in that case

Your company has invested heavily in developing an AIDS vaccine and wishes to embark on clinical trials. Applications have been made to numerous ethics committees in your developed country but all have refused approval on the basis that the risks of infection for the research participants are too great. You have learned of researchers in a sub-Saharan country who are keen to take up the research for your laboratory at a price which seems very reasonable to you in terms of research and development. The city in which the research would be conducted has 33% plus instance of HIV positive citizens. Its death toll from AIDS is already very high. Diarrhoea is the major cause of death in that country, by a factor of four followed by malaria. The country has no system of ethical review. What should you do?

commentary

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Vulnerability of Participants

The case illustrates a worrying development in international research practice. Developing countries and the former communist bloc countries are targeted by international organizations, especially in pharmaceutical development, as convenient locations for the execution of clinical trials. There are numbers of reasons for this trend, amongst which are the lack of stringent ethical review procedures in those countries and the economic privation suffered both by researchers and research participants in those places. I have come across such cases in the former Yugoslavia and sub Saharan Africa. In the first case the research was executed under the cover of providing aid, in the form of scarce but unlicensed pharmaceuticals, and in the latter the circumstances closely resembled those in this case. In addition these countries are useful targets for what has been described as 'biopiracy', where traditional medicines and genetic pools of the hosts offer promising material for exploitation.

Ethical review of research involving human participants has, as its primary function, the role to protect the interests and welfare of vulnerable participants. One means of doing this is to keep a careful eye on incentives offered to both researchers and participants. Undue incentives, that is rewards which put an unfair pressure on people to enter trials, are ruled out in New Zealand by the National Standard of Ethical Review. In this way the process protects people who are compromised by economic and health circumstances, like unemployed persons and students, who are natural candidates for Phase One drug studies, and sick people who make up the cohorts of participants in clinical studies of various kinds. Each of these kinds of privation are present in the case in point. What would seem to be a minor financial reward in New Zealand would constitute a major benefit in most African countries. Further, in countries where drugs cannot be afforded, patients will be sorely tempted to sign up to trials which would otherwise not attract them, in order to stand a chance of obtaining some kind of medication. Researchers too are vulnerable to the temptation to carry out research, which would be thought too risky in Western countries, because the rewards offered make it possible to do research at all. This puts a pressure on them which is not in the interests of participants.

Double Standards

In this case we are concerned with a prophylactic treatment which all the relevant Ethics Committees in the developed country of origin of the research consider to be too dangerous for their currently healthy citizens. Why then should be acceptable to the healthy citizens of another country? We might say that, given the incidence of HIV and AIDS in the target country, these participants are already at more risk of contracting the condition so that the additional risk is lessened. But that would be to conflate the chances

of each of these individual research candidates being harmed with the statistical chances of any individuals in that country of contracting the disease. For most of these people there is no chance of such an outcome, given that they are not involved in the delivery of health care to the sick and do not engage in risky lifestyles. To put them in the way of risk in the name of medical research would be to disregard the clinician's responsibility, as outlined in the Helsinki Declaration, to protect the health of the research participant.

What of the argument that the interests of the individual participant have to be weighed against the public interest? Such an argument would seem to entail that what might not be justified in the country of origin might well be justified in the target country. But there are good reasons to reject this defence. First, there is no guarantee that, if the drug turns out to be efficacious and becomes licensed, it will be available to the public of the target country. The chances are that that poor country will not be able to afford to purchase it. Second, the Helsinki Declaration (2000) says unambiguously that the interests of the research participant should not be sacrificed for the interests of science and society. Taking gross risks with the health of research participants for the benefit of others is beyond the pale. One is reminded of David Hume's account of the effect which separation in time and distance from people has on our moral concern for them. Double standards of this sort in clinical research are simply unacceptable.

Cultural Sensitivity

In this case the decisions of the home Ethics Committees about their citizens were disregarded in relation to citizens of the target country. But one might imagine a situation where a home committee was asked to consider the suitability of a trial for another country. This happens often when research is sponsored in other countries and the funding bodies subject the protocols to ethical review in their own country. Given a commitment to abide by the decision of such committees, would this make the procedure of foreign research acceptable?

One has to admit that it would be better than nothing, in that there would be some limits set on what was acceptable. However it would not be good enough. Within New Zealand we are careful to provide local scrutiny to multi-centre research, in order to do justice to the perceptions, concerns and interests of local populations. Yet we are not very far removed from each other in this country. The cultural dissonance between us and people in remote countries exacerbates the problem of respecting their cultural mores and heightens the possibility of doing them injustices. There is therefore a responsibility devolving on research funding bodies, who wish to carry out research in target countries, such as the one in our case, to support the setting up of ethical review procedures in those countries. The World Health Organisation engages in this activity. Commercial concerns which wish to use such countries for their research should make funding available for this purpose. This would add a very small percentage to their research and development costs and would demonstrate good intent on their part to execute ethical research. They should also commit themselves to the provision of the successful treatments to such countries at prices which those countries can afford. In this way they would not appear to be taking unfair advantage of the target populations.

This enterprise will not be straightforward. There will be occasions when cultural differences will place a question mark over the use of those countries for research. For example, I was once engaged in discussion with a sponsoring research organisation which wished to trial depot contraceptives in a developing country where spousal consent was required, because of the relation in which the wives stood to their husbands in that place. In the country of origin of the research such a relationship was thought to be subservient and gender biased. The women were keen to take part because they did not want to be pregnant constantly. Their husbands took a different view. The organization had to choose between three options: i) sponsor the research on terms which it considered to be unethical, ii) deny the benefits of the research to the women in that country altogether, iii) carry out the research disregarding the need for spousal consent and thus sacrifice cultural sensitivity and risk dire social consequences for the research participants. If any reader has a simple solution to this quandary then I shall be delighted to hear of it. However, the fact that respecting cultural diversity can lead to such difficulties does not entail that we are justified in disregarding it.

Reference

World Medical Association (2000). *Declaration of Helsinki* World Medical Association