CASE STUDIES

Case Study 2

Background

What are researchers' and institutions' responsibilities to the study community?

The National Institute of Cholera and Enteric Diseases-an Indian medical research center which is based in Calcutta-has recently received a grant from the Indian Council of Medical Research, Ministry of Health and Family Welfare, to study the effectiveness of a new vaccine against the cholera strain *Vibrio cholera 0139.* The new strain of *V.cholera* recently appeared in both Eastern and. Western Bengal. Cholera, a watery diarrhea that may have a mortality rate of over 30% in severe untreated cases, is endemic in the Bengal region of the Indian Subcontinent (West Bengal in India and Bangladesh). Although there is an effective treatment for cholera based on the principle of re-hydration and fluid maintenance there is a strong desire to develop a vaccine that would prevent cholera from occurring or limit the scope of outbreaks.

The new vaccine was developed at a large American university and has been through Phase I and II testing. At the present time the vaccine costs $1.00 per dose and three doses are required; however, it is estimated that cost will be reduced by 75% in the future. The government's per capita expenditure on health in this region is $5.00 per year.

The field site, a rural rice-growing area with a population of about 75,000, is a 2 hour drive from Calcutta by mainly country roads. A government clinic services the community but it is often short of medicines. It has no cholera cots, and has a physician population that changes every 12 to 18 months. There are a number of traditional practitioners and some "unlicensed doctors" in the area. Few of these providers have modern treatments for cholera or other diarrheas.
The vaccine will be given to children less than 5 years of age in a double-blind fashion with one group receiving the vaccine and the other a booster dose of tetanus toxoid. Even if the vaccine proves to be effective, there are still likely to be cases of cholera in the treatment group, and more still in the placebo group. Therefore, the Institute feels that a treatment facility should be established in the field site to provide state-of-the art care for all patients with cholera and other diarrheas. The Institute would provide the facility, the personnel, the equipment, and medicine free-at-charge to the community for the duration of the study. Others have suggested that it would be more sensible to upgrade the government clinic, rather than build a new facility. The Institute, however, would have no control over the selection of personnel or quality of care provided in the government clinic and is reluctant to endorse this idea. The Institute does not have an endowment and depends on government grants and research awards to finance its activities. Some of the investigators and research team members are concerned that the Institute may take on a long-term commitment to provide treatment that it can ill afford.

A group of public health activists in Calcutta has raised a number of concerns about the ethics of the study including some issues regarding informed consent and some study design issues. These concerns have been dealt with to the satisfaction of all parties. However, there are two outstanding issues on which agreement has not been reached: (1) What is the Institute's long-term commitment to providing health care to the community? Will the new clinic be abandoned after the study has been completed or will some form of on-going support be possible beyond the duration of the trial?; and (2) If the vaccine is effective, will all participants in the study who

received a placebo receive free doses? If so, for how long? Will the Institute commit to providing the vaccine to all the citizens of the community? Should this commitment extend beyond the community to the country as a whole?

Questions

You are the director of the National Institute of Cholera and Enteric Diseases. You have arranged a meeting of the other investigators to discuss the Institute's response to these questions. You have also invited a representative of the Indian Council of Medical Research, a senior official from the Ministry of Health and Family Welfare, the Institute's lawyer and the chair of the Institute's Research Ethics Committee. During this meeting, you will attempt to reach agreement on what obligations are reasonable/feasible for the Institute to commit to beyond the duration of the trial. In preparation for the meeting and to help establish the meeting agenda, you have circulated the following questions to the meeting participants in advance:

1. Who are the legitimate stakeholders in this process, i.e. whose interests are we trying to recognize and accommodate in making these decisions?

2. What are the practical constraints on any commitment made by the Institute (e.g. financial, authority, etc.) and the risks of over-stepping them? (One of your main concerns as Director is whether this type of / commitment is even within the scope of authority of the Institute)

3. What are the areas of uncertainty that must be considered before making any decision/proposal? (e.g. level of efficacy of vaccine, commitment of government, other potential sources of funding, etc. ?)

4. What are the areas on which there is (or can be) agreement from all stakeholders (e.g. baseline epidemiology of diarrhoeal diseases in the region/country, current government expenditures on health in the region, etc.)

5. What do the Indian (ICMR) Guidelines say about these post-trial obligations?

6. What do other International Guidelines say about these obligations?

7. What other examples exist that we might draw on to inform our decision- making?

8. What kind of framework might be useful for structuring the discussions/negotiations required to reach agreement among the stakeholders?

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