Developing a Vaccine for Malaria
Research Core-Science

Case Study 1: Principles of Research Ethics

Source: *Casebook on Ethical Issues in International Health Research,* World Health Organization

A North American university is planning to test a multistage, DNA malaria vaccine. Preliminary studies in North America have been encouraging; immunization of human subjects shows evidence of a strong immune response. Experimental challenge studies in North American volunteers will begin soon. Larger field studies, both Phase II and III, are being planned. A country in sub-Saharan Africa where malaria is endemic has expressed interest in participating in the vaccine research effort. The African and North American researchers begin working together to design a study protocol to assess the vaccine's efficacy in reducing deaths due to malaria in children under five years of age, particularly infants.

A district in the country with a population of approximately 150,000 has developed an effective epidemiologic surveillance system. Trained community health workers (CHWs) visit all homes in each village in the district every three months to record all births, deaths, major illnesses, marriages, and migrations. A centralized, computerized record-keeping system was created and is regularly updated with data from the CHWs reports. Nevertheless, most of the villages are remote, and there are only four health posts to serve the entire population. Furthermore, in addition to the high malaria burden (18 percent of annual income lost due to the disease), trained health care workers, laboratory facilities, and medicines are in short supply. Children under five years of age in the study area suffer an average of six bouts of malaria a year. Fatally afflicted children and infants often die less than seventy-two hours after developing symptoms.

The researchers will randomly select potential participants (infants) for the vaccine trial from the database gathered by the CHWs. A study vaccination team will visit each home, explain the study, and obtain informed consent from the appropriate caregiver. Researchers will administer the vaccine or placebo in double-blind fashion to those who agree to participate. Although many children will experience some soreness at the injection site, the risks of vaccination are minor. Once all participants receive the vaccine, the team will leave the village without implementing any other interventions. Using the system already in place—that is, monitoring patients who come to the clinic or hospital with symptoms of malaria, as well as the active surveillance regularly conducted by the CHWs—researchers can collect data on subsequent illness and death due to malaria. If the vaccine is found to be effective, the benefit is prevention of morbidity or mortality due to malaria.

There is no clearly defined immunological marker to measure protective immunity against malaria. As mortality is the most important outcome variable that can be measured, the researchers will look at deaths as a study endpoint. To the extent that health records and verbal autopsies allow, the researchers are specifically interested in those deaths known to be caused by malaria. If all cases of malaria in the study, Research Ethics Training Curriculum, 2nd edition (Case Studies 4) population were identified and treated, researchers could not measure the efficacy of the vaccine in preventing deaths. In the absence of a surrogate marker for mortality, the study researchers do not want to interfere with the "natural" consequences of malaria transmission in the study villages.

Questions

1. Is the use of a placebo appropriate in this context?

2. Is the study design appropriate to demonstrate the efficacy of the vaccine?

3. Should the researchers provide treatment for malaria cases in the community?

4. Should the researchers provide information on how to prevent illness?

5. The case study does not indicate that any provision has been made for an ethical review by the country where the research is being conducted. If the North American partners insist that the review conducted in North America is adequate, what should the host country do? If the host country does not have the capacity to provide ethical oversight, what options are available?