Advocacy for Research Participants

COMMUNITY ETHICS COMMITTEE
REPORT submitted to the
PRESIDENTIAL COMMISSION ON BIOETHICAL ISSUES
July 2011

SUMMARY of the CEC's Recommendations

The CEC makes four specific recommendations to the Presidential Commission on Bioethical Issues:

- We strongly recommend that empowered, informed and truly independent **Participant Advocates** be assigned to research participants and that those advocates stay with individual participants from the initiation of the informed consent process, through the clinical trial, and for follow-up after the trial closes.

- As an adjunct to providing independent Participant Advocates for individual research participants, the CEC also recommends local **Community Groups** be included as an authentic voice in the review, monitoring and management of clinical trials.

- While we recognize that numerous laws and regulations contain enforcement mechanisms for breaches of clinical trial protocols, we recommend that real and significant **Consequences**, such as loss of licensure and public censure, be imposed upon individual professionals involved in research which is not ethically supportable, as a way to minimize both community and individual harms.

- Lastly, given the pervasive nature of clinical trials in current medical practice, we highly recommend that medical schools **require a Course in Medical and Research Ethics** and clinical trial protocols.

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RE: **Protection of Human Subjects –**
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INTRODUCTION

The Community Ethics Committee (CEC) is a group of nineteen members living in the Boston metropolitan area who are representative of the diverse population served by the Harvard-affiliated teaching hospitals. The need for such a consultative group has been evident for a long time since the few community members on hospital ethics committees are not able to be representative of multiple communities, and there are almost no established ways to engage the lay public in addressing ethical and policy aspects of health care and biomedical research. Solicitation for membership on the Committee has been cast widely through civic, business, and religious groups, with a specific application process to ensure selection of a representative and effective working group, based on the demographics of our community.

The CEC's members are diverse as to socio-economic status, religious affiliations, cultural and language groups, and educational backgrounds. Twelve of the members are women and seven are men; we range in age from early twenties to seventies. Some have advanced degrees and some only have high school diplomas. Among the members are a high school administrator, a high school teacher and a recent college graduate; a rabbi and a prominent member of the Muslim community; individuals with disabilities and parents with medically involved children. Two of us are retired, one from a large Boston law firm. One of us is an Asian immigrant, several have ties to the African-American community, and one is of Guatemalan descent. The members are students and writers and small business owners. We volunteer in our communities - at a local rape crisis center, on an Institutional Review Board, in ministerial training, and in health care facilities. We belong to eight different religious traditions, including atheism, and we are fluent in seven different languages. Most of the members have attended the Harvard Bioethics Course, where the first CEC members met in 2007 and began our conversation as the Community Ethics Committee.

Acting under the auspices of Harvard University Medical School's Division of Medical Ethics, the CEC provides consultative services to all seven of Harvard's teaching hospitals. We have provided reports on such topics as pediatric organ donation on cardiac death, withholding non-therapeutic CPR, medical staff's use of social media, and continuous deep sedation as comfort care until death (aka palliative sedation). All of our reports have led to changes in hospital policies. We have also consulted with the Massachusetts Department of Public Health on the development of crisis standards of care in the event of a pandemic or catastrophic loss.

PROCESS

As a result of a brief conversation with the Deputy Director of the Presidential Commission on Bioethical Issues at the May, 2011 public hearing in New York City, the CEC was given the opportunity to submit this Report containing a community's perspective and recommendations about "Protections of Human Subjects" in federally-funded clinical trials in resource-poor countries. The Committee began its review with Susan Reverby's October 2010 article on the Guatemalan syphilis study done in the 1940s. We met on June 23, 2011 and discussed our individual concerns and varied perspectives, educating ourselves as thoroughly as possible beforehand. A majority of us came to the topic with no specialized knowledge of clinical trials or protections afforded human research subjects.

In addition to our one meeting to discuss this topic, the Committee members corresponded by e-mail and shared articles we had found and information we had gathered. As a valuable part of our process, one of the Committee members, who is a community representative on an active and accredited Institutional Review Board (IRB), was able to provide us with a brief introduction to the laws, regulations and context of how IRBs review, comment upon, and approve clinical trial research protocols, with particular focus on federally-funded trials conducted in resource-poor countries. That member stressed the rigors of the IRB processes, review and training. He noted that IRBs are very cognizant of their primary purpose – protecting research participants from harm, all while cultural sensitivities are respected, the voluntary nature of consent is rigorously maintained, and the information gathered is kept confidential.

Perhaps most importantly, the CEC members spoke about these issues with family, friends and colleagues – their communities. More than any other topic the Committee has addressed to date, the issues raised by clinical trials in resource-poor countries, especially as illustrated by the graphic and troubling abuses of the 1940s Guatemalan study, brought out the differences of our cultural sensibilities and the resultant trust and distrust of institutional medical systems.

Irrespective of our uniquely individual views of cultural and population vulnerabilities, our initial dilemma was the language used to discuss the topic. We deliberately chose to use the word "participant" in this Report rather than the objectifying word "subject", feeling strongly that the term "participant" implies informed consent while "subject" does not. We therefore use the term "participant" throughout this Report aspirationally.

(We should note that, as part of the development of our reports, we usually distribute a survey among the members of the Committee to ensure all voices on specific questions are heard - answers are provided anonymously and quotes from those surveys are typically included in our reports. CEC members also survey their own communities through our blog (http://medicalethicsandme.blogspot.com/) and individual Facebook pages to elicit broader public perspectives. Because of the time constraints attendant on providing this Report to the Presidential Commission by early July, we were not able to develop those Committee member and community surveys. We would be happy to respond to specific questions from the Presidential Commission and discuss this topic more fully in the future using the methodology we have developed.)

PERSPECTIVES and COMMENTS

Recognizing that this topic is especially multi-faceted and that we could not hope to address all the many concerns that arise when federally-funded clinical trials are conducted in resource-poor countries, the Committee chose to provide comment on four categories within this topic:

1. **Authentic Community Participation** by representative groups living where the research will be conducted – participation that includes collaborative partnerships, independent review, and respect for study communities;

2. **Vigorous Advocacy for Research Participants** provided by individuals who are empowered, informed and truly independent of institutional and governmental influences - advocacy that includes respect for recruited participants, as evidenced by transparency and voluntary informed consent;

3. **Social Value to the Community** that clearly justifies conducting a particular clinical trial in a resource-poor country within a particular community group; and

4. **Justice within the Community** that results in consequences proportional to harms suffered, including loss of professional licensure and public censure.

(We would highlight that these categories of concern include five of the eight Ethical Principles set forth in the seminal article on this subject by Emanuel et al in JID 2004:189 (1 March) 930. We deliberately did not comment on any aspects of the "science" underlying any clinical trial, assuming a robust review of the research methods had been done and a compelling justification for the study design had been proven.)

The responses set forth below are necessarily condensed and cannot completely reflect the richness of the Committee's discussion or the care with which we wrestled with these issues. These comments do, however, reflect the manner in which our discussion developed.

DISCUSSION

1. **Authentic Community Participation** by representative groups living where the research will be conducted – participation that includes collaborative partnerships, independent review, and respect for study communities.

Although the CEC's role has typically been one of independent review of a topic generated from a clinical ethics perspective, the members felt strongly that we should speak to this topic of Protections for Human Subjects. As an independent volunteer group of community members, we are perhaps particularly well-suited to submit this Report and we unanimously recommend the inclusion of an authentic and "real" community voice before, during and after participants are enrolled in a clinical trial protocol. The harder question is how to achieve truly authentic community participation within the hosting country. One question which arose in our discussion about "independent review" was whether the hosting community's IRB was vigorous in including broad and diverse community representation. The assumption of authentic community participation and independent review within the IRBs of both hosting and sponsoring communities was critical to our reliance upon the integrity of the IRB process.

The CEC's member who is of Guatemalan descent was certainly a proponent for community participation in reviewing and monitoring clinical trials. She noted, however, that many barriers exist to open communication in that culture – if someone says he or she "has nothing to say", that is not necessarily the case. Because there have historically been harsh consequences to citizens who speak against those in power, most are afraid to speak openly about feelings of anger and vulnerability. Even so, she recommended soliciting membership for community groups within Churches and community centers as well as including those who are more educated such as lawyers, doctors and health care workers. When the suggestion was made that schools might be an effective venue for initiating community participation and that when children can be made aware of public health issues, parents often follow, she noted that children do not have the same "voice" that adults do in her culture. She also noted, from the perspective of most Guatemalans, the United States still retains a culturally exalted position so that when American scientists and medical personnel come in ostensibly to help, her countrymen's natural inclination is to agree and be respectful and appreciative.

We discussed at length the required sensitivities to cultural norms that must be in place prior to entering a resource-poor country and enlisting participants in a clinical trial. According to the Committee's view, however, that sensitivity could not be absolute – meaning it could not extend to allowing especially vulnerable populations within a vulnerable population to remain unprotected. As one member noted, any model of IRB approval that respects local norms of morality may mean approving protocols that "throw women under the bus." So, while we were sensitive to the dangers of moral imperialism, the Committee advocated a position of "ethical pluralism" that honored local customs and norms, but only so long as those customs and norms did not render an indigenous group more vulnerable.

The ethical principles of collaborative partnerships, independent review, and respect for study communities can best be evidenced by the creation of strong independent community groups that have an authentic "voice" to review and approve the initiation of clinical trial protocols conducted within their communities; to monitor the clinical trial throughout its pendency; and to manage the effects, both for good or ill, on the community after the clinical investigators have withdrawn.

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2. **Vigorous Advocacy for Research Participants** provided by individuals who are empowered, informed and truly independent of institutional and governmental influences - advocacy that includes respect for recruited participants, as evidenced by transparency and voluntary informed consent.

The Committee concluded that obtaining oversight of clinical trials by community groups was necessary but not sufficient. A child of one of the Committee members has participated in numerous clinical trials and that participation was accompanied by consistent and vigorous participant advocacy. The "comfort level" which the presence of such an advocate provides helps to shift the balance from the public health benefits focus of a clinical trial to a focus on the individual participant's personal health benefits. The Committee concluded that was a good thing and highly recommends that, most especially in clinical trials conducted in resource-poor countries, the study design should include a strong corps of informed and independent Participant Advocates who are not employed by or affiliated with the research institution or with any institution that might receive some financial benefit from the research, including governmental agencies.

Echoing that sentiment, one member commented upon a 1995 article by Edgar and Rothman in the Milbank Quarterly that advocated for the deletion of the "I" in IRB, voicing a concern that the research participant should come before the institution. The Committee's discussion included many moments of "point/counterpoint" when some members expressed concern that IRBs (and particularly the hosting country's IRBs) might in some instances be "suspect" and an inadequate protector of vulnerable communities. Other members were much more comfortable with the protective role that IRBs performed and were convinced that "times have changed" and "significant legal and regulatory protections are in place." (Some of the Committee members' concerns regarding effective IRB oversight were based upon materials provided by the Department of Bioethics at the National Institutes of Health website at http://www.bioethics.nih.gov/research/protection.shtml, accessed June 23, 2011.)

In conjunction with effective IRB oversight and the inclusion of authentic community group perspectives, Participant Advocates would "fill in the gaps" which are perceived to exist in a vulnerable community's and individual participant's understanding of what is involved in participation in a clinical trial. While the Committee was glad to see international clinical trials are included in the website directory under clinicaltrials.gov, members were skeptical that such a computer-based registry was actually understood or always helpful to vulnerable populations that may be recruited for participation in clinical trials.

Transparency about what trials are being conducted, what populations are being recruited, and what the benefits and burdens are to the community and to the individual participant is essential to the integrity of the process and the strength of protections of the participant. (Committee members were especially concerned that individuals be informed of the fact they are not obligated to continue as research participants in a clinical trial, while also being fully informed of the potential consequences of withdrawal.) The Committee expects an independent Participant Advocate will be able to provide that needed transparency - giving context to and content about a particular clinical trial that will increase the likelihood participants are actually well-informed and their consent is truly voluntary.

The Committee's primary recommendation is for empowered, informed and truly independent Participant Advocates to be provided for all clinical research participants.

3. **Social Value to the Community** that clearly justifies conducting a particular clinical trial in a resource-poor country within a particular community group.

Several commentators in this area of providing social value to the communities in which clinical trials occur suggest: disseminating the data obtained through the study to enhance population health; providing training to local clinicians so they can conduct their own medical research; or enhancing the health care delivery systems within the host country. The CEC agreed that social value must be provided to members of the local community if a clinical trial in a resource-poor area is to be ethically supportable. We concluded the most effective and legitimate social value that can be provided to the local host communities is to educate individuals so that they can become active participants in their health care – becoming their own health advocates. Different models for community health education initiatives have been successful in Brazil, India, Mexico and Bangladesh and while the CEC does not have the background or information to recommend one such model over another, we recommend such participatory models as a way to educate local communities and research participants in becoming skilled in their own individual health care advocacy. (This community-based focus on local education and empowerment is part of what Coldwell and Coelho call the "participatory sphere" discussed in their book Spaces for Change: The Politics of Participation in New Democratic Arenas, 2007.)

Two questions were posed during our discussion that illustrate most powerfully the CEC's concern about inadequate protections for individuals recruited from vulnerable populations and the need for establishing the social value of research to the communities in which clinical trials occur.

The first question posed was – Could the horrors of the 1940s Guatemalan syphilis study happen again? A member of the Committee stated the issue this way – "We need to make sure that such abuses can never happen to another race or people group ever again, no matter what the perceived public benefits might be." As has been stated above, the protections provided by a well-trained and vigilant IRB are substantial, but an important question remains as to whether vigorous community representation is a part of hosting countries' IRBs. The protections provided by a well-established and truly representative community group are even better, but ensuring such groups have a substantial voice in the process is an admittedly difficult challenge. The CEC concluded the provision of Participant Advocates is the most effective tool to ensure research participants are adequately informed, protected and monitored. Research studies like the 1940s Guatemalan syphilis study, which are predicated on an astounding disregard for human worth and bodily integrity, are much less likely to occur if independent Participant Advocates accompany those individuals enrolled in federally-funded clinical trials in resource-poor countries.

The second question posed was – Are there some things doctors just should not do? It seemed so obvious to CEC members that scraping a prisoner's penis, lodging there a piece of gauze loaded with syphilis bacterium, and asking the gentleman to wait in this condition for hours, all as occurred in the Guatemalan study, was just something a doctor should not do!! A member of the Committee based her question on the thoughts expressed by Robert Truog in a May-July 2011 Hastings Center Report about physicians' participation in capital punishment. He states that "the physicians' role should always be defined in terms of the individual and collective well-being of patients", believing "that a coherent and internally consistent role morality for physicians can be constructed based upon the goals of medicine." The protections for research participants should be grounded not only in laws and regulations, and review boards and collaborations between host and sponsoring countries, and community oversight and even active Participant Advocates, but should also be inextricably woven into physicians' morality. The CEC understands that sensitivities to some aspects of morality are sometimes learned as an adjunct to a good medical education and we recommend that medical and research ethics and the development of sound clinical trial protocols become a part of the required medical school curriculum.

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4. **Justice within the Community** that results in consequences proportional to harms suffered, including loss of professional licensure and public censure.

Lastly, the Committee's discussion focused on what would be appropriate consequences for the harms to research participants that are sometimes a result of clinical trial protocols. Perhaps the Committee members were especially sensitized to this issue because most had recently viewed an exhibit sponsored by the United States Holocaust Memorial Museum called "Deadly Medicine: Creating the Master Race" and were struck by the fact that so many physicians who had crossed seemingly clear ethical boundaries were able to continue their medical practices, living with honor and prestige, dying in their own beds as old men. We were struck by the fact that the Nuremberg trials of those few physicians who were held accountable occurred at the very same time American doctors were practicing "bad medicine" in Guatemala. We were also moved by the Committee member with Guatemalan relatives who was visibly angry and upset, saying "A presidential apology is nice but it is not enough." Is it appropriate to impose consequences when irreparable harms are suffered by vulnerable communities and research participants? Is it especially appropriate when those harms are suffered in resource-poor countries? In addition to the already-existing legal sanctions that are in place for clinical research malpractice, the Committee felt strongly that significant professional consequences were appropriate, even though the specifics were not developed. Recognizing that not all cultures immediately seek reparation from lawsuits

or find relief in monetary damages, the Committee felt the scope of penalties that could be imposed upon sponsoring physicians and investigators of ethically unsupportable clinical trials could be expanded to include both the loss of professional licensure and public censure. In addition, one member of the Committee suggested academic journals should refuse to publish study results generated from ethically questionable trials. Whatever the consequences might be, the imposition of consequences is a recommendation the Committee submits is absolutely necessary to ensure a social value is provided by clinical trials conducted among vulnerable populations in resource-poor countries.

Committee members understood that their recommendations also had consequences – clinical trials are already costly and imposing requirements for community groups and participant advocates and consequences for harms result in more expense. We also recognized that not all clinical trials result in the successful or profitable medical outcome hoped for. Nevertheless, the Committee represents the community and is aware of the long-term consequences to communities which are traumatized by research abuses. One of the Committee members, who was particularly moved by the Tuskegee research narrative, spoke about a childhood friend who was from a troubled minority family in the South. Her friend was taken by the police to a medical office, consent was unwittingly signed by her father, and this healthy twelve year old was sterilized. Not only was the friend's life irrevocably shaped by this incident but a whole community of African Americans – North, South, East and West – suffer from a societal form of post traumatic stress disorder due to these sorts of abuses. The resulting distrust of the medical profession has profound consequences within our healthcare system to this day. The social value of research, as evidenced by increased public health and the development of effective treatments for individual patients, must significantly outweigh the potential harms and there must be direct consequences to the professionals who are involved when, due to culpable oversight and/or unprofessional conduct, harms occur.

Areas not included in the Committee's recommendations but considered

The Committee considered three additional areas within the topic of protections for research participants that should be mentioned – human rights, research relationships, and particularly vulnerable populations within resource-poor countries.

We considered the possibility of recommending a Human Rights Officer who would monitor clinical trials and provide advocacy for participants. We rejected that particular terminology because we recognized that many cultures do not place the same value upon individual rights and autonomous decision-making as they do upon communal structures and joint decision-making. We concluded that an independent Participant Advocate would most closely describe the role we are hoping can become part of all clinical trials.

We also considered the perhaps necessary but uneasy tension that exists in the realm of medical research – the fact that research participants are primarily entering a clinical trial for the "public good" and they are not necessarily receiving medical care for their "individual health". We felt perhaps it was an unsupportable dichotomy. The Committee recognized that there are potential harms that accompany all medical progress. Every medical innovation requires both the medical practitioner's skill and the patient's reliance on the "goodness of the physician". But concerns were voiced about the practice of "bad medicine" as a means to advance scientific knowledge and clinical trial treatments that do not treat a malady the research participant has.

Finally, we considered whether certain especially vulnerable groups within communities should be so protected from the potential harm of clinical trials that they be excluded from participation entirely. We were concerned by the question – Why not perform the clinical trial in the United States? We did not want the decision to conduct research in a resource-poor country to be driven by either reduced costs or increased access to vulnerable populations. That being said, we also did not want to exclude certain peoples because we evaluated their risk by our paradigms. Once again, we concluded that an independent Participant Advocate with particular sensitivities to protecting especially vulnerable populations was the most effective protection.

RECOMMENDATIONS

The CEC makes four specific recommendations to the Presidential Commission on Bioethical Issues:

- We strongly recommend that empowered, informed and truly independent **Participant Advocates** be assigned to research participants and that those advocates stay with individual participants from the initiation of the informed consent process, through the clinical trial, and for follow-up after the trial closes.

- As an adjunct to providing independent Participant Advocates for individual research participants, the CEC also recommends local **Community Groups** be included as an authentic voice in the review, monitoring and management of clinical trials.

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- Lastly, given the pervasive nature of clinical trials in current medical practice, we highly recommend that medical schools **require a Course in Medical and Research Ethics** and clinical trial protocols.