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BIOMEDICAL ETHICS

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benefit). This would be analogous to familiar concepts of subjects receiving continued access to treatment after their participation in a trial is completed.

I certainly support every reasonable effort to increase access to treatments which will reduce vertical transmission. But imposing the types of community-wide requirements that have been suggested, but not necessarily justified if the above analysis is correct, may prevent important trials from being run because of the potential expense. Such proposals should be treated as moral aspirations, and exploitation should be avoided by focusing on what is owed to the subjects who have participated in the trials. It is they, after all, who are primarily at risk for being exploited.

These observations are about research in developing countries in general, and not just about research on vertical transmission. Three lessons have emerged. The standard for when a placebo control group is justified is a normative standard (what they should have received if they were not in the trial) rather than a descriptive standard (what they would have received if they were not in the trial). Coercion is not a serious concern in trials simply because attractive offers are made to the subjects. Legitimate concerns about exploiting subjects should be addressed by ensuring their future treatment, rather than by asking what will happen in their community at large.

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FAIR BENEFITS FOR RESEARCH IN DEVELOPING COUNTRIES

Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries

This joint statement by participants in a 2001 conference challenges the thesis (embraced by Glantz et al.) that, in order to avoid exploitation, interventions proven safe and effective through research in developing countries must be made "reasonably available" in those countries. After analyzing the concept of exploitation for the

sake of explicitness, the authors argue that the reasonable availability requirement fails to avoid exploitation in many cases and wrongly regards interventions under investigation as the only relevant sort of benefits. In place of the reasonable availability requirement, the authors offer a Fair Benefits framework, which incorporates principles of collaborative partnership (between investigators and the local population), transparency (regarding agreements reached and community consultation), and fair benefits. The fair benefits principle distinguishes benefits to trial participants and benefits to the local population both during and following research. Extending well beyond the benefits of medical interventions validated in a trial, the benefits identified as appropriate to consider in avoiding exploitation include health services unrelated to the trial, public health measures, employment, and development of a community's research or medical care capacity.

Collaborative, multinational clinical research, especially between developed and developing countries, has been the subject of controversy. Much of this attention has focused on the standard of care used in randomized trials. Much less discussed, but probably more important in terms of its impact on health, is the claim that, in order to avoid exploitation, interventions proven safe and effective through research in developing countries should be made "reasonably available" in those countries.[1,2]

This claim was first emphasized by the Council for International Organizations of Medical Sciences: "As a general rule, the sponsoring agency should agree in advance of the research that any product developed through such research will be made reasonably available to the inhabitants of the host community or country at the completion of successful testing."[1] The reasonable availability requirement has received broad support, with disagreement focusing on two elements. First, how strong or explicit should the commitment to provide the drug or vaccine be at the initiation of the research study? Some suggest that advanced discussions without assurances are sufficient, while others require advance guarantees that include identifiable funding and distribution networks.[2–6] Second, to whom must the drugs and vaccines be made available? Should the commitment extend only to the participants in the study, the community from which participants have been recruited, the entire country, or the region of the world? Although these disagreements have ethical and practical implications, there is a deeper question about whether reasonable availability is necessary, or the best way, to avoid exploitation in developing countries.[7]

What constitutes exploitation? A exploits B when B receives an unfair level of benefits as a result of B's interactions with A.[8] The fairness of the benefits B receives depends on the burdens that B bears as a result of the interaction, and the benefits that A and others receive as a result of B's participation. Fairness is the crucial aspect, not equality of benefits. Although being vulnerable may increase the chances for exploitation, it is neither necessary nor sufficient for exploitation.

The potential for clinical research to exploit populations is not a major concern in developed countries since there are processes, albeit haphazard and imperfect, for ensuring that interventions proven effective are introduced into the health-care system and benefit the general population.[9] In contrast, target populations in developing countries often lack access to regular health care, political power, and an understanding of research. They may be exposed to the risks of research, while access to the benefits of new, effective drugs and vaccines goes predominantly to people in developed countries and the profits go to the biopharmaceutical industry. This situation fails to provide fair benefits and thus constitutes the paradigm of exploitation.[1,2,5,6,10,11]

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By focusing on a particular type of benefit, the reasonable availability requirement fails to avoid exploitation in many cases. First, and most importantly, the ethical concern embedded in exploitation is about the amount or level of benefits received and not the type of benefits.[8] Reasonable availability fails to ensure a fair share of benefits; for instance, it may provide for too little benefit when risks are high or benefits to the sponsors great. Moreover, it applies only to phase III research that leads to an effective intervention; it is inapplicable to phase I and II and unsuccessful phase III studies.[12] Consequently, reasonable availability fails to protect against the potential of exploitation in a great deal of research conducted in developing countries. Furthermore, reasonable availability embodies a narrow concept of benefits. It does not consider other potential benefits of research in developing countries, including training of health-care or research personnel, construction of health-care facilities and other physical infrastructure, and provision of public health measures and health services beyond those required as part of the research trial. Finally, insisting on reasonable availability precludes the community's deciding which benefits it prefers.

Reasonable availability should not be imposed as an absolute ethical requirement for research in developing countries without affirmation by the countries themselves. The authors,[13] who are from developed countries and African developing countries, have proposed an alternative to reasonable availability to avoid exploitation in developing countries: Fair Benefits. This framework would supplement the usual conditions for ethical conduct of research trials, such as independent review by an institutional review board or research ethics committee and individual informed consent. In particular, Fair Benefits relies on three widely accepted ethical conditions. First, the research must address a health problem of the developing country population, although, as with HIV/AIDS, it could also be relevant to other populations.[7] Second, the research objectives, not vulnerability of the population, must provide a strong justification for conducting the research in this population. For instance, the population may have a high incidence of the disease being studied or high transmission rates of infection necessary to evaluate a vaccine. Third, the research must pose few risks to the participants, or the benefits to them clearly must outweigh the risks.[7]

The Fair Benefits framework requires satisfaction of the following three additional fundamental principles to protect developing communities from exploitation.

Fair benefits. In assessing whether studies offer a fair level of benefits, the population could consider benefits from both the conduct and results of research. Among potential benefits to research participants are additional diagnostic tests, distribution of medications and vaccinations, and emergency evacuation services. Research might also provide collateral health services to members of the population not enrolled in the research, such as determining disease prevalence and drug resistance patterns, or providing interventions such as antibiotics for respiratory infections or the digging of boreholes for clean water. Conducting research usually entails the benefits of employment and enhanced economic activity for the population as well.

Reasonable availability of a safe and effective intervention may provide an important benefit for the population after the completion of some research trials. Alternatively, other postresearch benefits might include capacity development, such as enhancing health-care or research facilities, providing critical equipment, other physical infrastructure such as roads or vehicles, training of health-care and research staff, and training of individuals in research ethics. Furthermore, any single research trial could be an isolated endeavor or form part of a long-term collaboration between the population and the researchers. Long-term collaboration embodies engagement with and a commitment to the population; it can also provide the population with long-term training, employment, investment, and additional research on other health issues. Finally, profits from direct sales of proven interventions or from intellectual property rights can be shared with the developing country. It is not necessary to provide each of these benefits; the ethical imperative is for a fair level of benefits overall—not an equal level.

Collaborative partnership. Collaborative partnership means that researchers must engage the population in developing, evaluating, and benefiting from the research. Currently, there is no shared, international standard of fairness. In part this is because of conflicting conceptions of international distributive justice.[14,15] Ultimately, the determination of whether the benefits are fair and worth the risks cannot be entrusted to people outside the population, no matter how well intentioned. They may be ill-informed about the health, social, and economic context and are unlikely to appreciate the importance of the proposed benefits to the host community. The relevant population for the Fair Benefits framework is the community that is involved with the researchers, bears the burdens of the research, and would be the potential victims of exploitation. There is no justification for including an entire region or every citizen of a country in the distribution of benefits and decision-making, unless the whole region or country is involved in the research study. To avoid exploitation, it is the village, tribe, neighborhood, or province whose members are approached for enrollment, whose health-care personnel are recruited to staff the research teams, whose physical facilities and social networks are utilized to conduct the study who must receive the benefits from research and determine what constitutes a fair level of benefits.

The population's decision about whether research is worthwhile and fair must be free and uncoerced.[16] Practically, this means that a decision not to participate in the proposed research is a realistic alternative. Deciding if a population can really refuse will not be easy. Nonetheless, proceeding with a research trial requires that the population in which it is to be conducted genuinely supports it.

Transparency. The lack of an international standard for fairness and the disparity in bargaining power between populations and researchers in developing countries and sponsors and researchers from developed countries means that even in the presence of collaborative partnership, the community might agree to an unfair level of benefits. The Fair Benefits framework can be used to catalog the array of benefits that are provided in different research studies (see Table, this page). An independent body, such as the World Health Organization, could establish a central and publicly accessible repository of all the formal and informal benefit agreements of previous studies. This repository would allow populations, researchers, and others to make independent and transparent comparisons of the level of the benefits provided in particular studies to ensure their fairness.

To further facilitate transparency, this body should develop a program of community consultations that actively informs the communities, researchers, and others in developing countries likely to participate in research about previously negotiated agreements. These consultations would also provide forums in

The Fair Benefits Framework*

Fair Benefits
Benefits to Participants During the Research
Improvements to health and health care
Collateral health services unnecessary for research study
Benefits to Population During the Research
Collateral health services unnecessary for research study
Public health measures
Employment and economic activity
Benefits to Population After the Research
Reasonable availability of effective intervention
Research and medical care capacity development
Public health measures
Long-term research collaboration
Sharing of financial rewards from reseach results
Collaborative Partnership
Community involvement at all stages
Free, uncoerced decision-making by population bearing the burdens of the research
Transparency
Central, publicly accessible repository of benefits agreements
Process of community consultations

*It is not necessary to provide each benefit.

which all interested parties could deliberate on the fairness of the agreements. Over time, such a central repository and the community consultations would generate a collection of critically evaluated benefits agreements that would become a kind of "case law" generating shared standards of fair benefits.

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ANIMAL RESEARCH

THE CASE FOR THE USE OF ANIMALS IN BIOMEDICAL RESEARCH

Carl Cohen

Identifying himself as a speciesist, Cohen defends the extensive use of animals in biomedical research. Against the "animal rights" view, he contends that animals are incapable of moral agency and therefore lack moral rights. Against Peter Singer's view, which extends to animals the principle of equal consideration of interests, he maintains that animals' interests are not due equal consideration because animals lack the moral standing of humans; speciesism is therefore not analogous to racism and sexism. Indeed, Cohen argues, we have an obligation to expand animal research both to protect potential human subjects and to benefit future patients with advances in biomedicine. In his view, our obligations toward animals (e.g., not to be cruel to them) are minimal and do not compare in importance with our obligations to beings who have rights—namely, human beings.

Using animals as research subjects in medical investigations is widely condemned on two grounds: first, because it wrongly violates the *rights* of animals,[1] and second, because it wrongly imposes on sentient creatures much avoidable *suffering*.[2] Neither of these arguments is sound. The first relies on a mistaken understanding of rights; the second relies