Resolution No. 11-2001-299

RESOLUTION OF THE WHITE MOUNTAIN APACHE TRIBE OF THE FORT APACHE INDIAN RESERVATION

WHEREAS, members of the Tribal Council of the White Mountain Apache Tribe are duly elected representatives of the people of their respective districts; and among the many issues of concern to the Council are the health and well-being of its Tribal members; and

WHEREAS, the Tribal Council supports carefully designed research projects to evaluate health problems which exist in the population and to development appropriate interventions which seek to decrease or alleviate these problems; and

WHEREAS, diarrhea is a common illness among babies, and most diarrheas are caused by various types of bacteria and viruses; and

WHEREAS, rotavirus causes severe diarrhea in babies, and the cold months of the year is when many babies have rotavirus diarrhea; in fact, overall, it is estimated that ½ of all diarrhea in babies are caused by the rotavirus; and

WHEREAS, diarrhea, especially rotavirus diarrhea, is a common problem of Apache babies, especially very young babies who can have several rotavirus diarrhea illnesses in one year; and

WHEREAS, in 1998, a rotavirus vaccine was licensed by the FDA and distributed throughout the U.S., including on the Apache Reservation, but was subsequently withdrawn because the vaccine was thought to be connected with the occurrence of intussusception which is the folding of a short segment of intestine into itself; however, no Apache child developed intussusception after receiving the vaccine; and

WHEREAS, recently, an oral (taken by mouth) rotavirus vaccine was developed for babies, and was tested at several locations in the U.S. and seems to be safe and strongly suggests that it could prevent rotavirus diarrhea in young babies, and the vaccine is ready for final evaluation to see how well it can prevent rotavirus diarrhea; and

WHEREAS, representatives from Johns Hopkins have proposed a study of this new vaccine within the Tribe's Reservation; and

WHEREAS, under the study, three doses of the vaccine will be given by mouth, and each infant will be closely monitored by more than a dozen home visits for the occurrence of diarrhea, fever, vomiting, other reactions, and intussusception; and

WHEREAS, the newly developed rotavirus vaccine to be used in this proposed study was made

to prevent intussusception from occurring, and the protocol was written so that intussusception could be detected readily and the study stopped in the event this occurred; and

WHEREAS, this same study is being conducted on the Navajo Reservation and at several locations throughout the U.S., as well as in the country of Finland; and, only about 1,000 Apache and Navajo infants will be enrolled; and

WHEREAS, informed consent will be obtained from the parents/legal guardians of all infants taking part in this study, and the study will be explained to them in detail using the Apache language if necessary, and participation in this study is totally voluntary; and

WHEREAS, for more than 20 years, the Johns Hopkins University has conducted research projects on the White Mountain Apache Reservation to bring down high rates of Haemophilus, pneumococcal, hepatitis, and diarrheal infections in Apache babies and young children, and, as a result, many diseases in babies have been prevented, and many lives saved.

BE IT RESOLVED by the Tribal Council of the White Mountain Apache Tribe that it hereby supports and approves the proposed research project indicated above within Tribal lands to determine the safety and efficacy of the oral bovine-human reassortant rotavirus vaccine study among infants to be conducted by the Johns Hopkins University.

The foregoing resolution was on November 15, 2001 duly adopted by a vote of NINE for and ZERO against by the Tribal Council of the White Mountain Apache Tribe, pursuant to authority vested in it by Article IV, Section 1 (a), (b), (j), (k), (s), (t), and (u) of the Constitution of the Tribe, ratified by the Tribe September 30, 1993, and approved by the Secretary of the Interior on November 12, 1993, pursuant to Section 16 of the Act of June 18, 1934 (48 Stat. 984).

Chairman of the Tribal Council

ACTING Secretary of the Tribal Council

8/22/01

A Study to Determine the Safety and Efficacy of a Rotavirus Vaccine in Healthy American Indian Infants

Johns Hopkins Projects: White Mountain Apache & Navajo Reservations

Introduction.

Rotavirus is responsible for high rates of diarrhea in infants throughout the world including American Indian infants. In the past several years, a rotavirus vaccine was developed that has shown in preliminary evaluations to be safe and elicits favorable responses in infants. This vaccine is the pentavalent rotavirus vaccine which is taken by mouth.

Purpose.

The purposes of this research study are: 1. to find out how well the pentavalent oral rotavirus vaccine protects infants from rotavirus diarrhea, and 2. to continue to collect information about the safety of the vaccine, especially with regard to whether or not it is linked to the occurrence of intussusception (explained below).

Background and Rationale.

Rotavirus is responsible for high rates of diarrhea in infants and is the leading cause of severe diarrhea. Worldwide, it is estimated that about half of all diarrheal illnesses in infants is caused by rotavirus. It is also estimated that, by 5 years of age, each person throughout the world has had at least one diarrheal illness caused by rotavirus. Further, studies have indicated that Indian infants can have multiple episodes of rotavirus diarrhea during the first two years of life. In the US, rotavirus causes 50,000 hospitalizations and 40 deaths per year.

Rotavirus diarrhea is highly infectious and is thought to spread from person to person through respiratory secretions. In fact, many infants who have rotavirus diarrhea also have a cold. Because rotavirus spreads easily, epidemics of rotavirus diarrhea can occur.

There are five (penta-) different types of rotavirus (designated G1, G2, G3, G4, P1), and each type causes diarrhea. The rotavirus vaccine contains components of all five types (pentavalent). The vaccine is intended to protect against diarrhea caused by these five types. There currently is no licensed vaccine that can protect infants from diarrhea caused by rotavirus.

Since the late 1980's, research has been conducted to find a vaccine that could prevent diarrhea caused by rotavirus. The first vaccine evaluated was not efficacious in the US. The second vaccine, a rhesus-human reassortant oral tetravalent vaccine, was evaluated in the mid-1990's and was found to be quite protective against severe diarrhea and was licensed in 1998 by the Food and Drug Administration for general use among infants in the US. This vaccine, however, was also thought to be associated with the occurrence of intussusception in a few infants who received the vaccine.

Intussusception is the folding into itself of a segment of the small intestine. This can occur naturally, and

little is known about why or how this happens. Intussusception can block the passage of food through the intestine. Sometimes, intussusception can correct itself, but surgery is often required to fix the problem. How or why the rhesus-human rotavirus vaccine is linked with intussusception is not fully understood. Because of the association of the rhesus-human vaccine with intussusception, licensure of this vaccine was withdrawn by the FDA.

Because of the persistent high prevalence of rotavirus diarrhea in infants, research has continued to find a vaccine that could protect against this illness. In the past several years, a bovine-human reassortant penta(5)valent oral vaccine has been developed and evaluated and appears to be safer and generally better than the rhesus-human rotavirus vaccine. Infants 6 weeks to 9 months of age responded to the bovine-human vaccine by making greater amounts of antibodies against rotavirus. Complaints of fever and fussiness are fewer. Overall, better results were obtained with the bovine-human rotavirus vaccine.

In the testing of the bovine-human vaccine in over 5000 infants throughout the US, only one case of intussusception has occurred. Examination of information about this case suggests that intussusception was "classic"--that is, it likely would have occurred even if the person did not participate in the study. There is no certainty regarding this conclusion, however.

Procedures.

This study is to be conducted on the Navajo and Apache reservations, and about 1000 total infants will be enrolled from both reservations. The study has already begun at a number of other locations in the US, and in the country of Finland. This study is a randomized, double-blind, placebo, controlled study. The two major parts of this study are the efficacy and safety parts. The efficacy part will begin first, followed by the safety part in which participants will be monitored for adverse reactions, including intussusception, after having been vaccinated.

Only healthy infants will be enrolled. Infants will be randomly placed into the vaccine group (Group 1) or the placebo group (Group 2). Three total doses of vaccine or placebo will be given. Infants will be given the first dose of vaccine or placebo at any time between the ages of 6 weeks and 12 weeks. The second and third doses will be given 4 to 10 weeks (28 to 70 days) after the previous dose.

Five ml of blood will obtained on the same day as vaccinated for the first and third doses and 2 weeks after the third dose. Blood will be tested for rotavirus antibodies. Stool will be obtained 3 to 5 days after all three vaccinations and will be tested for viral shedding.

Three home visits will be made after each dose: at 6-5 days, 13-15 days, and 42-43 days post-dose. Inquiries will be made about adverse reactions experienced by the infant including diarrhea, fever, vomiting, rashes, blood in stool, abdominal pain, and symptoms compatible with intussusception. Study participants will also be visited at home every 6 weeks from day 43 post-dose 3 to 365 days to inquire about hospitalizations and clinic/ emergency room visits for intussusception. If intussusception occurs any time during the study period, it will be reported immediately to the DSMB (independent monitoring committee) and the sponsor.

Informed Consent.

Trained study personnel will carefully and thoroughly administer informed consents to all parents/legal

guardians of infant participants of this study. Two separate consents will be administered for this study. A consent form will be used for the part of the study in which the vaccine will be tested for how well it will protect (efficacy) infants from rotavirus diarrhea. safety information will be collected. Another consent will be used for the part of the study in which safety information will be collected.

Risks.

Safety data have been collected from over 5000 infants who have been given the bovine-human rotavirus reassortant pentavalent oral vaccine. Infants have tolerated the vaccine well. There is no difference between vaccine recipients and placebo recipients in the information and data regarding fevers and fussiness.

Risk of the occurrence of intussusception is not known. However, preliminary evaluations suggest that decreases in both viral shedding and reactogenicity with the bovine-human vaccine tend to suppress the development of intussusception. This study is designed to detect the occurrence of intussusception. If intussusception is detected, the study will cease if it is determined that a definite link has been made between the occurrence of intussusception and the administration of the bovine-human rotavirus vaccine.

Benefits.

Although it isn't certain, there is the possibility that those who receive the bovine-human reassortant pentavalent oral rotavirus vaccine (Group 1) may be protected from rotavirus diarrhea. Those randomized to receive placebo (Group 2) are not expected to receive similar benefits. All infants enrolled in this study, however, will have contributed valuable information regarding the bovine-human rotavirus vaccine, and may thus benefit those born in the future.

Confidentiality.

All information and data related to all participants, including their parents/legal guardians, will be held in the strictest confidence. A unique coded study number will be assigned each participant, and only this number will be used to identify participants. Computer entry of data and information of participants will be by coded study number. Only Johns Hopkins personnel connected with this study will have access to computer study files. Hard copies of documents will be stored by study code in locked file cabinets, and access will be limited to only study personnel.