vaccinomics (30). The variability in immunity results largely from differences in genes that control the immune responses. Variable immune responses depend on HLA genes, cytokine and cytokine receptor genes, killer cell immunoglobulin-like receptors, genes of the leukocyte receptor cluster, signaling molecules, the natural resistance-associated macrophage protein-1 gene, and many others (30). As new vaccines are developed and tested in the future, understanding the influence of polymorphisms in immune response genes will be critical to designing safe and effective vaccines and predicting vaccine efficacy. One might predict that in the future, vaccines will be designed that are expected to be safe and immunogenic in people of defined genotypes, and that vaccine testing will involve enrolling volunteers based on their genomic makeup.

Considerations for Studies Involving Children and Infants

Pediatric vaccine trials are carried out in healthy children who have no personal or family history of immune deficiency. The exception to this would be a vaccine targeted for a particular population, such as a *Pseudomonas* vaccine for children with cystic fibrosis. Screening of healthy children generally involves only a medical history and physical examination. Specific baseline data may be collected if there is specific concern about potential vaccine side effects; for example, liver function tests are performed if a live viral vaccine might cause hepatitis.

Transmission of live viral vaccine strains to contacts through the stools or respiratory secretions is a particular concern in studies involving young children. Until it is demonstrated that the vaccine virus is not transmitted, initial live viral vaccine studies should not include children attending group day care or children residing in a household with an immunosuppressed individual.

Recruitment of children into vaccine trials is usually carried out through outpatient settings providing well child care, such as private practices, hospital clinics, and health maintenance organizations. The optimal method of approaching families varies, depending upon the population served and the setting. In many centers, a study nurse and/or investigator approach the parent or guardian on the day they wish to enroll the child. Sending literature to the parents before the vaccine visit provides an important opportunity for the family to discuss the study, and to contact the study personnel by telephone for further information before they must make the decision whether or not to participate.

CONSENT

General Considerations

The FDA regulations concerning informed consent are contained in 21 CFR Part 50. Consent is not an endpoint but a continuing communication between participant and investigator during which the participant receives all the information he/she needs to participate in the study. The process should include ample opportunities for the free exchange of information and for the participant to ask questions. Consent should be obtained under circumstances that give the potential participant the opportunity to carefully consider the decision to participate with no coercion or undue influence. Such features as the place, the time, and the person who provides the information may affect a subject's ability to make an informed judgment. Some investigators use a formal mechanism to assess whether the volunteer adequately understands the key elements of the study. This could be a question and answer session, or a written test in which the volunteer must answer a specified proportion of questions correctly in to qualify for participation.

The principles of informed consent include the following: (*i*) the purposes, procedures, and experimental nature of the protocol are described fairly; (*ii*) the discomforts and risks to be expected are described; (*iii*) information about appropriate alternative procedures (for vaccine studies, this might be information about the existence of a licensed vaccine for the same disease); (*iv*) information about whom to ask for further information; and (*v*) the statement that an individual is free to withdraw his/her consent and discontinue participation without prejudice.

It is key that the information provided be understandable to the participants. This means that the information be presented in the participant's language and that technical and medical terms be explained or replaced with lay terms appropriate to the participant's level of education. Often a consent form can be simplified by using short, declarative sentences. In addition, the consent document should not include statements that release the investigator from responsibility or that waive the volunteer's rights. Consent must be documented in writing.

The FDA requires that the IRB reviews and approves advertisements and other materials used to recruit participants. Recruiting materials are considered an extension of the consent process. These materials, such as advertisements and fliers, should not be misleading. FDA recommends that the advertisement include only the following: (*i*) name and address of the investigator; (*ii*) purpose of the research and a summary of eligibility criteria; (*iii*) a description of the benefits (including payment); and (*iv*) the location of the research and person to contact for more information. It is important to avoid making claims about the vaccine.

It is also important that the payment of volunteers not be so much as to affect the ability of the volunteer to assess risks and benefits appropriately. Few research groups or organizations have specific standards (31–33). Volunteer compensation scales should be carefully conceived to ensure that economically disadvantaged individuals are not unduly influenced by the financial compensation offered. This concern applies not only to economically disadvantaged individuals, but students and middle class populations as well. Dickert and Grady describe three approaches related to volunteer payments (34). The first approach is the market model, which is grounded in the free-market principle that supply (availability of interested and eligible volunteers) and demand (the investigator's desire to complete a trial with a specified number of subjects within a defined time frame) determine how much subjects should be paid for participation. A second model is the reimbursement model, in which payment is provided simply to cover volunteers' expenses (travel, meals, parking, child care), similar to jury duty payments, such that the volunteers accrue no profit, thereby minimizing financial inducement. The third and most accepted model is the wage payment model. This model purports that participating in research is similar to many other forms of unskilled labor in that it requires little skill and training, but may involve some risk. In this model, subjects are paid for work that is valuable to society, on the basis of a standard wage for unskilled labor. In general, volunteers should have characteristics that make them suitable for other jobs in the community, particularly entry-level jobs, to ensure that the decision to participate in research is truly optional.