or the millions of subjects who participate in ICH GCP–regulated clinical trials each year throughout the world, the informed consent process is a fundamental rite of passage. Every volunteer must agree, in writing, to participate before he or she can enroll in a clinical trial. The agreement to participate is based on the fundamental right of all subjects to be told everything about the study, and to have their questions answered in easy-to-understand language and concepts. Subjects also must agree to participate voluntarily—they must not be pressured or coerced. By giving their consent to be in a clinical trial, volunteers are acknowledging that they understand and accept all aspects of the study—including the risks involved.

Not only is the informed consent process a mandatory and basic right of all study participants, it is also the most important way that investigative sites establish trust and confidence in their study subjects. Indeed, informed consent plays a critical role in influencing and shaping long-term relationships with the patient community and the general public.1

Several recent subject deaths in the United States have drawn the legal community into the clinical research arena. Industry insiders and observers speculate that litigation will increase dramatically because of failures to fully inform study subjects of research risks and benefits, of conflicts of interest including financial stakes in study outcomes, and of the validity and value of the research.

Our new survey of nearly 1600 study volunteers offers insight into ways that the informed consent process works—and where it breaks down. Wide differences appear to occur...
in the ways the informed consent process is being managed and in the motivation and comprehension levels of study volunteers. This variability speaks to the challenges of complying with informed consent guidelines.

The following findings suggest places where research professionals should focus in order to build upon and improve the current informed consent process. Insights from the results of this recent survey also suggest applied ways that investigative sites might enhance their subject recruitment and retention efforts.

Several key takeaways:

- The vast majority of study volunteers claim to understand the expectations of the study.
- A very high percentage of volunteers understand that they can withdraw from a clinical trial at any time.
- A high percentage of volunteers also say that they do not understand research risks or the availability of patient advocacy, and approach the decision to give consent without the assistance of a support network.

Too many subjects sign the consent form without reading and reviewing it, do not understand research risks or the availability of patient advocacy, and approach the decision to give consent without the assistance of a support network.

An online survey

In January and February 2002, we conducted an online survey among study volunteers who had completed a trial within the past six months. A total of 1561 respondents completed the survey, representing a 9% response rate. The average age of respondents was 51 years. Approximately 59% of respondents were women, and 41% were men. Respondents were evenly divided in terms of having participated in clinical trials in the past.

We posted the survey on our Web site for four weeks. The Web site receives visits from several hundred thousand patients and their advocates monthly. The survey screened for only those individuals who had completed a clinical trial within the past six months. Along with relatively even gender representation, the distribution of disease conditions was broadly based across 18 major therapeutic areas.

Web-based surveys have several biases that should be noted because they provide an understanding of respondent demographics. Web browsers tend to be more computer literate. In addition, the typical Web browser is better educated and has higher socioeconomic status than the national average.

What the survey shows

The results of the survey focus on form review, form discussion, and form comprehension.

Form review. The majority (86%) of study volunteers in our survey indicate they read the informed consent form prior to signing it. Despite the importance of this process, 14% of subjects report signing the informed consent document without reading the form. Based on our survey of volunteer subjects, many explanations for this result present themselves. Volunteers may be facing a dire condition for which their participation is perceived as the only option, for example. Alternatively, some subjects place an unusually high level of trust in research professionals. And some may be uncomfortable reading overly technical documents.

Although investigative sites approach the informed consent process differently, many common practices exist. How the consent process is handled depends on a variety of factors, including the individual clinical trial, the volunteer, and the standard operating procedures of the research center. Figure 1 illustrates our recent survey results. Study coordinators review the form with the volunteer 41% of the time. The principal investigator (PI) reviews the informed consent document with study volunteers 20% of the time. Interestingly, nearly one in seven study subjects report that no one reviewed the informed consent form with them.

Form discussion. A wide variability occurs between volunteers when it comes to asking numerous questions and to being engaged throughout a discussion of a study-specific informed consent form. Investigative sites report that some volunteers go out of their way to be as informed as possible. By contrast, a large number of volunteers reportedly do not ask any questions during the review of the informed consent form. In our survey, more than 70% of respondents indicate that they didn’t know what questions to ask. One in ten volunteers adds that they were simply too afraid to ask the PI or study coordinator certain questions. In a related survey item, one-third of subjects report that they asked few to no questions. Two-thirds of subjects report that they asked several questions during the informed consent discussion.

A previous survey of 1050 study volunteers in 2000 found that at the outset of a clinical trial, volunteers are most concerned about two things: receiving a placebo rather than an active drug, and the risk of side effects.

Form comprehension. Volunteer comprehension is one of the thorniest aspects of the informed consent process. Study per-
sonnel often cite low volunteer comprehension as the largest determinant of false expectations and misinformation. A number of professionals believe that often the study coordinator can sense when volunteers are uncomfortable asking questions and discussing participation risks. In these instances, study personnel may give only a cursory review of study risk factors and other complex items during the informed consent process.

Research professionals involved in the informed consent process appear to be doing a good job explaining the basic requirements of participation. A strong majority (85%) of study volunteers say they were made aware of the duration of the trial as well as the number of visits they would have to make. And 89% of respondents say they well understood that the study drug might not work for them. Additionally, as shown in Figure 2, a high percentage of respondents understood that they did not have to be in the study and could quit at any time. In our survey of 1561 trial participants, 10% report they did not understand that their participation was voluntary and could be terminated at any time.

Although a high percentage (86%) of subjects say they did understand that the study drug could cause side effects, 30% claim they did not understand that their trial could carry more risk and discomforts than the standard treatment. Nearly two-thirds (63%) say they were aware that the treatment and procedures in the study might not be standard for their medical condition. By contrast, one out of three subjects did not understand that the investigational drug might be a novel approach to treating their indication.

The informed consent form must provide contact information for the PI, the ethics review board, and, if appropriate, a study advocate. Despite this fact, nearly 40% of subjects did not know they had an advocate or an ethics board representative, other than the PI, to whom they could turn with problems or concerns. In addition, one out of five volunteers did not understand that certain authorized individuals would have access to their medical records.

In the recent survey, the majority of study subjects (83%) say they made the decision to participate on their own. Only 17% report they sought input from others into their decision to participate. The most common sources for input into this important decision were family members (30%), friends (7%), and a personal physician (30%). For those individuals seeking input into their decision to participate, study coordinators provided input less than 10% of the time. And one out of four study subjects report that they were never given a copy of the informed consent form that they signed.

The process still needs work

The results of this survey show a highly variable informed consent process. Wide differences in volunteer motivation and comprehension require more work on the part of investigative site personnel. Certain aspects of the process are well supported. A high percentage of volunteers understand the requirements of participation, for example, and the majority understand they may withdraw from a clinical trial at any time.

The informed consent process falls short in a number of areas, however. A relatively high percentage of subjects sign the consent form without reading and reviewing it. Volunteer understanding of research risk and the availability of patient advocacy are low. Volunteers also primarily approach the decision to give their consent individually, without the assistance of a support network.

The informed consent process presents major challenges for study staff personnel. At the same time that they face performance and cost pressures, study personnel must ensure that consent is voluntary and without coercion. This is particularly difficult at part-time sites and in academic settings where the physician is also the researcher. In these instances, subjects may feel that their decision not to participate in a trial could adversely affect the quality of their future care.

Study personnel must prevent undue influence and misrepresentation of the investigational treatment. Study personnel are also responsible for ensuring that subjects are competent to consent to treatment and must make sure that each volunteer is fully informed. Study information must be fully disclosed, and the participant must understand the information that has been disclosed.

In discussions with investigative sites about the results of this survey, many study staff indicate that they are, or will soon be, implementing a number of new approaches to address shortcomings in the current informed consent process. These new approaches target three broad objectives: volunteer preparation, consistent communication, and assessment of comprehension.
Several improvement approaches are designed to prepare study volunteers to be more comfortable with the process and to promote more active participation during informed consent form review. For example, many sites now send the informed consent form to their volunteers several days before staff review the form in person with the volunteer. This gives volunteers and their advocates time to look over the form and to formulate questions on their own. One site reported mailing a letter to volunteers with a glossary of research terms and a discussion to help shape volunteer expectations.

A number of sites report developing resources to assist in delivering a more consistent message to study volunteers during review of the informed consent form. For example, some sites distribute brochures that discuss a volunteer’s “bill of rights.” Sites have also mentioned using videotaped presentations of the informed consent form to ensure consistency across study volunteers. Several institutions report that their IRBs are evaluating the involvement of impartial witnesses to sit in with the volunteer during review of the informed consent form.

Many investigative sites now employ the use of quizzes and questionnaires following informed consent form review in order to gauge comprehension. A growing number of sites are also exploring the use of assessment mechanisms, implemented after a volunteer has completed his or her participation, in order to gather longitudinal information on informed consent process improvements. Our company, for example, conducts routine volunteer assessments on an ongoing basis for a number of investigative sites.

Providing an effective informed consent process is of utmost importance. Without an effective and efficient informed consent process—one based on complete disclosure that nurtures trust and a commitment to participate—enrolling subjects into clinical trials will continue to be difficult. Subjects who have been through a clinical trial are far more likely to participate again because they understand the subject experience. A more effective informed consent process will affect subject recruitment and retention efforts on a wide scale. Ultimately, an improved informed consent process could play a substantial role in shaping public perceptions of the value of clinical research.

References

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