or resources that they used in order to participate in a trial.

When compared to both reimbursements and compensation, the use of incentives presents a greater challenge to investigators and ethics committees since incentives require deciding not only what form the incentive should take, but also how much of the chosen form is given. To clarify, when using the term *incentive*, I am not referring to reasonable payments made to subjects for their participation in research or for the costs they incur as part of the trial. Rather, I am using this term to highlight the use of special incentives or bonuses provided to research participants as a mechanism for encouraging them to join or to remain in a study. Incentives, as I have just defined them here, are used to ensure that clinical research studies gather sufficient sample size necessary to maintain statistical power. If not used appropriately, incentives can have undesirable adverse effects for participants, such as eroding the informed consent process. In contrast, reimbursements and compensation do not typically lead to such problems. A reason for this differential experience is that payments for participation to research participants are not considered a benefit, whereas incentives usually are. For example, financial incentives are often used when health or other benefits to participants are remote or nonexistent.

While a large literature exists on the issues of compensation and incentives for participating in research, little has been written on compensation and incentives specifically within international research contexts, especially on research sponsored by developed countries that is conducted in developing countries (only) or alternatively is conducted in both types of countries. Justice and fairness are central concepts for discussion of compensation and incentives, and the centrality of such concepts is even more compelling in the case of international research. Of particular concern here is potential exploitation of a weaker party by a stronger party. With the expanded practice of developed countries sponsoring international research in developing countries, developing country ethics committees increasingly fear unwarranted exploitation of their populations. As compared to individuals from developed countries, individuals in developing countries are more easily compensated and incentivized. As such, developing country committees grow increasingly concerned that their populations will be used as cheap sources of data in research not intended for internal benefit, but instead to benefit developed countries.

I turn now to address issues of fairness in compensating and incentivizing research participants in international research specifically from the viewpoint of developing country ethics committees. I argue that because trial participants from developed countries and developing countries share equally in the burdens of research, we must have just and fair decisions regarding compensation and incentivization of developing country research participants.

Incentives can be examined from two levels: the micro level in which research participants actively participate in the research and the macro level in which communities or countries participate in research. At the micro level, incentives work either to encourage people to join a study or to persuade them to remain in a study so as to serve the aforementioned need to retain a statistically significant and valid number of participants. Risky research or research that is not of direct and immediate benefit to the individual can apply at both levels mentioned. There are strategies that investigators may use to incentivize potential participants to join or stay in trials including bonuses, raffles for prizes, grocery vouchers, cash, T-shirts, caps, food, drinks, gifts, and gift cards. It is important to note that in developing country settings such incentives may easily be viewed as undue inducements. Whereas developed country researchers might consider a T-shirt a simple gift, poverty-stricken community members may alternatively view it as a once in a lifetime treasure not to be passed over.

Returning to the issue of compensation, the notion that participants should be paid for inconveniences, such as time spent and reimbursement for expenses is uncontroversial. What is instead up for debate, and is in fact often overlooked, is the importance of ensuring that payments are realistic relative to the local economy. Indeed, it is crucial that payments are not so large so as to induce prospective subjects to consent to participate in research against their better judgment. Potential trial participants need to be provided with information about the research, including its attendant risks and benefits, sufficient to reach an informed decision regarding their voluntary participation. Researchers must ascertain if the payment levels or chosen material goods have unintended consequences, such as being coercive or resulting in undue inducement. Unfortunately in a developing country setting all such precautionary measures ultimately may not achieve their set goal. Too often, researchers in developing countries are faced with poor, hungry, and unemployed community members who, as a consequence of such impoverished circumstances, might instead view participation in a clinical trial as a way of earning quick money for survival.

The root cause of problems associated with the use of incentives in developing countries is poverty. The degree of poverty is especially high among those communities typically approached to participate in research and the perplexing problem of undue inducements is a direct consequence of such impoverishment. Potential participants are by circumstance forced to consider the benefits and ignore the risks associated with a study. Amounts offered to participants as compensation might appear reasonably non-coercive to sponsors and participants in developed countries, but prove irresistible in developing countries. For example, consider a $150 incentive. That amount may be regarded as appropriate, non-coercive, and non-inducive in a developed country setting. However, that same amount represents up to a year's earnings in a developing country. Advertising for clinical trials in developing countries is not openly posted on notice boards and in local newspapers. Successful recruitment is instead based more on power differentials between investigators and ordinary community members, trust of the authoritative medical profession, as well as the notion found in some cultures that declining an invitation is simply rude and unfriendly.

In general more participants are successfully recruited from developing country sites than from developed country sites. The two main reasons for this both stem from poverty. First, as already discussed, there are large numbers of potential participants in developing countries who are willing to join to make some quick cash (as well as for other reasons). Second, because the cost of compensation and incentives is less expensive per person in developing countries than developed countries, researchers can compensate and incentivize many more people in the developing world with a given amount of money and material goods than they could in the developed world. Let's consider a realistic example: 300 developed country participants and 1500 developing country participants are being paid $300 and $40 respectively as compensation for time and inconvenience and as incentives to remain in the study. This large pay difference between developing world participants and developed world participants is simply too obvious and unfair at both the individual and community/country level. Since research pragmatically contributes to development and international relations, sponsoring countries and researchers should be cognizant of current and historical exploitation of developing countries by developed countries. By participating in the global processes of income redistribution, current health research should ideally play a part in redressing imbalances.

I support a practice whereby resources are channeled through research grants into community development efforts. This channeling would provide an ethical way of dealing with the 10/90 gap, as it represents an effective form of income redistribution from developed countries to developing countries without having to expose individual participants to undue inducement. That

is to say, in the interest of protecting individuals in developing countries from undue inducement, some of the benefits of internationally sponsored trials should, if possible, be converted into community benefits, such as supporting local clinics or engaging in other community projects that promote good health; resultant benefits can then be enjoyed by all individuals within that community. Health research is about a few individuals sacrificing for the benefit of humankind. In that same vein, the self-sacrifice of the few individuals who participate in trials can result in the common good of those communities.

In addition to locally sponsored research, some African countries have internationally-known research centers sponsored by agencies from developed countries. Those research "centers of excellence" are situated largely in poor rural areas but with stable populations; all major studies within those countries are then conducted in such centers and their surrounding areas. Notably, due both to currency weakness in developing countries and to the limited resources set aside for health research, locally sponsored studies do not often offer incentives equal to those made available through internationally sponsored research. There have been reports of individuals who refuse participation in locally sponsored research because they feel that such research is poorly incentivized. They have grown accustomed to receiving cash incentives and other attractive gifts for participation in internationally sponsored trials. As individuals favor the better paying internationally funded trials, this disparity has then led to deterioration in the quality of locally sponsored research.

In the interest of protecting locally funded research, I think certain benefits from internationally sponsored research should be converted into community benefits; this might include supporting clinics, wiring community centers and schools with electricity, installing boreholes or piped water, and engaging in other community projects that promote good health. Funds from research grants could also be used in training and adequately remunerating personnel from developing countries as well as in technology transfer to those countries. Such strategies might then reduce the current brain drain to developed countries and could also reduce the exportation of specimens to developed countries "for further analysis." Moreover, such recommendations might then further the ultimate aim of improving developing countries' capacity to conduct research that directly addresses their own needs. One way of ensuring that locally funded research trials do not suffer at the hands of internationally funded research is to set strict, regulated levels of incentives to be adhered to by both locally funded and internationally funded trials. A percentage of the budget for internationally funded trials might then be diverted to other health promotion activities or to programs for those communities participating in such trials.

In this paper I put forward a view that at both the micro and macro level, compensation and incentivization for participation in research is the most fair and just procedure. Compensation and incentives should not only be monetary, but could also take the form of technology transfer (e.g., scientific, technical, and medical training, and installation and ongoing maintenance of infrastructure of laboratories, clinics, libraries, and other facilities). I end with one additional suggestion. Research ethics committees in developing countries need to be sufficiently strengthened so that they have the capacity to make informed decisions on negotiating compensation, individual incentives, and community benefits for their communities. The ethics committees should review advertisements, recruitment, and payment incentives associated with all studies to ensure that they are consistent with prohibitions on coercion and undue influence and so that internationally funded trials do not unduly affect individuals' willingness to participate in locally funded research. In order to achieve this end, research ethics committees must critically examine the population of the potential participants, the incentives, the conditions under which offers will be made, and the incentives offered for participation by other trials

conducted in their area. Lastly, ethics committees should encourage investigators to consider community benefits and other associated ways of ensuring that communities and institutions realize greater benefit from participation in international research.

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Exploitation in International Research

by Tom Tomlinson

In this short essay, I want to better understand the danger of exploiting research subjects in developing countries.

Concerns about exploitation lie behind a number of ethical principles applied to international research. The 2002 CIOMS Guideline 10, for example, mandates that

> "Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:
> - the research is responsive to the health needs and the priorities of the population or community in which it is to be carried out; and
> - any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community."

The commentary on the guideline explains that this requirement is necessary to avoid exploitation.

> "Even when a product to be tested in a particular country is much cheaper than the standard treatment in some other countries, the government or individuals in that country may still be unable to afford it. If the knowledge gained from the research in such a country is used primarily for the benefit of populations that can afford the tested product, the research may rightly be characterized as exploitative and, therefore, unethical."
> (Found at http://www.cioms.ch/guidelines_nov_2002_blurb.htm, 01/02/06)

The requirement is motivated by a number of studies in developing countries in which the principle beneficiaries of a successful clinical research trial appeared to be persons in the developed world who have the means to purchase any resulting treatment. One possible example is a trial of adjuvant breast cancer treatment following mastectomy in Vietnam, in which the control group received mastectomy alone. Since adjuvant therapy following mastectomy is standard practice in the US, such a trial would not be permitted here. Yet, since Vietnam could not afford to provide adjuvant therapy to all mastectomy patients, whatever knowledge might be gained about the usefulness of this therapy is likely to mostly benefit women (and possibly their insurers) in the US and other developed countries.[1] It might be said, then, that the Vietnamese women in the trial suffered all the risks of the research, but will not enjoy all of its benefits. CIOMS Guideline 10 would remedy this unfair exchange by pledging to make beneficial treatment available to the subjects or to similarly situated patients.

The idea that post-trial benefits help to remedy exploitation raises a number of questions. What form of post-trial benefits best addresses the sorts of exploitation produced by research?

Are there situations in which post-trial benefits might increase the risk of exploitation? And, when is research in a developing country exploitative in the first place?

In this essay, I will only have space to discuss this last question. In my discussion, I will be drawing on, and at times departing from, an article on post-trial benefits produced by participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries, and published in the Hastings Center Report.[2] (Henceforth, the "Conference Report.") Readers who want to pursue some of the other questions raised are referred there.

Let's start by asking what counts as "exploitation." Note first that it is not exploitative merely to "use" another person for my benefit. I do that with my auto mechanic whenever I take my car in to be serviced. Of course, he gets something out of it as well. Since he's "using" me to make his living, there is at least some rough parity of benefits.

This leads to the idea that exploitation occurs when there is an inequality of benefits (or harms). This might indeed be a necessary condition, but it is not sufficient. Imagine a company which hires a management consultant, who collects her standard fee, while the company goes on to save millions using the consultant's recommendations. There's a great inequality of benefits, but we wouldn't say the consultant had been exploited without having more information about the conditions under which the deal was struck.

We also should recognize that if inequality of harms or benefits were a sufficient condition for exploitation, much human subjects research would be exploitative by its nature. Research is not therapy; it is not conducted primarily to benefit its subjects. It's conducted to gain knowledge that will often be of benefit only to others, while the subjects endure the risks. There is thus an inherent inequality in the distribution of harms and benefits produced by medical research, but it would go too far to condemn it all as "exploitative."

We might attempt to address this by incorporating a requirement of informed, voluntary consent into our conception of exploitation. Neither the consultant nor the research subject is exploited so long as they freely agreed to the "bargain." But this isn't quite right either. Together with inequality of harms/benefits, the lack of consent may contribute to exploitation. But it's not a necessary condition. To borrow an example from the Conference Report, if I run into a snow bank and find myself at the mercy of a tow truck operator who demands three times the usual rate to tow me out, I'm a victim of exploitation even as I freely pull the cash out of my wallet.

So what then is "exploitation?" Borrowing from Alan Wertheimer[3], the authors of the Conference Report claim that "Party A exploits party B when B receives an unfair level of benefits as a result of B's interactions with A" (Conference Report 19). But what makes a different level of benefits an unfair and hence exploitative one? According to the Conference Report (and Wertheimer), "Fairness in individual interactions, which is the concern of exploitation, is based on ideal market transactions. Thus a fair distribution of benefits at the micro-level is based on the level of benefits that would occur in a market transaction devoid of fraud, deception, or force" (Conference Report 20).

This is an unsatisfactory answer. It can't easily make sense of the tow truck example, which is a market transaction involving neither fraud, deception, nor force. Neither is it clear how to translate this market model into the context of clinical research, which doesn't involve markets of the usual kind and so doesn't offer paradigm examples of what counts as a fair market transaction.

What produces exploitation is not just inequality of harms or benefits, but also how that inequality comes about. Here the role of vulnerability becomes critical, because exploitation involves "taking advantage" of another person. John exploits Sam when

- Sam is vulnerable or disadvantaged (from desperation, ignorance, incapacity, poverty, etc.).
- John uses that vulnerability to his advantage in order for John to end up with a larger share of benefits, or Sam a larger share of burdens, than would otherwise have occurred.

The authors of the Conference Report, however, brush aside the relevance of vulnerability: "Since exploitation involves the distribution of benefits and burdens, vulnerability is neither necessary nor sufficient for its occurrence" (Conference Report 20). Of course, by itself vulnerability is not sufficient for exploitation. There can be a parity of harms/benefits despite the vulnerability of one of the parties. But by itself, inequality of harms/benefits is not sufficient for exploitation either. It's the *relationship* between inequality and vulnerability that produces exploitation.

Given this conception of vulnerability, when is research in developing countries exploitative? Perhaps less often than assumed. Certainly we can no longer conclude that research is exploitative merely because it promises much greater benefits for developed countries than it does for developing countries. It will depend as well on the reasons for that disparity. Compare two studies. One is a surveillance study of HIV-discordant heterosexual couples in Africa which seeks in part to determine the relationship between HIV viral load and seroconversion of the HIV negative partner.[4] Uganda could not afford the resources for viral load testing and for the antiretrovirals needed to reduce viral load in HIV positive patients. For these reasons, any results showing a strong relationship between viral load and infectivity would prove much more useful for HIV-positive persons in the US than in Uganda. The other is Phase I testing of a potential treatment for oral cancers, using patients recruited at a cancer center in India.[5] If successful, the drug, being developed by a commercial start-up company, would likely be beyond the reach of most Indian cancer patients.

In both these cases, the benefits of the research will go disproportionately to patients in developed countries. But the Ugandan study is less exploitative than the Indian study, for two reasons. The first has to do with the reasons for conducting the research in the developing country and the way these rely upon vulnerability. The question posed by the HIV seroconversion study would be much more difficult to answer in the US, since for scientific validity the study requires a high rate of heterosexual transmission, together with an incidence of HIV-discordant heterosexual couples sufficient to recruit the numbers required. By contrast, I will suppose, the questions posed by the Indian cancer trial could have just as readily been answered by trials conducted in the US. Arguably, they were conducted in India because there participants are more easily and cheaply recruited, due to poverty, illiteracy, and desperation. Of course, the high incidence of HIV transmission in Uganda is a disadvantage suffered by those who will be recruited into the study. But the trial relies only on there being a high incidence of HIV transmission, not on this high incidence being a disadvantage relative to other subject populations. Unlike the Indian trial, the Ugandan research does not rely on the subject's being disadvantaged in order to further its aims.

The second reason is that the HIV study has a much more benign risk-benefit ratio for the subjects than the Indian study. The Ugandan subjects are exposed to little or no additional risk, and may benefit from the additional HIV education and counseling provided by the research project. The Indian subjects are at risk for whatever toxic side-effects may be caused by the agent being studied, with no prospects for any therapeutic benefit. This enlarges the disparity in harms/benefits between the subject population and the populations of patients who will benefit from the knowledge obtained. This implies that one way to reduce the danger of exploitation is

to maximize the benefit-risk ratio for the study subjects. (And this can't be accomplished by luring subjects into ignoring the likelihood or significance of real risks.)

This discussion has only begun to scratch the surface. Even if my analysis of exploitation is headed in the right direction, there are still plenty of questions. What counts as a "vulnerability?"[6] Under what circumstances has someone improperly relied on or used a vulnerability in gaining an advantage? And, of course, how do we translate the answers to these questions to the international research context?

References

1. See Love, RR, and NC Fost. 1997. Ethical and regulatory challenges in a randomized control trial of adjuvant treatment for breast cancer in Vietnam. *Journal of Investigative Medicine* 45(8):423-31.

2. Participants. 2004. Moral standards for research in developing countries: from "reasonable availability" to "fair benefits." *Hastings Center Report* 34(4): 17-27.

3. Wertheimer, A. 1999. *Exploitation*. Princeton, NJ: Princeton University Press.

4. For example, see Gray, RH, and MJ Wawer MJ, and R Brookmeyer, et al. 2001. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. *Lancet* 357(9263):1149-53.

5. I'm thinking of the Phase I trial of M4N conducted by a Johns Hopkins researcher without approval of the Hopkins IRB. For more disturbing details, see Bagla, P. and E. Marshall. 2001. Hopkins reviews investment in Indian cancer drug trial. *Science* 293, 1024.

6. For more on the concept of "vulnerability," see Kipnis, K. 2001. Vulnerability in research subjects: a bioethical taxonomy. In Ethical and Policy Issues in Research Involving Human Participants, Volume II: Commissioned Papers and Staff Analyses, National Bioethics Advisory Commission, pp G1-G13. (available at http://www.georgetown.edu/research/nrcbl/nbac/pubs.html)

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How Much Are We Reporting about Ethical Misconduct: A Critical Review of Cyranoski's Article "Chinese Clinical Trials: Consenting Adults? Not Necessarily"

by Edward Chigwedere
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David Cyranoski's recent article in *Nature*, "Chinese clinical trials: Consenting adults? Not necessarily," reveals how certain clinical research in China has violated ethical research regulations. In this paper, I briefly outline what the article reports, disclose Cyranoski's sources of information and consider how authoritative they are, highlight significant omissions in the report, discuss how the report deals with controversial issues and their interpretations, and finally look at the implications of the report.

In 1999 China passed the Good Clinical Practice (GCP). This international standard demands a variety of regulations, including informed consent, approval of trial protocols by independent Institutional Review Boards (IRBs), and strict monitoring of trials. Despite these formal regulations, their enforcement is patchy. A classic example of a poorly regulated Chinese trial is the VGV-1 trial, which sought to study the effects of VGV-1 on participants who had never had antiretroviral therapy. Cyranoski reports a number of flaws with this trial, notably:

- The trial was carried out without the drug being approved by the State Food and Drug Administration (SFDA) of China.
- The trial protocol was not properly explained to the participants. Participants later reported that they found the informed consent process unclear and that doctors made no effort to explain it or the trial to them.
- Participants were deceived. They were told that the treatment would grant them good health without the need for further treatment for up to 20 years.
- Participants were never informed of trial results.

While the above list includes many significant flaws, one that Cyranoski fails to point out is the scientific justification for using research participants who had never been exposed to antiretroviral therapy. The only other VGV-1 trial that Cyranoski mentions relied upon participants who had previously been on antiretroviral therapy. Given that we do not have any information about the effectiveness (and the risks) of VGV-1 on people who had never taken AIDS treatment, I am unsure of what the scientific basis was for carrying out this trial.

In order to assess and critique this trial, Cyranoski draws from four distinct sources. First, he spoke to trial participants, quoting directly what they viewed as the flaws in the VGV-1 trial. Second, he communicated with Ruotao Wang, the IRB chairperson for the National Center for AIDS/STD and Prevention and Control. Wang states that rather than being cautious when making decisions about new drugs, many IRBs in China are ineffective due to "inexperienced members" with "little training in bioethics" and a tendency of getting "carried away with

enthusiasm" (139). Third, Cyranoski got in touch with the public relations representative for Viral Genetics, the company that supplied the drugs. Fourth, Cyranoski sought information and perspectives from people not directly linked to the trial, like the director of the Aaron Diamond AIDS Research Center in New York who is conducting research in China on IRBs.

Despite consulting this wide range of sources, Cyranoski has two serious omissions in his method. First, he did not attempt to contact the Ditan Hospital IRB, which was the IRB that approved the VGV-1 trial. Second, given both the magnitude of the problems that the Chinese bioethics committees reported and how poorly the case was handled after reports were made to the National Center for AIDS/STD Prevention and Control IRB, Cyranoski should have sought independent legal views. I will return to this second point later.

Now that I have pointed out all these problems with this trial, what might explain them? According to Cyranoski, ethical misconduct in Chinese clinical trials is largely a function of two interrelated factors: first, an alarming lack of knowledge regarding ethical regulations; and second, ineffective IRBs — IRBs that rubberstamp proposals that come before them instead of enforcing bioethical standards. Despite the existence of these problems in the Chinese biomedical system, medical researchers are queuing for clinical trials in China. Indeed, among countries sponsoring research, China is a favorable destination in Asia. According to the National Institute of Health (NIH), China received the highest NIH award in international research for all Asian countries in 2003—an amount equivalent to 13.2 million American dollars (Bartlett 2005).

Why this level of interest and support for clinical research in a country with questionable ethical standards? Cyranoski believes that this interest is due to "plentiful clinical opportunities" as a result of a "debilitating" disease profile: infectious diseases (including AIDS), lifestyle ailments, and rare genetic disorders (138). Additionally, China is an attractive place for clinical research because of the sheer size of its population. Such a large population, especially one with chronic medical needs, translates into good business for the pharmaceutical industry. Specifically, China is an appealing open market for antiretroviral pharmaceutical companies given that it is estimated that approximately 10 million Chinese—almost the size of the Zimbabwean population and three times the size of the population in Botswana—will have AIDS by the turn of this next decade.

Some argue that developing countries attract clinical trials because conducting research in such countries (or countries in transition as is said to be the case with China) is less cumbersome than in developed countries (Angell 1988). Cyranoski's article lends further support to this position, as he describes how Chinese IRBs typically approve proposals that come their way without adequate consideration to ethical standards. Cyranoski overlooks another reason why receiving research approval in developing countries is not as cumbersome—their IRBs are poorly staffed. Instead of a well staffed committee consisting of people from diverse backgrounds, and importantly including people who are not affiliated with or invested in the trial in any way, as is the model in developed countries, IRBs in developing countries are all too often one-person committees. There have been reports in developing countries of committee members with personal interests in the trial protocols, as well as of committees receiving a significant portion of their funding from protocols they approve, which means they benefit from approving rather than rejecting trials (Ndebele 2005).

In light of my discussion, it seems that the approval of the VGV-I trial was a result both of the aforementioned factors and of scientists' limited knowledge of bioethical standards. As Wang observes, most IRBs in China consist of scientists who lack adequate substantive knowledge of bioethics. He asserts, however, that under normal circumstances they should still avoid using any

drug whose profile is unknown. In other words, while serving on IRBs and working in clinical trials, they are still expected to abide by the Hippocractic oath of "do no harm."

Cyranoski offers two recommendations for alleviating such ethical misconduct: first, provide bioethics training to all IRB board members and second, if they want to avoid tarnished reputations, international funding organizations need to be more cautious of where and whom they fund. While these recommendations are laudable, it is also important to note that they do not include a legal voice. This cogent omission implies that Cyranoski does not recognize the interconnected relationship between bioethics and the law. A legal perspective, for example, would be helpful in determining the legal obligations that both China and sponsoring countries have in ensuring ethical research trials. Moreover, by excluding a legal perspective, Cyranoski's recommendations do not address the possible legal consequences of both physicians and investigators knowingly misleading VGV-1 research participants.

In conclusion, Cyranoski's article sheds light on ethical misconduct in China, but still and yet it perpetuates a disturbing divide between bioethics and law particularly in the developing world. Ethical misconduct, especially in the research field, should necessarily attract attention within academic circles. However, such attention should also be inclusive of legal perspectives. This calls for vigilance on the part of bioethicists in developing countries and for support from their colleagues in the developed world.

References

Angell, M. 1997. The Ethics of Clinical Research in the Third World. *N Eng J Med* 337(12):847-849.

Angell, M. 1988. Ethical imperialism? Ethics in International Collaborative Clinical Research. *N Eng J Med* 319(16):1081-1083.

Cyranoski, David. 2005. Chinese clinical trials: Consenting adults? Not necessarily. *Nature* 435:138-139 (12 May).

Bartlett, E.E. 2005. International Research: Promises and Pitfalls. Conference on Ethical Dilemmas in Human Subject Research, Michigan State University. October 28, 2005.

Ndebele P. 2005. The Problem of "False Confidence" in Microbicide Trials in Zimbabwe and Elsewhere. Invited lecture. Michigan State University, October 6, 2005.

Ndebele P. 2005 Health Research Oversight in Zimbabwe: Responding to International Developments and Current Challenges. Invited lecture. Michigan State University, October 7, 2005.

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InkLinks *is a regular column in which readers reflect on issues related to the previous lead article. In the last issue of The Medical Humanities Report, Len Fleck wrote about the complexities in deciding who to help. Identifying the "least well off," he wrote, is not all that matters; there are also questions about how much good will be accomplished. His discussion of finite health care resources has echoes throughout all "helping" spheres: there is only so much time, attention, energy, and money. The contributors to today's InkLinks have extensive experience in community and international development. They share their own reflections on choosing what to do.*

Working in Africa: Whom to Help, and How?

by Lexine Hansen
Resource Development, M.A. candidate
Former Peace Corps Volunteer, Morocco

Reading Fleck's essay about our obligation to provide assistance to the medically least well-off is intriguing to those who deal with international development because the issues of how to use limited resources to assist those least well-off (in the third world as well as in our poorer communities) is the same. We struggle with moral claims around *which* least well-off take priority and *how* best to help them.

Large scale humanitarian efforts in countries or locations that lack social infrastructure or capacity have a lot of competing claims for assistance. Many organizations use a triage system whereby those "least well off" are prioritized for help. We make pragmatic decisions to alleviate famine, provide disaster relief, etc. But in the day-to-day work of development, women and children are the least well-off (according to UN indicators) and so programs focus on them. In situations of conflict, some aid organizations have begun to prioritize aid to those victimized the most and deny it to those who engage in violence (which is probably easier in theory than to see or control on the field).

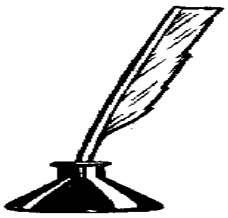
As we see from this example, *who* we focus on also significantly impacts *how* we help them. Here is where Fleck raises an interesting point—he suggests that the effectiveness of the aid is part of the moral question. In effect, he suggests that it is morally permissible to provide aid only to those that the aid can help—which is a reverse of the usual aid mantra to find ways to provide aid that does help. If we consider it a moral imperative that the aid be effective, that it help move those least well-off to a better place, then humanitarian aid that helps the perpetrators of violence more than the victims is actually morally reprehensible.

But what about more mundane situations? Let's return to the women and children example. Over the years, development programs have moved from programs that specifically provide services to the poor to those that attempt to help the poor access more resources. When focused on women, this quickly becomes a social structure issue: it isn't whether there is enough food in the household to feed women, it is convincing male house heads that women deserve an equal share of the food there is. Pragmatic developers soon realize that women and children are marginalized because of complex social processes and structures that limit not just women's

roles but also those of men. Therefore fundamental changes in women's social conditions, rights and abilities are required to improve their lives materially. In effect, women's role in society must be changed—we are calling for a social revolution. Suddenly we discover that helping the least well-off is deeply challenging.

What is most interesting in terms of the question of helping the least well-off is the concept that aid is only morally justified if it is effective. We see that just doing "something" to help isn't sufficient to fulfill our moral obligations—we have to do something effective, or we simply cause more damage.

MEDICAL HUMANITIES REPORT



InkLinks *is a regular column in which readers reflect on issues related to the previous lead article. In the last issue of The Medical Humanities Report, Len Fleck wrote about the complexities in deciding who to help. Identifying the "least well off," he wrote, is not all that matters; there are also questions about how much good will be accomplished. His discussion of finite health care resources has echoes throughout all "helping" spheres: there is only so much time, attention, energy, and money. The contributors to today's InkLinks have extensive experience in community and international development. They share their own reflections on choosing what to do.*

Working in North America: Worries about Worrying

by Bill Hannah
Philosophy, Ph.D. candidate
Community Activist, Canada

I worry about three things when I think about treating the poor: First, that the implied separation between us and them when talking about treatment will go unnoticed and unaddressed; second, that most such discussions simply intensify efforts to preach to the converted; and third, that agonizing about how we (and others) should go about it will in the end paralyze all efforts.

First, the question "How ought we treat the poor?" implies an unhealthy separation between the poor and us. Of course there is a difference between people who are poor and people who are not poor, but differences in responsibility are not so clear. We create and perpetuate the conditions that result in poverty—in poor people. We cannot separate ourselves and our actions from conditions of poverty as easily as one might from someone who has a broken arm. There, one's obligations could be only to treat the injury. Treating the poor as an overarching goal helps to distance us far too much from our culpability for what we treat. We need to ask how to eliminate the conditions that result in there being a separation between the ultra-poor and the well-off.

At this point my second concern crops up. People who are devoted to treating the poor understand both the need and the complexities involved in meeting the need. So discussions about it may not be helpful. The International Committee for the Red Cross is not naive in its traditional commitment simply to helping those who were suffering without concerning itself with guilt, innocence, or root causes. Sometimes treatment is the best one can do and in order to treat one will have to remain neutral, or even subjugate oneself to local powers.

My third concern is this. If you find yourself "merely" treating the poor, or "merely" making people aware of the roots of the problem, do not stop! Strategically, it makes sense that some of those who want to help act as neutral parties devoted to triage while others engage in activism against the source of the problem.

To achieve the goal of eliminating poverty we have to stop preaching to the converted and *continue* with the efforts we are currently involved in. Apathy is often blamed for inaction, but

paralysis stemming from “but what can I do?” must be addressed. The challenge is to educate and motivate those who are doing nothing, while making more pluralistic our own efforts.

MEDICAL HUMANITIES REPORT

The Center Remembers Beth McPhail

by Barry DeCoster
University of Louisville

This past November, the Center for Ethics lost a good friend and coworker. Beth McPhail passed away after a two-year struggle with cancer.

Beth and I began working at the Center around the same time in 1999. We shared an office over the following years. If you have ever shared an office with another person, you likely know that sharing a close work space is a wonderful way to get to know someone—if the relationship is right. With Beth, that relationship was always one of easy friendship, joking, and seemingly continuous good moods. Well, that's to exaggerate; like all of us, Beth got upset. I remember her occasional frustrations with her computer. As she hurled insults at the computers—always deserved, of course—Beth would end up chuckling away her irritations. Beth also had the habit of "thinking out loud" as she worked. At first, I was often distracted by her comments and confused as to whether I should respond to her questions. Although I never really learned *not* to reply to her questions not directed to me, like the rest of the Centerfolk, I came to enjoy the sound of her voice, her cheerful whistling, and occasional humming, as part of the background to the Center's daily environment. Her pleasant mood and concern about others continued during her illness. Most often Beth would quickly divert attention away from herself, and instead she would ask about your day—or she might brag about the many accomplishments of her children that brought her no end of vicarious parental joy.

During her time with the Center, Beth was a wondrous resource. She was one of the gems scattered throughout Michigan State University that allow academic units to run smoothly and efficiently. Without her effort and skills, many of the Center's projects would never have seen the light of day. Beth worked to organize the Center's Brown Bag Speaker Series, to overhaul the Center's website, to ensure distribution of the *Medical Humanities Report*, and as many of you reading this will know, she was often the voice who greeted callers and guests to the Center. We at the Center miss Beth dearly. Her absence is painfully noticed, but we are grateful for the time we had with her sharing her infectious laughter and enjoying life.

MEDICAL HUMANITIES REPORT

News & Announcements

JUDY ANDRE

- Presented “Incorporating Ethics Case Studies into Science Courses” at the Lilly Seminar on Teaching Ethics, Michigan State University (October 2005).
- Gave a three hour workshop, titled “Confidentiality,” for hospital ethics committees, University of North Florida, Jacksonville (January 2006).

LIBBY BOGDAN-LOVIS

- Presented a collaborative paper (with Chad Gandiya, M.Div. and Joseph-Matthew Mfutso-Bengo, Ph.D.) titled "Bioethics' Truths?: A Transnational 'E-Dialogue' Between Medical Students in the United States and Students in Sub-Saharan Africa," at the 2005 American Anthropological Association Annual Meeting, Washington, D.C. (December 2005).

HOWARD BRODY

- Presented “Physicians, Ethical Principles, and the Drug Industry” to Michigan State Medical Society, Annual Bioethics Conference, Traverse City (October 2005).
- Gave the talk “Ethical Issues in Working with the Pharmaceutical Industry” for the11th annual Bioethics Grand Rounds, York Hospital, Pennsylvania (November 3).
- Presented “Physicians and the Pharmaceutical Industry: Issues of Professionalism” for Professionalism conference for house staff, Beaumont Hospital, Royal Oak, MI (January 2006).
- Published a commentary on “Clinical Case: Informed Refusal” in Virtual Mentor: Ethics Journal of the American Medical Association, 8(1):24-29, January 2006.
- Gave the talks “Is Futility About the Just Use of Resources?” and “Ethics and Resource Allocation: The Return of Grass Roots Bioethics” for MidMichigan Medical Center, Midland (January 2006).
- Presented “Can We Talk? Religion, Bioethics, and End of Life Care in America” for the Albert J. Shipka Speakers Series, Youngstown State University, Ohio (February 2006).

LEN FLECK

- Published “Creating Public Conversation About Behavioral Genetics” in Wrestling with Behavioral Genetics: Science, Ethics, and Public Conversations, edited by Erik Parens, Nancy Press, and Audrey Chapman (Johns Hopkins University Press, 2006), 257-85. This was one of the documents to emerge from a three-year NIH ELSI project that was a collaboration between the Hastings Center and the American Academy for the Advancement of Science.

MARGARET HOLMES-ROVNER

- Spoke on (with co-authors D.R. Rovner, J. Pylar, C.E. Wills, J. Lillie, and K. Kelly-Blake) "Accuracy of graph interpretation in a decision aid" at the 27th Annual meeting of the Society for Medical Decision Making, San Francisco (October 2005).
- Presented (with co-authors A.M. O'Connor, G. Elwyn, D. Stacey, R. Volk, R. Thomson, A. Barratt, M. Barry, A. Coulter, H. Llewellyn-Thomas, N. Moumjid, and T. Whelan) "International Patient Decision Aids Standards Collaboration [IPDAS] Reaches Consensus On Criteria For Judging The Quality Of Patient Decision Aids" at the 27th Annual meeting of the Society for Medical Decision Making, San Francisco (October 2005).
- Gave a talk on (with co-author A. Siddiqi) " Euroqol Vs Domain-Specific Measures To Predict Cardiovascular Disease Outcomes" at the Annual Scientific Meeting of the International Society for Quality of Life Research (ISOQOL). San Francisco (October 2005).
- Published (with co-authors C. Price, D.R. Rovner, K. Kelly-Blake, J.A. Lillie, C. Wills, and V. Bonham) "Persistence of men's theories about BPH and prostate cancer following a decision aid" J Gen Intern Med: (2006)21:56-60.
- Published (with co-author C.E. Wills) "Integrating Decision-Making and Mental Health Intervention Research: Research Directions" in Clinical Psychology. Science and Practice (2006) 13(1): 9-25.

HARRY PERLSTADT

- Serves on the CDC Research Agenda Steering Subworkgroup, Advisory Committee to the Director of CDC. This group is advising on the creation of the new CDC Health Protection Research Guide, 2006-2015.

GERALD S. SCHATZ

- Published "International Health Regulations: New Mandate for Scientific Cooperation," American Society of International Law Insight (August 2, 2005).
- Published "Introductory Note to World Health Organization: Revision of the International Health Regulations," International Legal Materials (September 2005).
- Coauthor, with Howard Brody, "Letter: Learned Intermediary Doctrine," Federal Lawyer on contrast between pharmaceutical industry's marketing strategies and its liability defense that the physician makes the decisions (January 2006).