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Clinical Research Ethics Question of the Month: Pediatric Study

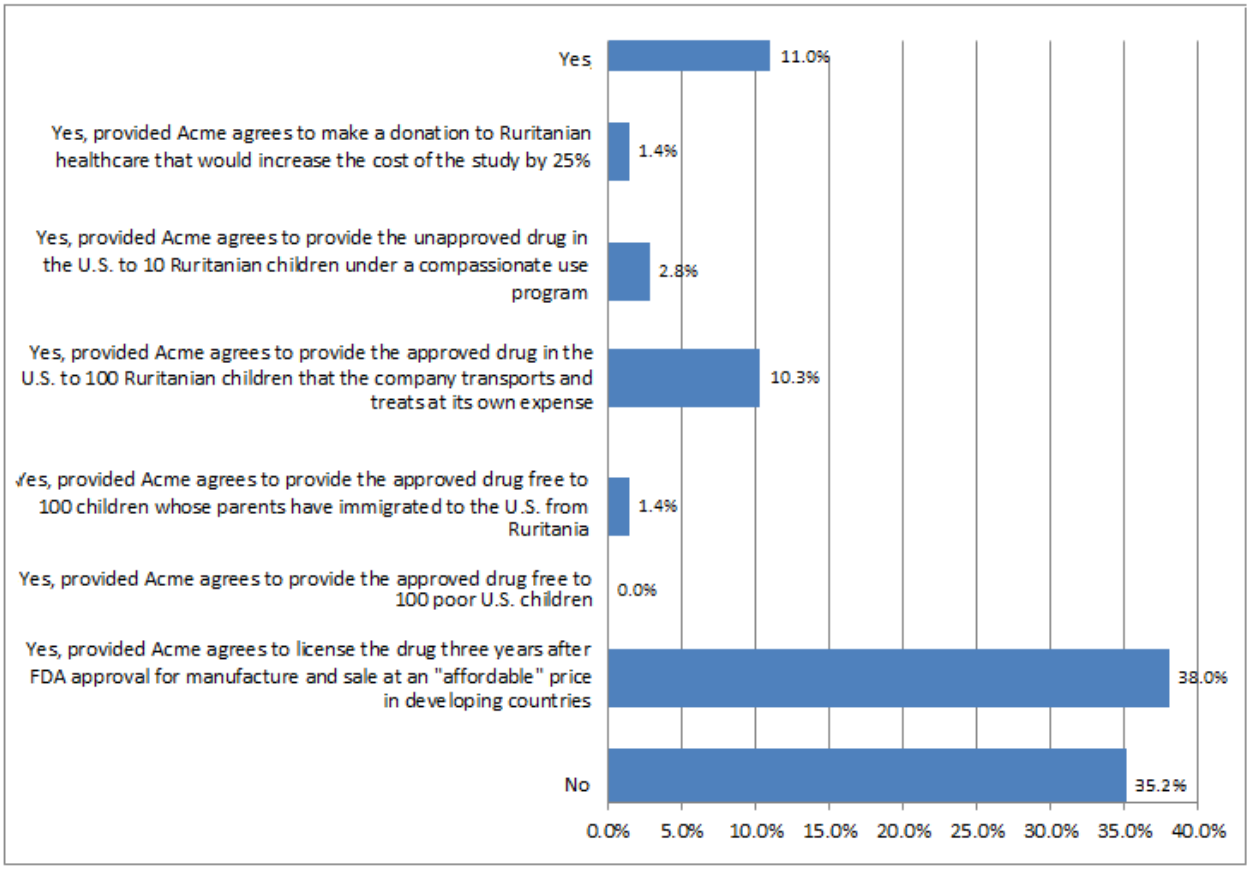
By Norman M. Goldfarb

You are the President of Ruritania, a developing country. Acme, a U.S. pharmaceutical company, has applied to conduct a study in your country for the treatment of a life-threatening pediatric disease. In the U.S., a drug from a different company prevents such deaths, but that treatment is not available in Ruritania. If the study is conducted, the 100 children who receive the active drug will likely live, and the 100 children who receive the placebo will likely die. If the study is not conducted, all 200 children who would have been in the study will likely die. Acme cannot conduct a placebo-controlled study in the U.S. because the other drug is available there. Acme does not intend to market the new drug in Ruritania because of its high cost and Ruritania's unsuitable healthcare infrastructure. If the study is successful, Acme will use the results in a marketing application to the FDA for U.S. patients. If you do not approve the study, another country might. You have no other information to make your decision and no clever way to dodge it.

Results

The 145 respondents answered the following question:

Will you vote to approve the study?



Discussion

Only 11% of respondents would approve the study without conditions. Thirty-eight percent would approve it provided Acme agrees to license the drug three years after FDA approval for manufacture and sale at an "affordable" price in developing countries. Ten percent would approve it provided Acme agrees to provide the approved drug in the U.S. to 100 Ruritanian children that the company transports and treats at its own expense. Thirty-five percent would not approve it, even with conditions. In other words, most respondents, acting as President of Ruritania, would pass on the opportunity — or take the chance of losing the opportunity — of saving the lives of 100 Ruritanian children.

This scenario puts the President of Ruritania in a very tough spot: Decide whether to accept a study of questionable ethics that will likely save the lives of 100 Ruritanian children.

As President of Ruritania, your job is governance, with ethics being only one consideration. Your primary responsibility is to your citizens. If you do not approve the study, you would have to explain to your citizens how letting 100 Ruritanian children die is a good decision. Imagine trying to explain this to actual parents who would have eagerly enrolled their children in the study to have a 50% chance of living. On the other hand, if your ethicists advise you that that study is unethical and exploitative, should you accept exploitation by Acme? Imagine trying to explain to the political opposition why you conceded to exploitation by a U.S. drug company. You could approve the study with conditions, but what is your tolerance for the risk that Acme might go elsewhere?

An active-drug-controlled study is not an option for Ruritania. We can assume that Acme is aware of the ethical issues. Acme could conduct a non-inferiority study in the U.S. with an active control but believes it must conduct a placebo-controlled study to support its marketing applications. If it proceeds with a U.S. study, Ruritania would not have the opportunity to save the lives of 100 of its children. Acme has chosen Ruritania for the study because the standard of care in Ruritania is no treatment. Article 11.3 of the Declaration of Helsinki states, "In any medical study, every patient, including those of control group, if any, should be assured of the best proven diagnostic and therapeutic methods and no patient should suffer from unnecessary pain [or death]." Ethicists debate whether the U.S. standard of care, the local standard of care, or some other standard of care should apply in this scenario. Whatever the reason for Acme's decision, as President of Ruritania, is the Declaration of Helsinki reason to reject the study?

Some respondents would approve the study, provided participants receiving the placebo can obtain the drug after the study is completed. This is a valid option, provided study participants survive the study. Another possible option might be to change the endpoint of the study to allow rescue medication for study participants who are faring poorly.

One respondent would not approve the study because "the rights, safety and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society." However, the study offers 200 Ruritanian children the right to a 50% chance of survival, which is a lot better than nothing.

One respondent points out that clinical studies cannot be conducted ethically without equipoise, i.e., genuine uncertainty as to the outcome of the study. This is valid criticism, but, as President of Ruritania, would you turn down the study for this reason? Or, would you see the lack of equipoise as an advantage?

This scenario raises difficult questions about the application of ethical principles to real-world situations. The numerous revisions of the Declaration of Helsinki speak to the challenges.

Next Month's Question:

You are on the national ethics review committee of Pauvistan, a developing country. Researchers have proposed a clinical study in your capital city of Belostadt. To recruit an adequate number of study participants, they need to include the entire metro area, including outlying villages. The study will provide bus tickets to the research center, which will be highly prized by villagers, many of whom struggle to afford transportation to the city…

Read the rest of the question and give us *your* answer at:
https://www.surveymonkey.com/r/HSKMCGL

Please send your ethical conundrums to editor@firstclinical.com.

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