Introduction

The requirement to obtain voluntary informed consent from individuals before they are enrolled in a research trial is a fundamental principle of research ethics. This requirement is reflected in all published national and international codes, regulations, and guidelines pertaining to research ethics, including those in many developing countries, such as India, Thailand, and Uganda. It also appears in a major international human rights instrument—the International Covenant on Civil and Political Rights—to which the United States is a party. Article 7 of this covenant provides that “no one shall be subjected without his free consent to medical or scientific experimentation” (United Nations 1996).

The requirement for freely given and informed consent to participate in research reflects important substantive ethical principles, including respect for persons, human dignity, and autonomy. However, it is possible to respect persons and their dignity or autonomy and affirm the requirement to obtain voluntary informed consent and at the same time allow for the modification of the procedures that are involved in obtaining consent, such as those stipulated in the Federal Policy for the Protection of Human Subjects, known as the Common Rule (45 CFR 46.117(c)).

Despite the ethical centrality of voluntary informed consent and its underlying principles, problems of interpretation and application exist for researchers and ethics review committees in both developed and developing countries. Some problems regarding informed consent are particularly difficult when the host country has little experience with clinical trials and has markedly different cultural values and ethical commitments than the United States. It is important, therefore, for U.S. sponsors of international research to address pressing issues concerning the application of U.S. research regulations for informed consent in settings with different cultures and customs.

This chapter addresses a number of related topics, including the following:

- whether cultural factors create a barrier to complying with the substantive ethical standard of informed consent and whether it is permissible to depart from that standard if the research could not otherwise be carried out;
- how investigators obtain voluntary informed consent in settings in which the belief system of potential research participants does not explain health and disease using the concepts and terms of modern medical science and technology;
- how voluntary participation can be ensured in settings in which community leaders may exert pressure on the entire community to enroll in a proposed clinical trial;
- how cultural differences can be addressed between the United States and other countries that make it difficult or impossible for other countries to adhere to U.S. federal regulations stipulating specific procedures for obtaining voluntary informed consent; and
- the means by which the United States could modify its informed consent regulations to adapt to various cultural circumstances in other countries without compromising the substantive ethical standard of informed consent.

Although individual voluntary informed consent by competent adults is a widely accepted standard in most research environments, it is not universally embraced.
Nonetheless, the National Bioethics Advisory Commission (NBAC) remains convinced that U.S. sponsors of research in developing countries should adhere to internationally agreed-upon ethical standards of voluntary informed consent for research, even in the face of cultural diversity. Obtaining adequately informed voluntary consent from individual research participants is a necessary requirement in preventing exploitation, and it should be possible to remain sensitive to cultural differences without departing from these standards.

The justification for the need for obtaining informed voluntary consent is simple: The use of human beings as a means to the ends of others without their knowledge and freely granted permission constitutes exploitation and is therefore unethical. NBAC recognizes, however, that disagreement still exists about this claim. One commentator has argued that “[i]t is ‘ethical imperialism’ at its worst to assume that the informed consent requirement, which does indeed serve one (only one) moral principle in the Western setting, is in itself such a universal ethical standard” (Newton 1990, 11). This same commentator contends that growing doubt surrounds the values of individualism and individual rights, so “the investigator might better stick to the research, and accept the local assessment as to adequate protection of individual rights” (Newton 1990, 11).

Two other commentators, Ijsselmuiden and Faden, take an opposing view: “Appeals to cultural sensitivity... are no substitute for careful moral analysis. We see no convincing arguments for a general policy of dispensing with, or substantially modifying, the researcher’s obligation to obtain first-person consent in biomedical research conducted in Africa” (1992, 833). They add that defenders of such a policy “have relied on limited and often dated anthropologic literature that does not reflect the rapid cultural changes brought about by colonialism and independence, warfare, and urbanization” (1992, 833).

The recommendations developed in this chapter focus on three traditional elements of informed consent (Faden and Beauchamp 1986): 1) disclosing information to potential research participants (see Exhibit 3.1); 2) ascertaining their understanding of what has been disclosed; and 3) ensuring that their agreement to participate in research is voluntary. The basic elements of disclosure in the informed consent process as presented in the Federal Policy for the Protection of Human Subjects are listed in Exhibit 3.1. References in this chapter to the basic elements of disclosure in informed consent are to these eight requirements.

### The Ethical Standard of Informed Consent

Various descriptions of the process and nature of informed consent can be found in the Common Rule (45 CFR 46.116 and 46.117), Food and Drug Administration (FDA) regulations (21 CFR 56), the Council for International Organizations of Medical Sciences (CIOMS) *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (CIOMS 1993), the International Conference on Harmonisation (ICH) *ICH Harmonised Tripartite Guideline, Guideline for Good Clinical Practice* (GCP) (ICH 1996), and the World Medical Association’s (WMA) *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects* (WMA 1964, as amended in 1996 and again in 2000). Principle 9 of the 1996 revision of the *Declaration of Helsinki* states that “[i]n any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject’s freely given informed consent, preferably in writing” (WMA 1964, as amended in 1996). In the October 2000 revised *Declaration of Helsinki*, Principle 22 addresses the informed consent process, stating that:

> [I]n any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician
should then obtain the subject’s freely given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed (WMA 1964, as amended in 2000).

Substantive changes between the 1996 and 2000 revisions of the Declaration include 1) informing each potential subject about any possible conflicts of interest and the institutional affiliations of the researcher; 2) ensuring that research participants have understood the information presented to them; and 3) requiring that if the consent cannot be obtained in writing, the nonwritten consent must be formally documented and witnessed.

For this report, NBAC adopts, as the clearest and most appropriate guides for discussion, the following definitions of informed consent and the substantive standard of informed consent: Informed consent is a process by which an individual voluntarily expresses his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the decision to participate. This definition is adopted from the ICH Guideline for Good Clinical Practice, GCP Guideline 1.28 (ICH 1996). An important feature of this definition is that it focuses on the process of obtaining consent rather than on the documentation of that process using, for example, a written, signed, and dated form.

Exhibit 3.1: Disclosure Requirements in the U.S. Common Rule

The disclosure requirements found in the Federal Policy for the Protection of Human Subjects at 45 CFR 46.116(a), under the heading of “basic elements of informed consent,” are as follows:

1) a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject’s participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
2) a description of any reasonably foreseeable risks or discomforts to the subject;
3) a description of any benefits to the subject or to others which may reasonably be expected from the research;
4) a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
5) a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
6) for research involving more than minimal risk (as defined in 45 CFR 46.102(i)), an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
7) an explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject; and
8) a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled (45 CFR 46.116(a)).

It should be noted that these requirements could be modified or waived by an Institutional Review Board (IRB) under certain circumstances. In addition to the basic information listed above, the U.S. regulations require that participants be given other information that may affect their participation in research, depending on the nature of the project itself. The U.S. regulations list six such additional disclosures (45 CFR 46.116(b)).

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In an ethically sound consent process, a member of the research team provides information to the potential participant, determines that the individual understands the information provided, and ensures that the individual voluntarily agrees to participate. Although consent traditionally has been documented by the signing of a consent form, other methods of documentation often are acceptable or even preferable, such as oral consent with a witness signature. In many settings, it is also required that the person obtaining the consent sign the consent form or other related documents and that a witness (or person designated by the participant) attests to the process. It is always essential to make a distinction between the consent document and the consent process and to not allow the document itself to constitute the process.

The phrase substantive standard of informed consent refers to the requirement to obtain voluntary informed consent and reflects the principle that competent individuals are entitled to choose freely whether to
participate in research. This definition was adopted from the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects, Guideline 1, Commentary, para. 2 (CIOMS 1993, 13). In general, voluntary informed consent protects the individual’s freedom of choice, respects his or her personhood, dignity, and autonomy, and reduces the chances of exploitation.

Objections to this substantive ethical standard are rarely, if ever, voiced, even in parts of the world in which less cultural emphasis is placed on individual rights and freedom of choice than is common in Western and most developed countries. However, various objections often arise about the need for certain procedures for obtaining and documenting informed consent, including those stipulated in U.S. research regulations and other documents, such as the ICH Guideline for Good Clinical Practice. As noted, it is important to distinguish substantive ethical principles and standards from the procedures that implement them. Although procedures are important, they often can be modified without compromising ethical principles or standards. Examples of procedural aspects of the informed consent process and its documentation include the following requirements: the informed consent documents should be in writing and signed by the research participant; the consent form should be signed by the person obtaining consent or by the principal investigator; and there should be a witness to the signing of consent forms. Other examples of procedures that are not always central to meeting the substantive ethical principles and standards of voluntary informed consent are involving family members in the consent process or obtaining a community leader’s permission before approaching individuals in the community. Although it is necessary—and not always easy—to determine which procedural aspects are ethically required and which might be altered or waived altogether, procedural requirements should be viewed as less fundamental than matters of substantive ethical standards or principles.

**Recommendation 3.1:** Research should not deviate from the substantive ethical standard of voluntary informed consent. Researchers should not propose, sponsors should not support, and ethics review committees should not approve research that deviates from this substantive ethical standard.

### Cultural Barriers Relating to Disclosure Requirements

Requirements for disclosing information in research settings usually exceed those for disclosing information in clinical contexts. In the United States, the requirements for disclosure of information to potential participants in research are specific and detailed. (See Exhibit 3.1.) The extent of medical information that is disclosed to patients in clinical settings differs among cultures and can influence judgments about the amount and kind of information that should be disclosed in research settings. Three principal types of disclosure are central to the process of informed consent in the research setting: 1) disclosure of diagnosis and risk; 2) disclosure of the use of placebos and randomization; and 3) disclosure of alternative treatments. In addition, NBAC considers a fourth type of disclosure—that of the possibility of access to any post-trial benefits—a central issue discussed in Chapter 4.

#### Disclosure of Diagnosis and Risk

In some parts of the world, it is still customary for physicians to withhold certain information from patients. Clinicians often provide diagnoses (as well as prognoses) of cancer or other serious conditions to family members, but they withhold such information from patients. As a result, the patient’s consent to certain procedures, if sought, may not be fully informed. Jeremy Sugarman and his colleagues noted in their report to NBAC that “[i]n one country, complete information about medical diagnoses and prognoses are withheld routinely from patients with certain diseases, such as cancer. Consequently, valid informed consent (for either treatment or research participation) can be difficult or impossible.”

Nancy Kass and Adnan Hyder describe a similar situation in their study for NBAC: “…in some developing country settings, a diagnosis of cancer would never be revealed directly to the patient but rather to members of the patient’s family.” Although this observation was made in reference to clinical care, these cultural practices are relevant to research participants, who may have similar expectations. Similarly, different cultures have different attitudes toward the disclosure of risks in the clinical context,
and some researchers believe that it is not always appropriate to disclose to patients the full ramifications of their situation.

In another study conducted for NBAC, Nigerian researchers indicated that consent documents attached to certain research protocols included information that potential participants might find extraneous, irrelevant, or culturally inappropriate. These researchers called particular attention to the emphasis placed on explaining the potential risks to study participants, noting that in the United States, there is much greater interest in communicating the possibility of harm to research participants than there is in Nigeria. One physician noted that, given Nigerian cultural norms, disclosing all possible risks would unnecessarily alarm potential research participants associated with the research. Based on such observations, some people believe that, at least in some cultures, it would be impossible to enroll research participants by adhering to the basic elements of disclosure as presented in 45 CFR 46.116(a).

NBAC believes that cultural standards regarding the inappropriateness of providing diagnoses and prognoses to patients or research participants do not justify deviation from the substantive ethical standard of informed consent in research. Even if the custom of routinely withholding complete information about diagnoses and prognoses from patients with certain diseases could be defended in ordinary medical practice, it poses a severe challenge to the need to adhere to the substantive ethical standard of disclosure required for research involving human participants. Those who lack information about their diagnosis and prognosis cannot be expected to understand the purpose of the research, any potential direct benefits, the risks of not participating, or the alternatives to participation. Similarly, potential participants cannot make an informed decision to participate without knowing that they may not receive a proven treatment that could be beneficial. Enrolling individuals in research who are not given the opportunity to understand such important information represents a deviation from the substantive ethical standard of disclosure required for adequate informed consent and should not be permitted. Diversity in the practice of disclosing information in the clinical context does not alter the requirements for such disclosure in the research context.

These matters must be studied in more detail to learn about how cultural variations affect the meaning and effectiveness of the consent process and the use of particular consent documents. It is critical that we find innovative and culturally responsive ways to disclose information to potential participants. NBAC heard testimony from U.S. and developing country researchers who have succeeded in adhering to this standard, even though doing so often takes more time and effort than researchers typically expend in the informed consent process. Even in cultures in which a diagnosis of serious illness is not normally revealed in the treatment context, researchers often can find ways to overcome this barrier to disclosure in the research setting.

Disclosure About Control Interventions and Randomization

In some cultural contexts, questions also arise regarding the appropriateness of requiring information to be disclosed about the use of a placebo in one arm of a clinical trial, the randomization of participants, and any uncertainty that may exist regarding the efficacy of an experimental intervention. Sugarman and his colleagues reported on “local perceptions concerning cultural barriers to randomization and the use of placebos.” Indeed, investigators sometimes struggled with these barriers, responding in different ways. For example, in one case, investigators who believed that it would be impossible to obtain valid informed consent for a randomized trial abandoned the use of randomization in their research. However, in another case, investigators used placebos, even though they did not believe that the research participants understood the implications of doing so. Despite these barriers, cultural differences do not provide adequate justification for foregoing the requirement to disclose key elements of the nature of the clinical trial, such as the use of a placebo or the randomization of participants into different trial arms.

Disclosure of Alternative Therapies

An example from the literature illustrates a particular disclosure problem. Love and Fost (1997) describe a struggle that occurred in one U.S. IRB that reviewed a proposal for a randomized clinical trial of adjuvant treatment for breast cancer to be conducted in Vietnam. The
informed consent process should be culturally appropriate. Researchers should develop culturally appropriate ways to disclose information that is necessary for adherence to the substantive ethical standard of informed consent, with particular attention to disclosures relating to diagnosis and risk, research design, and possible post-trial benefits. Researchers should describe in their protocols and justify to the ethics review committee(s) the procedures they plan to use for disclosing such information to participants.

**Disclosure About Possible Post-Trial Benefits**

The basic disclosure requirements for satisfying the informed consent provisions in U.S. research regulations (see Exhibit 3.1) focus on information needed by a potential participant to decide whether or not to participate in a study. Of the eight basic disclosure requirements, one focuses on potential benefits: “a description of any benefits to the subject or to others which may reasonably be expected from the research” (45 CFR 46.116(a)(1)). Traditionally, such a disclosure has been required to ensure that potential participants understand which benefits they might receive by participating in the research. However, there is no specific mention of post-trial benefits in U.S. research regulations. The Commission recognizes the importance of informing participants about potential benefits they might receive after their participation in the research ends. Therefore, Recommendation 3.3 requires ethics review committees to ensure that researchers disclose information about post-trial benefits to participants.

**Recommendation 3.3:** Ethics review committees should require that researchers include in the informed consent process and consent documents information about what benefits, if any, will be available to research participants when their participation in the study in question has ended.

**Other Cultural Issues Relating to the Informed Consent Process**

Additional issues in the informed consent process include the ability of potential participants to understand the scientific and technical aspects of research protocols—given the culture and belief systems within which they live—and the influence and involvement of others in the consent process.

**Innovative Ways of Presenting Information to Participants**

In some cultures, the belief system of potential research participants does not explain health and disease using the concepts and terms of modern medical science and technology. This is significant, because when people do not understand or accept scientific explanations of health and disease, the challenge of obtaining informed consent can be daunting. Patricia Marshall’s report to NBAC quotes one physician as follows: “…[W]hat I worry about is whether we are really informing them. We are talking to a society that does not believe in the germ theory of disease so it’s difficult to explain.” The researcher provided an example of the pervasive belief that a person’s death is a result of sorcery rather than a lethal infection. In noting that he had encountered a cultural belief that spirits cause epilepsy, Alfred Sommer, Dean of the Johns Hopkins University School of Hygiene...
and Public Health, told NBAC that “we do not want to fight a belief system. We simply say we have this pill. We believe it is safe. We think it may reduce the recurrence of the following thing. We would like you to take it.”

Despite this potential barrier to adequate understanding, if they are willing to devote the time and effort to do so, researchers often are able to devise creative measures for overcoming these barriers. An example appears in the Kass/Hyder report for NBAC: “…the concept of immunology, an immune response, that there’s something in your blood that’s going to attack bacteria and viruses which you also don’t have a concept for…. [H]ow much can someone really focus on the consent form when they have this whole new idea that there’s this battle going on in their bloodstream?…. When we go and translate, we try to use, for example, immune cells, we talk about people who guard houses... it’s a particular kind of watchman. So you have a particular kind of watchman in your blood…. “12 Even in countries with very low literacy rates (e.g., 30 percent for men and 10 percent for women in Senegal), one group found that widespread illiteracy is not a barrier to comprehension, especially since informed consent is more an interactive process than one that depends on reading” (Preziosi et al. 1997, 372). However, the authors of this study concluded that understanding abstract scientific concepts, such as double blinding and randomization, could be difficult. To help explain these complex issues, researchers used terms and concepts that were understandable to the community involved: “To illustrate the principle of randomization and the possibility that one of the vaccines might fail, the presenters used a familiar agricultural example: the evaluation of fertilizers or of seed varieties on randomized plots, a procedure familiar to farmers in the area” (Preziosi et al. 1997, 370).

Another illustration emphasizes the importance of educating individuals and the community about the study and its specific purpose and procedures. Investigators and research assistants interviewed by Marshall noted that education should begin at the community level. “You approach some person as a contact person...you often start with the local governance...we need to obtain permission from them and we need their help to get to community leaders...they need to work with community leaders...we spend time discussing [the study]...you have to explain [it] fully.” Researchers may find, for example, that, in circumstances where they do not speak the local language, the use of intermediaries can be an effective means of ensuring adequate understanding among potential participants.

In some countries, a process of community education acts as a precursor to the process of obtaining individual consent. For example, one study reported that in Senegal, the field staff and physicians held meetings in each village to provide information about a study of a new pertussis vaccine and to obtain consensus about its use. A physician then provided additional information and sought individual informed consent at the monthly vaccination session. A clinical trial for vaccination against Haemophilus influenzae type b in The Gambia was preceded by an intensive publicity campaign involving radio, newspapers, and discussions with village leaders (Leach et al. 1999). When mothers attended the first child health clinic, they received an information sheet about the clinical trial to take home for discussion with their families. When a mother returned for the first vaccination, the trial worker explained the study again, and, if the mother gave oral consent, the trial worker signed the information sheet.

Translation and back translation of a written consent form may be one way of ensuring that information is correctly disclosed; however, this may not always be effective. Jean Pape, a researcher from Haiti, who is also on the Cornell University faculty, described the complexity of this process. In preparing to begin HIV vaccine trials in Haiti, his research group needed approval from its own IRB in Haiti, as well as from the IRB at Vanderbilt University—one of the collaborators—and from the IRB at Cornell University Medical School. To be understandable to participants, the consent form had to be in the Creole language. Yet, the document also had to be in French, the language of the Haitian researchers. Because the consent form had to be reviewed by the Cornell IRB, a translation in English was also required. Pape said that the back translation of a consent form “does not guarantee that volunteers have really understood the objective of the study, the risks and advantages, and their voluntary participation,” a difficulty reported in another study in Nigeria.
NBAC also heard about the desirability of testing research participants to understand whether and how much they understood regarding the informed consent process. Pape described the process he regularly undertakes to ensure understanding. This process includes a person who counsels potential participants about all aspects of the project, helps to develop a test questionnaire that all potential participants must pass before being given the actual consent form, and is available to address participants’ concerns and questions. The period before obtaining ethical clearance from the various review committees is used to counsel and inform potential volunteers, who should pass this test of understanding before receiving a simpler informed consent form. These mechanisms—the counseling sessions and test questionnaires—illustrate some of the ways in which informed consent can and should be a process that takes place over time and that is much more than the mere signing of a document that may be imperfectly comprehended. Despite the acknowledged difficulties of administering tests of understanding, NBAC supports the idea of incorporating these tests into research protocols.

Recommendation 3.4: Researchers should develop procedures to ensure that potential participants do, in fact, understand the information provided in the consent process and should describe those procedures in their research protocols.

Recommendation 3.5: Researchers should consult with community representatives to develop innovative and effective means to communicate all necessary information in a manner that is understandable to potential participants. When community representatives will not be involved, the protocol presented to the ethics review committee should justify why such involvement is not possible or relevant.

Involvement of Others in the Informed Consent Process

In some cultures, several barriers might arise to ensuring free and individual choice to participate in research. Among those identified by Kass and Hyder were deference to physician/health personnel; low economic status of potential participants; low level of awareness or education of potential participants; limited decisionmaking power for women; community leaders’ disapproval; family disapproval; and cultural customs that prohibit “refusing a guest” (rules of traditional hospitality). A subset of these barriers is discussed in this section—barriers that pertain to the involvement of community leaders and family members in the consent process.

Community Leaders

In some cultures, investigators must obtain permission from a community leader or village council before approaching potential research participants. Yet, it is important to distinguish between obtaining permission to enter a community for the purpose of conducting research and for obtaining individual informed consent. In their reports, NBAC consultants all noted that the role of community leaders or elders is an integral part of the process of recruiting research participants. Although these reports typically use the terminology of consent to refer to the community’s permission or a leader’s authorization for the researchers to approach individuals, NBAC will use this term to refer to the permission or authorization given by the individual being recruited as a research participant.

The need to obtain permission from a community leader before approaching individuals does not need to compromise the ethical standard requiring an individual’s voluntary informed consent to participate in research. Gaining permission from a community leader is no different, in many circumstances, from the common requirement in this country of obtaining permission from a school principal before involving pupils in research, from a nursing home director before approaching individual residents, or from a workplace supervisor before initiating an experimental screening program. An ethical problem arises only when the community leader exerts pressure on the community in a way that compromises the voluntariness of individual consent. The reports commissioned by NBAC describe a number of situations in which community leaders have been involved in the informed consent process. (See Exhibit 3.2.)

Nevertheless, recruitment procedures in some cultures involve community leaders whose authority does not allow individual members of the community to refuse to participate in research for which the leader has
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Exhibit 3.2: Involvement of Community Leaders in Informed Consent

During the course of its deliberations, NBAC sponsored a survey in which researchers who conducted international research were asked about the process of obtaining informed consent in different cultural settings.\(^2^0\) The following excerpts highlight some of the issues raised when cultural practices require the involvement of community leadership in the informed consent process.

- “There are very positive informed consent stories where you would never go first to the individual. You can approach the individual after you have explained the research to the chief or local leader. Then they explain the informed consent process to their people without exerting the pressure. The best evidence of the effectiveness of this approach is when people refuse to participate. That’s a good sign. They are able to refuse.”\(^2^1\)

- In contrast, in some settings, the head of the village or a group of elders makes a collective decision for the village. “If they make the decision in favor of participating in the trial, virtually everyone will participate. The people in the community are then extremely reluctant to withdraw from the trial because of the collective nature of community activities.”\(^2^2\)

- In other settings, there is authorization by a community leader that is compatible with individuals’ right to refuse and authorization in a context in which the Chief’s word is law. One physician described “two levels” of consent or permission: “One is community and the other is individual….When you leave [the Chief], the Chief is expected to open households so there is really another level of consent [in between]…the Chief and council, the household head, then the individual.”\(^2^3\) In answer to the question, “then how will the community respond?” the physician said that most of the time the members agree to participate. At the same time, there is some uncertainty on the part of the physicians interviewed about the extent to which individual agreement to participate is voluntary.\(^2^4\)

- “Regarding whether the community leaders should be asked to approve the study depends on 1) whether you are working in a healthy community, and 2) the level of corruption of the community leaders. I have been conducting a study in an African city since 1987. There, we have ‘laid low,’ trying to avoid the gaze of the community leaders and state or national politics. Had we been noticed there, the tremendous corruption would have destroyed the study. However, working in an African village would be an entirely different matter. In that situation, a study could not be conducted without the approval and active support of the community leaders.”\(^2^5\)

- An American researcher conducting malaria studies in Mali and in Malawi noted the difference between the two settings. In Mali, the study was conducted in a remote rural area in which community leaders were heavily involved. In contrast, the Malawi study took place in a large city with an established health care system and a more educated population. In this latter setting, community consent at the national or institutional level is removed from individuals and the local community, and it seems likely that consent by community leaders would not have an undue impact on the decisions of individuals. In addition, in an urban context, it is more difficult to identify appropriate spokespersons for the larger community, especially as individuals in urban areas tend to associate themselves with many different kinds of communities.\(^2^6\)

granted permission. Also, in some settings, authoritarian governments may limit autonomous decisionmaking by their citizens, which may affect their participation in research.\(^2^7\) The question then arises regarding whether there are some countries in which U.S. researchers should not engage in international collaborative research. In NBAC’s view, if a country’s political system or a local situation makes it impossible for individuals’ consent to be voluntary and that fact is known in advance, then, because U.S. researchers cannot adhere to the substantive ethical standard of informed consent, it would be inappropriate for them to choose such settings.

Recommendation 3.6: Where culture or custom requires that permission of a community representative be granted before researchers may approach potential research participants, researchers should be sensitive to such local requirements. However, in no case may permission from a community representative or council replace the requirement of a competent individual’s voluntary informed consent.
**Recommendation 3.7:** Researchers should strive to ensure that individuals agree to participate in research without coercion or undue inducements from community leaders or representatives.

**Family Members**

It is customary although not required in some societies for other members of a potential research participant’s family to be involved in the informed consent process. In most instances, the need to involve the family is not intended as a substitute for individual consent, but rather as an additional step in the process. An example of a multistep process involving the family is described by Loue and colleagues (Loue and Okello 2000) in their report on a workshop in Uganda that addressed the problem of acquiescence by another family member in order for an individual to participate in research. (See Exhibit 3.3.)

Researchers in other countries also have reported on their efforts to involve the family in the informed consent process in ways that do not undermine the standard of individual consent. Marshall reported, for example, that in Nigeria in areas where traditional cultural norms are strong, the permission of a woman’s husband might be required before she can enroll in research. A Nigerian physician involved in a breast cancer study noted that cancer patients often need the approval of their husbands to participate in research. However, the physician also emphasized that in such cases, the woman’s individual consent is still essential. Indeed, most investigators have developed strategies that accommodate and encourage discussion regarding study participation with family members.

NBAC recognizes that this situation does not apply in cases in which a family member lacks the capacity to give informed consent. Indeed, there is consensus that having the capacity to decide is an important precondition (or threshold element) for informed consent (Beauchamp and Childress 1994; NBAC 1998).

In many cases, family members may be approached before asking an individual directly to participate in a research project. However, seeking permission from family members without engaging the potential research participants at all clearly departs from the ethical standard of informed consent. On the other hand, potential participants might also choose to involve others, such as family members, in the consent process. Indeed, involving family or community members in the informed consent process need not diminish, and might even enhance, the...

**Exhibit 3.3: New Ugandan Guidelines for Informed Consent**

Uganda has a new constitution that specifically recognizes the rights of women and minorities, which had not been recognized in that country. A more specific development regarding research was the adoption of guidelines protecting the individual rights of research participants. In July 1997, the representatives of the National Consensus Conference on Bioethics and Health Research in Uganda voted unanimously to adopt the *Guidelines for the Conduct of Health Research Involving Human Subjects in Uganda* (National Consensus Conference 1997). Participants in the consensus conference came from a wide range of governmental and nongovernmental agencies.

The Ugandan guidelines for research specifically prohibit an investigator from relying on the permission of a community leader for the participation of community members in research. The development and adoption of this requirement of individual consent necessitated a reexamination of various aspects of Ugandan customary laws, which traditionally have demanded the subordination of an individual’s wishes to those of a specified family leader, usually the father or husband. An individual’s wishes could be further subordinates to those of the community or the tribe. Although these guidelines clearly require individual consent, it is not known whether this provision is always adhered to in practice. The process that led to adoption of these guidelines was informed by Uganda’s own recognition of its history, including its experience with tyranny, torture, and the elimination of targeted groups.

The Ugandan guidelines for research reflect efforts to achieve some balance between the older traditions and the ethical standard of voluntary and informed individual consent. The guidelines include a provision that allows potential participants sufficient and adequate time to confer with anyone else of their own choosing to discuss the particular features of the research and to minimize the possibility that they may be subjected to undue influence or coercion.
individual’s ability to make his or her choices and to give informed consent (or refusal).

These examples show that it is often possible to obtain individual informed consent, which may require and indeed benefit from the involvement of family or community members, while at the same time preserving cultural norms. Such involvement ranges from providing written information sheets for potential participants to take home and discuss with family members to holding community meetings during which information is presented about the research and community consensus is obtained. When the potential participant wishes to involve family members in the consent discussion, the researcher should take appropriate steps to accommodate this desire.

Recommendation 3.8: When a potential research participant wishes to involve family members in the consent process, the researcher should take appropriate steps to accommodate this wish. In no case, however, may a family member’s permission replace the requirement of a competent individual’s voluntary informed consent.

Consent by Women

Some cultures customarily require the permission of a woman’s husband, if she is married, or her father, if she is unmarried, before she can enroll in a research protocol. A strict requirement that a husband must first grant permission before researchers may enroll his wife in research treats the woman as subordinate to her husband and as less than fully autonomous. If the requirement of spousal authorization, in addition to individual informed consent, were applied equally to enrollment of men and women as research participants, it would at least constitute gender equity. But in cultures in which spousal authorization for participation in research is customary, it appears always to be the woman who must obtain her husband’s permission. If women wish to consult with their husbands or to seek voluntarily to obtain their husbands’ permission before deciding to enroll in research, this is not only ethically permissible, but in some contexts highly desirable. However, a strict requirement of spousal authorization violates the substantive respect for persons principle, which mandates that equal respect be accorded to women as persons.

Much research is directed at conditions that affect both women and men. Yet, it is important not to neglect research on diseases or conditions that affect only women. In reality, without involving the husband in the consent procedures, it may be impossible to conduct some research on common and serious health problems that affect only women. In such cases, a likely consequence would be a lack of knowledge on which to base health care decisions for women in that country. The prospect of denying such a substantial benefit to all women in a particular culture or country calls for a narrow exception to the requirement that researchers use the same procedures in the consent process for women as for men, one that would allow for obtaining the permission of a man in addition to the woman’s consent.

Recommendation 3.9: Researchers should use the same procedures in the informed consent process for women and men. However, ethics review committees may accept a consent process in which a woman’s individual consent to participate in research is supplemented by permission from a man if all of the following conditions are met:

a) it would be impossible to conduct the research without obtaining such supplemental permission; and

b) failure to conduct this research could deny its potential benefits to women in the host country; and

c) measures to respect the woman’s autonomy to consent to research are undertaken to the greatest extent possible.

In no case may a competent adult woman be enrolled in research solely upon the consent of another person; her individual consent is always required.

Voluntary Participation in Research

A fundamental principle of research ethics is the requirement that participation be voluntary—that is, “free of coercion and undue influence” (National Commission 1979). However, among the most difficult requirements to ensure is the voluntariness with which participants consent to enroll in a study. Pressure from a community
leader, the power and authority of the medical professionals who serve as investigators, and the fear of loss of health benefits that people would normally expect to receive may compromise individuals’ freedom to refuse to participate in research. The provision of medical care and treatment during a study may constitute an incentive for individuals to enroll in a study, but it should not be construed as a coercive offer that would unduly compromise the voluntariness of participation.

Undue Inducement

It is likely to be difficult to decide when a study design constitutes an undue influence. One definition states that “undue influence...occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance” (National Commission 1979, 14). There are many circumstances that can cause undue inducements to participate in clinical trials, including offers of medical care not otherwise available or offers of money. Discussions in the literature traditionally have focused on monetary payments to research participants and address the question of whether any amount of money is an acceptable inducement, and, if so, at what point the acceptable inducement becomes undue (Dickert and Grady 1999; Macklin 1981; Macklin 1982).

Other aspects of research design that may pose a problem of undue influence have received considerably less attention. As the CIOMS Guidelines document acknowledges: “It may be difficult to distinguish between suitable recompense and undue influence to participate in research....Someone without access to medical care may be unduly influenced to participate in research simply to receive such care” (CIOMS 1993, 19). This situation is likely to exist in developing countries in which large numbers of people have little or no access to medical care and treatment even for ordinary illnesses, a concern expressed to NBAC in testimony.

It is necessary, then, to answer the threshold question of whether the very offer to participate in research constitutes an undue inducement to citizens of developing countries who have little or no access to medical care and treatment (Bernstein 1999). Even a placebo-controlled trial offers such individuals a 50 percent likelihood (in a two-arm trial) of receiving an intervention that, although unproven, may be beneficial. If the solution to this fundamental problem is to forgo research entirely in such places, it might make those populations worse off than they would be if research goes forward. This consideration requires the review of the ethical consequences of not conducting research and the determination of whether those consequences outweigh the ethical problems alleged to exist in the conduct of the research. But the need to attempt such a balance can be avoided if a proper distinction can be made between acceptable inducements and those that constitute undue influence or coercion.

No hard-and-fast criterion can be stipulated for making this distinction. However, one approach would be to consider the possible motivations for participating in research, according to the following schema. People may, for example:

a) Act out of self-interest, when there is a potential benefit to them.

b) Act out of rational or enlightened self-interest, when there is potential benefit to others as well as to themselves, and some risk to themselves.

c) Act out of pure altruism, when they expect no benefit to themselves but expect benefit to others, and accept some risk to themselves.

d) Refuse to act because of perceived high risk or great inconvenience, only agreeing to undergo the risk when offered considerable material reward.

e) Act out of fear of the consequences of refusing to participate.

All of these situations apply to some extent in research. Situation (b) is the standard presupposition in Phase II or III clinical trials. Prospective participants weigh the risks and potential benefits, recognizing that there may be some risk to themselves but also some possible benefit and that the research as a whole may provide benefits to others. Situation (c) is the standard for research not designed to provide direct benefit to participants, but, for example, to determine the safety of drugs in Phase I studies, to discover basic physiological mechanisms, or to arrive at baseline data. Situation (d) captures the idea of undue inducement when people make a rational refusal based on perceived risk, but then agree to
accept the risk only when provided with a considerable material reward. Situation (e), by definition, is the paradigm of coercion: In hierarchical groups, in coercive settings, or under threat, individuals agree to participate in research because they fear the consequences of refusal. In this situation, their participation is coerced, not voluntary. Situation (e), therefore, is ethically prohibited.

In principle, there is no difference between the sort of motivation that prompts people anywhere to volunteer for research—situation (b)—and what may induce people in developing countries to agree to participate. The more difficult challenge lies in situation (d): Does the prospect of receiving medical care as a benefit during (or possibly after) the research prompt people in developing countries to undertake serious risks they would otherwise refuse to accept? There can be no general answer to this question, which can be determined only on a case-by-case basis. In studies with the usual range of risks, the provision of medical care may be an inducement to participate, but there is little reason to believe it is an undue inducement. Recalling the definition of undue influence cited earlier—"an excessive, unwarranted, inappropriate or improper reward"—it is reasonable to conclude that providing medical care to research participants is warranted, appropriate, and proper.

One might object that this definition is embedded in a document created in the United States—a wealthy, industrialized country—and therefore is irrelevant to resource-poor countries. The reply to this objection is twofold. First, poor people exist in every country, and participation in a clinical trial often is the only way that uninsured individuals in the United States can gain access to some medical care. Yet, no one could reasonably maintain that the poor or uninsured should be excluded from participation in research or that it would be ethically acceptable to deny them medical benefits that they could not otherwise obtain.

Second, the problem may not lie in the idea that an offer to possibly receive medical care is an inducement, but rather in the difficulty of determining when such an offer—admittedly an inducement—becomes undue. Those who argue that participation in research constitutes an undue inducement for poor people in developing countries would have to maintain that offering high-quality medical care and treatment that participants would not otherwise receive is unwarranted and inappropriate. However, the provision of medical care or treatment that would not otherwise be available to research participants should not, in principle, be construed as an undue influence to participate. This conclusion is supported by developing country researchers surveyed by Kass and Hyder: 64 percent stated that participants joined research projects in order to obtain benefits.33 Many researchers interviewed in focus groups for this same study seemed to believe that this was acceptable, given the overall risk/benefit ratio of the research; some focus group respondents remarked that providing significant benefits essentially left potential participants with no reasonable choice except to participate, but they did not specifically refer to this as undue inducement.34 NBAC concludes that although the potential benefits of participation in research may be an inducement for those in developing countries who lack access to medical care to participate in research, this does not sufficiently diminish the voluntariness of their decision in a way that would make their consent ethically invalid.

Somewhat more problematic are clinical trials studying a new intervention in which members of a control group receive an established effective treatment that is unavailable outside the trial. Does provision of the established effective treatment constitute an undue inducement to participate?

This situation can be cast in the form of a dilemma. If providing treatment otherwise unavailable to members of a control group receive an established effective treatment that is unavailable outside the trial. Does provision of the established effective treatment constitute an undue inducement to participate?

The dilemma arises because of the tension between the potential loss of full voluntariness on the part of participants and the probability of harm befalling those in the control arm who receive the placebo instead of an established effective treatment.
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As in any ethical dilemma, this one requires that moral considerations be weighed in order to determine which alternative is more acceptable. An appeal to certain ethical principles offers some insight. The well-accepted principle of nonmaleficence (Beauchamp and Childress 1994; National Commission 1979) requires that harm to participants be minimized; however, it could never be used to justify coercion of research participants, which would entirely preclude their voluntary participation. NBAC concludes that in this situation, it is more acceptable to allow the possibility of somewhat diminished voluntariness of participation than to risk harm to participants in the control arm, who are denied an established effective treatment. This is a position consistent with other guidelines, such as those of the Medical Research Council of the United Kingdom (MRC-UK 1999).

Minimizing the Therapeutic Misconception

One barrier to understanding the relevant, important aspects of any proposed research is what has been called the therapeutic misconception (Appelbaum et al. 1982; Churchill et al. 1998; King 1995). This term refers to the belief that the purpose of a clinical trial is to benefit the individual patient rather than to gather data for the purpose of contributing to scientific knowledge. The trust that patients have in their physicians in the clinical setting depends on an important element of the physician-patient relationship—that physicians should choose the most appropriate treatment for their individual patients. To apply that same concept to the research setting is to fall prey to the therapeutic misconception, which surfaces even when participants have received complete information (ACHRE 1996). In short, the therapeutic misconception rests on confusion between the aims of research and those of individualized medical treatment.

The therapeutic misconception has been documented in a wide range of developing and developed countries. For example, in a study conducted in a clinic in Brazil, all of the women who were interviewed said that they entered the study because they “thought that the contraceptive being offered would be good for them” (Hardy et al. 1998). In some parts of the world, a different kind of complication arises from the language itself. One American respondent to the study conducted by Kass and Hyder stated the following: “In many African languages, there is no word for ‘research’ or ‘science.’ The word used is generally the same as the word for ‘medicine.’ There is no concept of an experiment, placebos, etc., and despite the best translation of the most simply worded consent form, many adult subjects still have no understanding of the difference between being a research subject and receiving medical treatment.” The researcher went on to say that “[t]his should not be a reason to exclude these people from research; in fact they are often the population who will benefit most from the research and the only population in whom the studies can be done, e.g., persons at risk of naturally acquired malaria or other tropical diseases.”

It is important to distinguish the confusion that arises from the therapeutic misconception from a related consideration. In the research setting, participants often receive beneficial clinical care. In some developing countries, the type and level of clinical care provided to research participants may not be available to those individuals outside the research context. It is not a misconception to believe that participants probably will receive good clinical care during research. But it is a misconception to believe that the purpose of clinical trials is to administer treatment rather than to conduct research. Researchers should make clear to research participants, in the initial consent process and throughout the study, which activities are elements of research and which are elements of clinical care.

Recommendation 3.10: Researchers working in developing countries should indicate in their research protocols how they would minimize the likelihood that potential participants will believe mistakenly that the purpose of the research is solely to administer treatment rather than to contribute to scientific knowledge (see also Recommendation 3.2).

Documentation of Informed Consent

Distinguishing between the substantive need to obtain informed consent and the particular process by which consent is documented is critical. The U.S. requirements for documentation of informed consent (45 CFR 46.117) can pose unnecessary barriers to research that conforms
to the substantive ethical standard for informed consent. Problems arise, for example, from the need for written, signed consent forms and from the amount of information that is typically provided on U.S. consent forms for a complex clinical trial. In some developing countries, the requirement of documenting informed consent on a written form signed by the research participants is thought to be inappropriate. One obvious circumstance is that of illiterate participants, who may be able to understand information presented orally, but who find a written form on which they are required to make their mark useless. Moreover, in some cultures, people distrust any signing process. This distrust is common even in countries with a high literacy rate, such as Argentina and other Latin American countries, where people have lived under oppressive regimes and fear that signing a document could place them in jeopardy. Several examples that illustrate these situations are provided in Exhibit 3.4.

At the same time, there is some evidence that researchers can overcome many of the obstacles to participants’ understanding of lengthy complicated consent forms by devoting more time and effort to the consent process. Several empirical studies of informed consent carried out in developed countries describe a fairly elaborate, multistage consent process aimed at overcoming these barriers. Studies conducted in Chile, the Netherlands, and Switzerland found that researchers could overcome these barriers with three separate

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**Exhibit 3.4: Examples of Documentation of Informed Consent Requirements**

- Sugarman and colleagues provided two examples in which requiring a signed informed consent document was especially problematic: “…in one project involving many illiterate subjects, although thumbprints might be considered to be an appropriate means of documenting individual informed consent, local investigators did not use such an approach because it too closely related to past police tactics and [was] believed to frighten potential research participants. In another setting, where guerilla warfare was ongoing, the use of written informed consent posed a risk to participants because these documents linked them to particular institutions.”

- The Ugandan document *Guidelines for the Conduct of Health Research Involving Human Subjects in Uganda* rejects a requirement for written informed consent. This rejection stems from Uganda’s past experience of torture and persecution of individuals found to be associated with particular enterprises and recognizes the sensitivity to individuals’ reluctance to sign a piece of paper that attaches their name to an enterprise. Individuals who do not wish to sign may put an “X” in place of a signature. This is a good example of how procedural requirements can be made sufficiently flexible to reflect social and cultural sensitivities.

- Jean Pape, a Haitian researcher, discussed the complexity of the consent forms. He said that the forms are clearly too lengthy and that over the past 22 years, he has found them to be increasingly complicated. He stated that “[t]hey appear to be more concerned about legal implications for sponsor agencies than…with the welfare of the volunteers. We cannot read them to volunteers because the only time a volunteer had a document like this read to him was when he was in a court of law and had to sign some kind of papers. So this is changing the trust relationship that we have with our participants and, therefore, we have to explain it step by step.”

- Grace Malenga said of consent forms used in Malawi that providing too much information is likely to scare patients. “You start asking questions or telling them to sign…some papers and immediately…they will look at them, some of them have actually withdrawn.” Some people were willing to participate until they were asked to sign a piece of paper.

- Nigerian researchers pointed to the length and complexity of informed consent documents and the need for written consent as obstacles for those attempting to obtain consent from potential study participants. In Marshall’s study for NBAC, investigators agreed that individuals may have some anxiety about writing their signature or placing their thumbprint on a formal document because of uncertainties about whether the document could be used against them. One investigator noted the following: “Even if they use a thumbprint, they [can] get suspicious. They can’t read so they wonder why [you need their thumbprint]. It’s a big fear…the issue [has to do with] government documents. [It’s threatening] because they don’t know what they are signing or what they might be giving away.”
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preparatory sessions conducted with potential participants (Rodenhuis et al. 1984; Sánchez et al. 1998; Tomamichel et al. 1995). For example, in approving protocols, IRBs may waive documentation of informed consent through a signature or a thumbprint, provided that the researchers provide adequate justification for the waiver and ensure adherence to the substantive ethical standard of informed consent. It is NBAC’s view that in such cases, the justification, while important, also must pass public scrutiny, and we would encourage a process by which these waivers were audited by a competent body. Commentators to NBAC remarked that waivers of written consent documentation should include safeguards to ensure that individual consent is obtained. The FDA requires that clinical trial data entail some form of documentation of the consent process (21 CFR 312.62(b) and 21 CFR 812.140(a)(3)(i)), which means that an alternative form of documentation is needed for those trials submitted to the FDA that do not use individual signed consent forms. At the same time, more information is needed to determine the extent and magnitude of cultural differences in the informed consent process.

Recommendation 3.11: U.S. research regulations should be amended to permit ethics review committees to waive the requirements for written and signed consent documents in accordance with local cultural norms. Ethics review committees should grant such waivers only if the research protocol specifies how the researchers and others could verify that research participants have given their voluntary informed consent.

Recommendation 3.12: The National Institutes of Health, the Centers for Disease Control and Prevention, and other U.S. departments and agencies should support research that addresses specifically the informed consent process in various cultural settings. In addition, those U.S. departments and agencies that conduct international research should sponsor workshops and conferences during which international researchers can share their knowledge of the informed consent process.

Conclusions

In many countries, cultural barriers can prevent the informed consent process from being conducted in precisely the same way stipulated by U.S. research regulations. Investigators can, however, for the most part overcome these barriers without violating the substantive ethical standard that requires them to obtain individual and voluntary informed consent from competent research participants. One mechanism for addressing problems in a culturally sensitive way—without compromising ethical standards for obtaining voluntary informed consent—is to work collaboratively with the community in which the research will be carried out. Informing and educating the local community before the research begins can be helpful in recruiting volunteers and ensuring that this recruitment is noncoercive. Community education and consultation are important in protecting the rights of potential participants during recruitment, in promoting their understanding of the research, and in providing additional information about the study when relevant and necessary.

During the course of its deliberations, NBAC found that there is a great deal of support in developing countries for the requirement of voluntary, individual informed consent. The surveys conducted by Kass and Hyder lend considerable support to the view that both developed and developing country researchers view the requirement to obtain voluntary informed consent as a critical ethical standard. Adherence to this standard requires that researchers disclose relevant information, take steps to determine that potential participants understand what they have been told, and ensure that each individual’s consent is voluntary. Nevertheless, for some customs and traditions, some of the specific procedures related to the process and documentation of informed consent as stipulated in the U.S. regulations must be modified. These procedures should be sufficiently flexible to be adapted for use in various developing countries. The requirements of written consent and the participant’s signature, mark, or thumbprint on consent forms are procedures that ethics review committees should be allowed to waive when researchers provide adequate justification for such waivers.
Every competent adult should be able to decide freely whether to participate in research, a position adopted in previous NBAC reports (NBAC 1998; NBAC 1999). Those who wish to cede that decision to another should be able to do so, but the initial choice is still theirs. Often, personal and local circumstances complicate this choice, and many obstacles remain to achieving an ideal process. Nevertheless, adherence to a country’s customs and traditions need not compromise the ethical standard of informed consent. In some circumstances, researchers should have greater flexibility in determining how they inform participants about the research and in the methods they use to document consent. In addition, potential participants may wish to involve family members in their decision to participate, and researchers may need to obtain a community leader’s permission before approaching individuals in the recruitment process. NBAC believes that these recommendations represent only the first steps toward eventually reaching a point at which every competent individual, based on adequate information, can voluntarily make his or her own decision about participating in research.

Notes

1 The material in this chapter benefited from reports prepared by several NBAC consultants, articles published in the literature, and two unpublished studies provided to NBAC by researchers from South America (Hardy et al. 1998; Sánchez et al. 1998). The consultants’ reports are as follows: Kass, N., and A. Hyder, “Attitudes and Experiences of U.S. and Developing Country Investigators Regarding U.S. Human Subjects Regulations,” Marshall, P., “The Relevance of Culture for Informed Consent in U.S.- Funded International Health Research,” and Sugarman, J., B. Popkin, F. Fortney, and R. Rivera, “International Perspectives on Protecting Human Research Subjects.” These background papers were prepared for NBAC and are available in Volume II of this report.

2 We acknowledge that the principle of respect for persons also permits the foregoing of voluntary informed consent in certain situations, such as research involving those who lack the capacity to give consent, research involving only minimal risk, or emergency research. These areas pose their own unique issues, which will not be addressed in this report.

3 See Kass and Hyder; Marshall; and Sugarman et al.

4 See Sugarman et al., 10.


6 See Marshall, 18.


8 See Sugarman et al., 17.

9 See Kass and Hyder.

10 See Marshall, 34.


12 See Kass and Hyder, 6.

13 See Marshall, 17.


15 Ibid., 32.

16 See Marshall, 15.


19 See Kass and Hyder.


21 See Kass and Hyder, 43.


23 See Marshall, 34.

24 Ibid., 22.


27 See Kass and Hyder, 43.

28 Sugarman and colleagues state that “investigators in one country repeatedly noted that patients who might be asked to enroll in a medical study would be skeptical of an investigator who did not involve the family in the decision making process.” See Sugarman et al., 9.
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29 See Marshall, 28.


33 See Kass and Hyde, 56.

34 Ibid., 57.

35 This same principle is implicit in 45 CFR 46.111(a)(1), stating that in reviewing research, IRBs must determine that risks to subjects are minimized.

36 See Kass and Hyde, 41.

37 Ibid.

38 See Sugarman et al., 11.


42 See Marshall, 24.

43 Ibid., 26.

References


National Bioethics Advisory Commission


