ABSTRACT: The ethical conduct of community-engaged research (CEnR), of which the Community-Based Participatory Research (CBPR) model is the partnership model most widely discussed in the CEnR literature and is the primary model we draw upon in this discussion, requires an integrated and comprehensive human subjects protection (HSP) program that addresses the additional concerns salient to CEnR where members of a community are both research partners and participants. As delineated in the federal regulations, the backbone of a HSP program is the fulfillment of nine functions: (1) minimize risks; (2) reasonable benefit-risk ratio; (3) fair subject selection; (4) adequate monitoring; (5) informed consent; (6) privacy and confidentiality; (7) conflicts of interest; (8) address vulnerabilities; and (9) HSP training. The federal regulations, however, do not consider the risks and harms that may occur to groups, and these risks have not traditionally been included in the benefit: risk analysis nor have they been incorporated into an HSP framework. We explore additional HSP issues raised by CEnR within these nine ethical functions. Various entities exist that can provide HSP—the investigator, the Institutional Review Board, the Conflict of Interest Committee, the Research Ethics Consultation program, the Research Subject Advocacy program, the Data and Safety Monitoring Plan, and the Community Advisory Board. Protection is best achieved if these entities are coordinated to ensure that no gaps exist, to minimize unnecessary redundancy, and to provide checks and balances between the different entities of HSP and the nine functions that they must realize. The document is structured to provide a “points-to-consider” roadmap for HSP entities to help them adequately address the nine key functions necessary to provide adequate protection of individuals and communities in CEnR.

KEY WORDS: human subjects protections; risks; informed consent; justice; data safety monitoring plan; conflicts of interest; subject selection; community-engaged research; community-based participatory research

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The new United States National Institutes of Health/National Center for Research Resources (NIH/NCRR) Clinical and Translational Science Award (CTSA) infrastructure for academic medical centers presents a valuable opportunity to broaden the more traditional biomedical focus on individual human subject protections (HSP) and develop an integrated and comprehensive HSP program that addresses the additional concerns salient to community-engaged research (CEnR) where members of a community are both research partners and participants. We draw on the Community-Based Participatory Research (CBPR) model as the partnership model most widely discussed in the CEnR literature to serve as the primary model for analysis because of its emphasis on collaboration at all stages of the research process.

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The backbone of an HSP program is the fulfillment of nine functions that are delineated in the federal regulations (Department of Health and Human Services, 2005):

1. The risks of the research are minimized;
2. The risks to subjects are reasonable in relation to anticipated benefits;
3. The selection of subjects is fair;
4. Each participant gives a voluntary and informed consent;
5. When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects;
6. There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data;
7. Conflicts of interest are transparent and appropriately managed;
8. Consideration is given to what additional protections, if any, are needed for vulnerable populations; and
9. Proper training in human subjects protections is provided for research personnel.

The federal regulations, however, do not consider the risks and benefits that may occur to groups, and these risks have not traditionally been included in the benefit-risk analysis nor have they been incorporated into an HSP framework. In our accompanying article entitled “Human Subjects Protections in Community-engaged Research: A Research Ethics Framework” (this issue), we examined risks under three categories: risks due to process (participation in the research); risks due to outcomes; and risks to agency (the autonomy and authority to make decisions). We considered these risks from the perspective of the individual participant (A-level risks) the traditional focus in clinical research), and from the perspective of the groups to which the individual belongs. Individuals belong to many unstructured groups on the basis of shared traits including geography, race/ethnicity, shared culture, language, health care needs, economic status, alumni status, common social interests, religion, culture, sports affiliation, or a combination of several factors. Individuals may also belong to structured groups (communities) with their own leadership and decision-making capacity (e.g., one can belong to the religious Methodist group, but belong to a particular Methodist Church community). There are research risks to individuals as members of groups, whether structured or unstructured (B-level risks). When a community engages as a research partner, however, there are also risks to the community itself (C-level risks). Whereas C-level risks are unique to structured groups or communities with a defined organizational structure and leadership, B-level risks occur at the intersection between the individual and the group in which he or she is a member. B-level risks may occur to an individual if the group participates in research, even if he or she does not. B-level risks may also occur to non-participating group members groups if individuals participate and the results are extrapolated to the whole group. The analysis of these risks led to the creation of a $3 \times 3$ grid that is reprinted in Table 1 (and explained in detail in the accompanying article).

Using this expanded conception of risk, we reframe the discussion of the nine key functions to account for the additional types of risks and harms that may arise from research partnerships, to both the individuals who participate and the groups in which they are members.

There are seven distinct entities or mechanisms that can provide HSP: (1) the individual investigator(s); (2) Institutional Review Board (IRB); (3) Conflicts of Interest Committee (COIC); (4) Research Ethics Consultation (REC) program; (5) Research Subject Advocacy (RSA) program; (6) Data Safety Monitoring Plan (DSMP) for all research, and a Data Safety Monitoring Committee (DSMC) when constituted; and (7) Community Advisory

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<th>Table 1. Risks to Well-Being and Agency at the Individual and Group Level.</th>
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<td><strong>Process Risks to Well-Being (1)</strong></td>
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Boards (CABs), when constituted. Only three of these components are mandated in the federal regulations (the responsibilities of the individual investigator, the structure and functions of the IRB, and the formulation of a DSMP), and not all CTSA programs currently employ all seven mechanisms. We begin by exploring the seven mechanisms below, although our main focus is on how an integrated HSP program addresses the nine key functions to provide adequate protection of individuals and communities who engage in CEnR. We provide key questions that an integrated and comprehensive HSP program should consider to ensure adequate consideration of each of the nine responsibilities.

**Method**

A seven-member writing team convened to develop a framework for providing HSP in CEnR. The team consisted of one academic researcher and one community research partner; four with specialization in human subjects protections with three who self-identify as ethicists and one in research subject advocacy; and one research associate with interest in HSP.

Through iterative collaboration, the writing group developed a taxonomy and framework for the risks presented by CEnR. Implications were explored, and appropriate safeguards discussed. Two stakeholder meetings were held with numerous academic researchers, community research partners, community activists and other HSP program personnel. At the first meeting, 6 additional academic researchers involved in CEnR were invited, as were 10 community research partners/community activists, and 8 persons engaged in HSP. The stakeholders were asked to give presentations about the process of CEnR from the perspectives of the academic research partner and the community research partner, respectively. Some were asked to describe the benefits, burdens, incentives, and obstacles that those involved in CEnR face, while others were asked to discuss specific ethical challenges that arise when doing research with communities that are both partners and participants. There were both large group and small group break-out sessions to give all attendees a chance to express themselves. Following this meeting, the writing team developed a taxonomy of risk, with a particular focus of exploring the breadth of risks faced by disparate groups. At the second stakeholder meeting, the writing group (minus the RSA) met with 5 additional academic researchers involved in CEnR, 7 community research partners/community activists and 7 HSP experts to seek feedback on the ethical framework and supplemental documents developed to serve community-academic partners and HSP program personnel respectively. While there was much overlap in the participants who attended the first and second meetings, we intentionally made some changes to increase the diversity of viewpoints. All stakeholders at the second meeting were asked to comment on written drafts and most were asked to give oral presentations regarding strengths and weaknesses of the three documents.

**Entities that Provide Human Subjects Protections in CEnR**

*The Individual Investigator(s)*

Traditionally it is the conscientious and respectful investigator who has primary responsibility for ensuring the realization of all of the nine HSP functions delineated above. However, there are data to show that even conscientious investigators may not appreciate the full range of potential harms to which they expose participants of research (Pappworth, 1967), nor appreciate how personal and professional conflicts of interest (COI) may threaten their ability to protect human subjects. Other HSP entities are designed to complement the individual investigators to provide a comprehensive HSP program.

To ensure adequate protection in CEnR, academic investigators and their community research partners need to be educated not only about traditional HSP requirements but also to be sensitized and educated about the previously under-appreciated group risks and issues of group agency encountered in CEnR. These concerns at the level of the group may require new HSP strategies and additional resources to ensure adequate protections. The federally mandated requirement that all researchers receive some training in HSP and scientific integrity provides an incentive to develop an HSP curriculum enhanced to address the additional risks in CEnR. The importance of this educational opportunity cannot be understated because in CEnR the investigators (both academic researchers and community partners) share the primary responsibility for ensuring the ethical integrity of the research. Standard HSP training may need to be modified in how it is presented to be useful and comprehensible for community research partners, some of whom may have limited knowledge of medical terminology and traditional HSP language.

*The Institutional Review Board (IRB)*

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission) was established in 1974 in the
aftermath of various abuses of human subjects in the US and internationally (Levine, 1986). The federal regulations for the protection of human subjects, based on the National Commission’s reports, were first promulgated in 1981, and remain in effect with slight modifications over the years (Department of Health and Human Services, 1981; revised 2009). The federal regulations require the review of all federally funded research by an institutional review board (IRB). Although the structure and functions of IRBs have been interpreted within the framework of more traditional research and a focus on individual rights and welfare, the federal regulations offer enough latitude to accommodate some of the additional concerns raised by CEnR. These concerns include the psychological and social harms that are more typical of behavioral and social science research. The structure also allows for a greater role of community representatives than currently serve on IRBs (Dresser, 2001). However, the IRB is constrained with respect to some of the ethical considerations raised by CEnR because the federal regulations require that “the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research)” (Department of Health and Human Services, 2009). The federal regulations also state: “The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility” (Department of Health and Human Services, 2009). This is not to suggest that these concerns are not legitimate, only that they are not within the purview of the IRB. Rather, it may be that another HSP entity such as the RSA program or CAB that may be a better entity to consider these group risks (see below).

**Conflict of Interest Committee (COIC)**

While IRBs have an oversight role with regard to the financial conflicts of interest (COI) of the research, many academic institutions have established distinct conflicts of interest committees (COIC) “to provide a somewhat independent review of financial interest in research and to suggest appropriate management strategies, including what should be disclosed to potential research participants” (Weinfurt et al., 2006, p. 582). At some institutions, both the IRB and the COIC investigate COI, whereas at other institutions, one or the other committee has sole responsibility (Dinan et al., 2006). While there may be some overlap between IRBs and COIC in function and membership, there is also diversity in responsibilities and authority. In the past decade, both the Association of American Universities (AAU) and the Association of American Medical Colleges (AAMC) have published guidelines for oversight of individual and institutional financial conflicts of interest (the Association of American Universities, 2001; Association of American Medical Colleges, 2002). Neither organization requires a COIC, but they do recommend a written COI policy with a focus on disclosure, management, and in certain circumstances the prohibition of research at a particular institution or the performance of such research by a particular researcher. While communities as research partners may also have conflicts of interest, to-date there is no literature about COI policies within community organizations.

**Research Ethics Consultation (REC) Program**

Research ethics consultation (REC) involves a collaboration between investigators and research ethicists in the design and implementation of a research project that poses novel or complex ethical issues in HSP. REC was first described in the literature in 1989 when a surgical team consulted with an ethics team to develop a protocol to remove part of a parent’s liver that would serve as a graft for a child with liver failure (Singer et al., 1990). In the two decades since this initial description, while clinical ethics committees and clinical consultation services proliferated, research ethics consultation services were provided informally and rarely discussed in the literature. Since the establishment of CTSAs, the number of REC programs has expanded and REC is integrated within the Clinical Research Ethics Key Function Committee of the National CTSA program (Beskow et al., 2009). In the CEnR context, the REC could easily adopt its strategies to work with community partners and address ethical concerns raised by the participation of the community as partner and participant in the research. However, it is not a mandatory component of CTSA programs and not all CTSA programs provide this service.

**Research Subject Advocacy (RSA) Program**

Following several highly-publicized cases of HSP violations, including the Jesse Gelsinger tragedy (Ciment, 2000), the RSA program was established by the NIH in 2001 as an additional resource for HSP at NIH-funded General Clinical Research Centers (GCRCs) (National Center for Research Resources, 2001). Initial areas of key focus were (1) the development of data and safety monitoring plans
including the reporting and tracking of adverse events; (2) assurance of compliance with regulatory obligations; and (3) interactions with research participants to assess informed consent process and comprehension. With the move from the GCRC to the CTSA, the emphasis has moved from an RSA (individual) per se, to a group of research subject advocacy functions endorsed by the CTSA consortium as part of a comprehensive HSP. The emphasis has also moved from an exclusive focus on bench to bedside research to a shift within the CTSA to include more translational research that moves the research from the bedside into the community. Some centers maintain the RSA program solely for its role in research performed within their clinical research center while others have expanded the scope of the RSA to include outreach and monitoring in CEnR, and still others have dismantled their RSA program, incorporating the RSA functions into the responsibilities of other HSP entities.

Data Safety Monitoring Plan (DSMP)

The federal regulations require, when appropriate, the constitution of a Data Safety Monitoring Plan (DSMP) as another potential source of HSP (National Institutes of Health, 1998; NIH Clinical Trials Committee, 1979). Such plans can be quite variable in structure, depending on the risks and specifics of the research, but they force the investigator(s) to consider potential unanticipated results and to develop a plan for how to address them.

A DSMP should outline how adverse events will be addressed, when review and possible modification of the methodology may be required, and when, if ever, interim data will be examined. A DSMP should also outline the circumstances in which the research project might be halted: if an alternative treatment is shown to be so much better that the risks in the project (or in one or more arms of the project) are no longer justified; or if adverse effects dictate that the risks in proceeding with the research have become overwhelming.

The constitution of a Data Safety Monitoring Committee (DSMC) as part of the DSMP is usually reserved for studies in which the endpoints are morbidity and mortality, which involve blinding of researchers to the intervention, or involve multiple academic centers. Such studies often involve clinical trials of new drugs or devices. A more informal monitoring plan is acceptable for low-risk research. Most CEnR does not require a formal DSMC because most CEnR employs a broad range of low-risk interventions including social, behavioral and environmental modifications with only a subset including any invasive biomedical interventions. However, even for research that does not pose serious clinical risks, the DSMP serves to ensure that the rights of all parties are being respected and that the research has not created unanticipated harms.

Involving the community partner in the development and oversight of the DSMP could have multiple benefits, including an evaluation of particular risks in the community's cultural context and ensuring that decisions to continue or suspend research are based in part on the cultural values of the community with which, and in which, the research occurs.

The federal regulations deliberately provide sufficient flexibility for institutions to form DSMPs according to the scope of research efforts (National Institutes of Health, 1998). Thus in light of the physical and social risks that may emerge over the course of a CEnR project (A-1, A-2, B-1 and B-2 risks), the DSMP can be incorporated into a memorandum of understanding (MOU) between the academic researchers and the community research partners so that there is a way for the community to protect itself and its members. However, even with an MOU, some unforeseen risks may present. The DSMP should include periodic review so that emerging risks are examined and a decision can be made whether or not to continue the project, and whether or not to revise the consent form, or even revise the MOU.

Community Advisory Boards

As more communities engage in research partnerships, some have considered how they can promote the protection of their own members. Although the federal regulations require some community membership on an institution's IRB, some communities may criticize the fact that the current sources of HSP emanate solely from the academic institution. In order to equalize responsibility, the community may want its own source of HSP, ranging from oversight by an established political body to the creation of a community-IRB or, less formally, by the creation of a community advisory board (CAB). While one form may fit in a specific community—e.g., the role of the Indian Health Services Institutional Review Board in research on Native American communities—in other communities formal leadership and community representation may be more nebulous and necessitate different accommodations. CABs can serve as a powerful supplement to IRBs and have much greater flexibility than a community-IRB while retaining the ability to ensure culturally sensitive human subjects protections. The CAB may also be an invaluable component of oversight in the DSMP. Its legitimacy may depend upon its ability to be responsive and inclusive of the communities that it represents (Montanaro, 2009).
Generally, CABs are created to develop and enhance collaboration between the academic institution and its community partners and to serve as an oversight board. In some situations the CAB may serve as the research partner, but this creates a COI that lessens its ability to serve as an oversight body for ensuring HSP. Rather, from an HSP perspective, the value is in an independent CAB which can evaluate foreseeable risks and agency concerns for both individual participants and the groups in which they are members. Additionally, the CAB can provide insight into the risks and harms that may accrue to non-participant group members who may experience stigma or other social harms due to group membership. Non-participants are mostly at risk for B-level harms, although the active participation of other group members may also present C-level risks to the communities to which they belong or to other established communities relevant to the CAB. The CAB should consider the larger implications of the research for participants and non-participants, but in general the HSP focus must be on the risks to the participants at both the individual and group level. To the extent that research findings can be presented in ways that do not implicate an entire group but only a subset of the group, the risks to the non-participants may be reduced, although not eliminated.

The CAB may seek to have a continuing role throughout a community-academic research partnership. This role may be minimal (e.g., a request for interim reporting on progress) or it may be more demanding and include authority to review interim data, to monitor participant understanding, or to review research findings before they are reported. What authority the CAB will have during data collection, data analysis, and data dissemination and what role it will play in a DSMP needs to be specified in a MOU. This includes decisions about how to handle unflattering data findings. Once research is done, it is hard to justify vetoing publication based on community concerns; however, community concerns should be taken seriously and may require modifications to the way in which the data are presented and disseminated.

The CAB needs to be informed of all conflicts of interest (COI) and potential conflicts of interest of the individual academic investigators and the academic institution with respect to the research project in order to determine the implications of the COI for the groups that it serves. A CAB may recommend non-participation if there are concerns that the COI, or the appearance of conflict of interest (whether realized or not), poses threats to the community. The CAB should also evaluate whether the DSMP adequately addresses the community concerns that a COI may raise.

Nine Functions to Be Realized by an Effective HSP Program for CEnR

Given the diversity of HSP mechanisms in academic institutions, and the diversity in role-responsibility between similar mechanisms at different institutions, we cannot provide a one-size-fits-all organizational roadmap for coordinating the different entities that provide HSP nor delineate what functions each entity should fulfill. Clearly there needs to be some oversight within the academic institution regarding the various functions or at least significant dialog between the entities. To the extent that HSP is best achieved by involving the community research partners in the fulfillment of these HSP services, a CAB can help inform the various HSP entities within the academic institution about community needs, and delineate what roles it might play to ensure that HSP are provided in a culturally sensitive manner. While different mechanisms can perform most functions, the real crux of a HSP program is the fulfillment of the nine functions that we explore below.

Risks Are Minimized

The first obligation in HSP is to ensure that the research risks are minimized to the individual (A-level), to individuals as members of groups (B-level), and to the community (C-level). Risk assessment must be holistic. In CEnR, risk assessment must include risks to the individual and to the group. When a group participates as a community partner, risks can be minimized by developing an MOU regarding the rights and responsibilities of each party at each stage of the research process to ensure that the community understands and accepts the risks posed to it and its members. Both individual and group risks should be discussed with prospective individual participants so that they can make a voluntary and informed decision about whether to participate. Another way to minimize risks is to enroll adults who can consent for themselves, and only to enroll more vulnerable populations (e.g., children) if necessary (e.g., because the research focuses on a problem that is specifically targeted to address a youth health problem).

Risks are further minimized if all research personnel are provided appropriate HSP training. The CAB can ensure that the training is culturally sensitive and provided in a way that is comprehensible to the community research partners. Risks are also minimized if a DSMP is developed that is appropriate for the risks posed. Depending on the risks, such a plan may be informal (review as necessary by the research personnel) or formal (as in the establishment of a DSMC). The IRB may
have some authority in determining how formal a plan is necessary and whether stopping rules should be objectively defined or can be more loosely determined. Again, this should be done in conjunction with the CAB, if one exists.

**Points to Consider**

- Is the study designed to minimize the risks to the individual participant?
- Is the study designed to minimize the risks to individuals who are members of unstructured groups based on inherited traits like race/ethnicity, gender, or ancestry?
- Is the proposed degree of collaboration, which can introduce B- and C-level risks, appropriate for the potential benefits that the research can produce?
- If there are plans to collaborate with community partner(s), have the community risks been identified and has a management plan been developed?
- If there are plans to enroll members of a community, is the study designed to minimize the risks to the community (as well as the individual participants)?

**Risks Are Reasonable Relative to Benefits**

The second mandate is to evaluate the risks and determine whether the benefit: risk ratio is favorable. The question of whether the risks are reasonable in relationship to the benefits is critical to the IRB. Investigators are obligated to try to identify all foreseeable risks, both to the individual (A-level), to the individual as a member of a group (B-level), and in CEnR, to the group itself (C-level). However, as the risks or vulnerability of the community increases, the IRB may seek additional consultation from other HSP entities or seek advice directly from the community or CAB regarding the risks and benefits. The IRB must then determine whether these risks can be justified by the potential benefits.

In its determination of risks and the benefit: risk ratio posed by CEnR, collaborating investigators should explore the social context in which the research will be performed, to understand potential process risks {B-1} and the social context in which the research results may be interpreted {B-2}. Both B-1 and B-2 type risks must be transparent to the community in the discussions in which partnership rights and responsibilities are delineated. To some extent, the community as a research partner may provide some protection to the community because of its authority to engage or not to engage with particular academic researchers {C-3}. Community partners can enlighten the academic researchers about group risks and benefits that the academic researchers may not perceive or anticipate {B and C level risks}.

Both the likelihood and degree of risk and how these risks are justified by the anticipated benefits of the research must be made clear in order for both the academic researchers and the community partners to develop accurate expectations and a realistic MOU. Other HSP entities can provide complementary review. The CAB can work with the community and with individual members to ensure that the benefit: risk ratio is acceptable for the community as a group and for potential individual participants. By engaging the community throughout the research project, emerging unanticipated risks can be identified and incorporated into a revised benefit: risk calculation. As another check, the IRB should query investigators during continuing review about newly emerging or intensifying risks over the course of research. If the emerging risks are significant, the investigators may need to revise the informed consent forms and process. Depending on the expectation of emergent risks in the CEnR project, the IRB may require formal review more frequently than the typical annual review.

The meaning and frequency of anticipated risks may also change during the course of the research. In clinical trials, a DSMC may decide that the degree of risk has become too great or that the relative risk of one arm is too great, and may decide to stop the research. Even in research in which a DSMC is not constituted, the DSMP should delineate who will monitor the risks and how an evolving understanding of the risks will be monitored and reported. Such review may lead to requests to modify the consent form and process, greater consent monitoring to ensure adequate participant understanding, or even consideration of early termination.

Groups may participate in research to promote the traditional goals of research: the advancement of scientific knowledge and/or improved health care. In addition to these traditional benefits, benefits may also accrue to the community in CEnR in terms of job opportunity, empowerment, access to services, and collaboration in a research endeavor. While IRBs cannot consider these additional benefits, communities may include them in determining whether the benefit: risk ratio justifies community endorsement of, and participation in, the project. An independent CAB can help ensure that the terms of agreement between the academic researcher and community research partners consider short-term and long-term benefits and what obligations the academic institution may have to ensure that the benefits accrued can be maintained, even after research funding expires.
POI NTS TO CONSIDER
• What are the risks to individual members as individuals and as members of communities?
• What are the risks to participating communities?
• What are the expected benefits to the individual (A-level), to the individual by association to the group (B-level) or to the group as a whole (C-level)?
• Is the benefit: risk ratio favorable for the individual? For the community?
• Are there ways to increase the benefit: risk ratio?
• Is there a DSMP that provides for appropriate monitoring of the risks and the benefit: risk ratio?
• Do the academic researchers have an obligation to ensure that the benefits accrued during the research can be maintained, even after research funding expires?

Fair Selection of Subjects

The third requirement is the fair selection of subjects. Traditionally the focus has been to ensure that the risks of research are shared by all who can be expected to benefit. Data show that disparities exist even at the stage of who is invited to participate (Baquet et al., 2008; Shavers-Hornaday et al., 1997). The question of fair subject selection in CEnR is about both (1) whether the members of the partnering community are appropriate participants in the research; and (2) how participants within that community are selected. While IRBs are mandated to evaluate fairness in subject selection, the question should also be examined by the community research partner, and when constituted, with consultation from the CAB. The community research partner should also help to ensure that the recruitment strategy promotes a fair selection of subjects within the community. Research personnel, whether academic employees or community research partners, should be trained in HSP to ensure that there is neither undue influence nor coercion in recruitment practices and that they respect the potential individual participant’s right to decline enrollment. Recruitment should be equitable in providing unbiased access to enrollment for eligible individuals as well as exclusion or accommodation of vulnerable subjects as deemed appropriate by the research partners, the IRB and the CAB. The decision to include vulnerable subjects should be based in part on whether there are special benefits that can only accrue to those who participate.

POI NTS TO CONSIDER
• Is the population from which the research participants are selected the same population that can be expected to benefit from the research?
• Are the community members appropriate subjects of investigation for the project?
• Who will recruit potential participants? How will undue influence, favor, or exclusion be avoided?

Consent Is Informed and Voluntary

The fourth requirement focuses on the need for a voluntary and informed consent. In traditional research, the voluntary and informed consent of the individual participant is needed [A-3] and the focus was on risks and benefits to individuals [A-1 and A-2]. An adequate consent in CEnR must explore the risks and benefits of the research for the individuals and the community, an explanation of the alternatives to participation, an explanation that the participant has the right to refuse to participate, and that if the participant consents to participate, the participant retains the right to withdraw without affecting his relationship with the community or the academic medical center where he or she may receive medical care. While the IRB has the responsibility to affirm that the consent form includes all of the elements of consent delineated in the federal regulations (45CFR46.116), there are no formal requirements to monitor the consent process to ensure that these components are included in the consent conversations. Clearly, those involved in recruitment should receive appropriate HSP training about both the elements of consent that need to be addressed with potential participants, and how to engage potential participants in a robust consent process.

In CEnR, the partnership can be understood as community consent or more properly, community endorsement of participation by community members. Community endorsement, however, does not obviate the need for individual consent. Awareness that the community has agreed to participate may influence the participation of individual community members and may create tension about the freedom of individuals not to participate [B-3]. For instance, when community members are hired to recruit research participants, individual community members may feel some degree of pressure to participate [B-3]. It is critical that the recruiters are well trained in HSP and the importance of the voluntariness of research participation. In addition, the whole research team must provide opportunities for potential participants to excuse themselves, with minimal social effect, from specific components of the research study or from the whole research project. The IRB can require that all research personnel complete some type of HSP training, and the investigators or CAB may require additional training to ensure cultural competency and
appropriate engagement of potential participants by research personnel.

**Points to Consider**
- Have the risks and benefits been made transparent to the potential participants as individuals and as a group?
- Do the individual members understand that their individual consent is necessary and that their participation is voluntary?
- Do the individual members understand that they can withdraw at any time from the research without affecting their community membership or their right to seek care at the academic institution?
- How will group decisions be made by the community? If made by community representatives, can the community representatives be expected to be inclusive and responsive?
- Have the recruiters had adequate HSP training to understand that potential participants must give a voluntary consent and that their right to refuse should be respected?
- What type of monitoring, if any, will occur in the consent process?

*Data Monitoring*

The fifth requirement focuses on data monitoring. In the broadest sense, there should be a DSMP for all research. In general, the research performed in CEnR has less clinically significant endpoints than morbidity or mortality, and therefore rarely requires the constitution of a formal DSMC. However, even for research without such clear markers, a DSMP serves to ensure that the rights of all parties are being respected and that the research has not created unanticipated harms. In CEnR, new concerns may arise about privacy and confidentiality with respect to data storage and future use, and should be clarified in an MOU before data are collected. The IRB must ensure that due consideration has been given to research personnel training in research methodology and human subjects protections, and that there are adequate safeguards with respect to data storage and access.

Certificates of confidentiality [COC] are sometimes obtained to permit researchers to collect data that, “if disclosed could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation” (Department of Health and Human Services, 2000). The CAB may also seek to play a role in data monitoring. This role may be minimal (e.g., a request for interim reporting on progress), or it may include authority to review interim data, to monitor participant understanding, or to review research findings before they are reported. What authority the CAB will have during data collection, data analysis and data dissemination needs to be specified in a MOU. To what extent the CAB will have access to data or to have authority regarding the DSMP should be negotiated before the research begins.

**Points to Consider**
- Who is responsible for ensuring data monitoring?
- Who is responsible for reporting adverse events?
- Who will monitor emerging social risks to individuals and community structures?
- How will the researchers respond to adverse events?
- When are specific stopping rules needed?
- Who should be able to halt research, even if temporarily, if data monitoring suggests unexpected risks, adverse events, or breaches of privacy and confidentiality?

*Privacy of Subjects and Confidentiality of Data*

The sixth criterion focuses on the need to protect the privacy of participants and to maintain the confidentiality of data. This may be more complicated when the community is a partner with respect to data storage and future use, and should be clarified in an MOU before data are collected. The IRB must ensure that due consideration has been given to research personnel training in research methodology and human subjects protections, and that there are adequate safeguards with respect to data storage and access.
Conflicts of Interest

A conflict of interest (COI) occurs when a primary interest (e.g., validity of research) is unduly influenced by a secondary interest (e.g., financial gain, academic success, community leadership) (Thompson, 1993). While secondary interests are legitimate, the problem arises when the importance of the secondary interests become so great or appear to be so great as to threaten the primary interest. Several policy changes in the past two decades have expanded the potential for COI of academic researchers and their institutions. First was the passage of the Bayh-Dohl Act in 1980, which sought to stimulate translation by permitting institutions and investigators to own patents resulting from federally funded research. Second is the growth of industry funding in biomedical research. Whereas federally funding was the primary source of research dollars in the decades following WWII, today, approximately 60% of research funding comes from industry sources (Moses et al., 2005).

Conflicts of interest are common, and most COI policies and/or COI committees focus on transparency regarding the severity of risk that COI may pose, and on devising appropriate management plans. All conflicts and potential conflicts must be disclosed to the IRB or some other institutional agency (e.g., COI Committee) that can provide appropriate oversight. The appropriate management plan for a research study will depend on the severity of risk that the research poses as well as the severity of risks that the COI may pose. If the severity of risk from the research and the COI is negligible, one may depend upon the researchers’ integrity alone and require a mere disclosure of COI. However, in general, there needs to be some oversight and the IRB should insist upon a plan. In cases where the COI may be or may appear to be significant, the IRB may request that particular investigator(s) not participate in the conduct of the research itself. More frequently, the IRB may request that a DSMC be constituted, and that specific stopping rules be agreed upon before the research begins.

While the traditional focus on COI was on the individual investigator’s COI and relative inattention was paid to the potential for an institutional conflict of interest, today institutional COI may be quite significant (Slaughter, Feldman, & Thomas, 2009). An institutional COI arises “when health care institutions have a financial stake in the research conducted in their laboratories and clinics” (Emanuel & Steiner, 1995, p. 262). Two major categories of such conflicts are: “(1) potential conflicts involving university equity holdings or royalty arrangements and research programs, and (2) potential conflicts involving officials who make decisions with institution-wide implications” (Association of American Universities Task Force on Research Accountability, 2001, p. 10). Between 1998 and 2008, over 1.75 million patents were granted, 37,467 of which were granted to U.S. universities (National Science Foundation, 2010). In 2005, 24 universities reported earning more than $10 million from licensing income; a few earning over $100 million (Association of University Technology Managers, 2006). The Association of American Universities Task Force on Research Accountability recommends disclosure and management of most conflicts at both the individual and institutional level, but also acknowledged that there may be circumstances where an activity must be avoided to protect the public interest or the interest of the university. Clearly best practices include transparency; separation of functions and duties; and the appointment of an external institutional COI committee if certain triggers are present (e.g., university ownership of intellectual property or investment in areas in which the institution is running clinical trials or otherwise involving human subjects) (Slaughter, Feldman, & Thomas, 2009).

When the community is a research partner, the community must be aware of all individual and institutional COI that may influence the academic researcher or the
academic institution. A community research partner may decide not to participate if there are concerns that the appearance of conflict of interest (whether realized or not) poses threats to its agency {C-3}. The academic researcher and the community research partners should be involved in developing a DSMP that adequately addresses the concerns that the community may have. A CAB may also want input in both the development of the plan and in compliance oversight. There should be an oversight plan to ensure compliance with the DSMP.

Conflicts of interest may also exist within the community or between the community and the community leadership or a community-based organization (CBO) that represents it, as well as within the research–community partnership. It is critical that there is some oversight so that community members are not exposed to undue pressure to participate and that their participation serves their own interests. A CAB may be best suited for this type of oversight.

**POI NTS TO CONSIDER**

- What are the primary and secondary interests of the academic investigator?
- What are the secondary interests of the community research partner or the organization (e.g., CBO) that represents the community?
- Does the academic institution have a financial conflict of interest with respect to the proposed research?
- Do individual community members or the community itself have a conflict of interest with respect to the proposed research?
- Who is responsible for disclosing the various conflicts of interest (academic researcher, academic institution, community research partner, community)?
- Who is responsible for managing the various conflicts of interest and/or determining the adequacy of COI management plans?
- When is a conflict of interest so great that the research should not go forward?

**Vulnerable Populations**

Vulnerable individuals such as “children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons” deserve special consideration in all research engagements (Department of Health and Human Services, 2009). Given the focus of CEnR on health care disparities, many of the participants and the groups to which they belong may be vulnerable. It is important to ensure that vulnerable populations and individuals are the appropriate research subjects; that research benefits and risks are fairly distributed, especially within vulnerable communities; and that adequate safeguards are in place that promote voluntary participation for all eligible participants.

When the research seeks to enroll vulnerable individuals, the IRB must assess whether additional safeguards are needed. For research involving a group that is vulnerable by virtue of its lack of structure, a CBO or other advocacy group may provide the structure for the group’s participation. One requirement may be to ensure that the community partner is being inclusive and responsive to the needs of the group {B-3} (Montanaro, 2009). This can be achieved by asking the academic researchers to have an open meeting and allow interested community members to participate or, if the research raises significant risks, to seek input directly from the community through town-hall meetings, focus groups, or other public meetings. Given the CAB’s expertise about the community, it would be appropriate to seek input from the CAB regarding whether the CBO or advocacy group is being inclusive and responsive to the needs of the prospective participants, and whether additional safeguards are necessary.

A mandated IRB function is to determine whether it is appropriate for the vulnerable individuals to be recruited as research participants. In general, it is best to recruit those who can consent for themselves and are at lowest risk of undue influence. However, there may be situations in which it is appropriate to recruit vulnerable members of a group; for example, when the research offers significant benefit that may not be available outside of the research setting. When recruitment targets vulnerable individuals, there should be adequate HSP training and consent monitoring to ensure a robust consent process so that the vulnerable individuals, or the surrogates who represent them, understand that participation is voluntary and that they can withdraw at any time.

**POI NTS TO CONSIDER**

- Does the community partner adequately represent all of its community members? In particular, does the community partner adequately represent its vulnerable members?
- Is it appropriate to enroll vulnerable populations? That is, does the research address a problem that is particular to the vulnerable population or does the research offer significant benefit that may not be available outside of the research setting?

**Proper Training of Research Personnel**

The IRB requires that all research personnel receive training in HSP. It can and should also require such training...
for its own members and for other HSP entities. The responsibility of providing such training, however, need not be solely within the purview of the IRB. Other HSP entities may have responsibility for training (or at least for developing appropriate training tools) and for ensuring ongoing compliance with human subjects protections.

When the community is a partner, it is critical that culturally sensitive training exists and that the training does not assume extensive biomedical research knowledge or biomedical terminology. Consultation with the CAB, if it exists, may help ensure that the training is being offered in a way that the community partners can be expected to understand. Ideally, a training manual would be developed in conjunction with the CAB, and training could be provided by community members trained to serve as community trainers. Plans for ongoing training should be provided as the research moves from one stage to another.

Often communities may wish to undertake recruitment and data collection responsibilities both to contribute to the research partnership and to provide employment to some persons as a benefit of the collaboration. Community members trained as research assistants can be quite effective (Brugge et al., 2009). However, some researchers may see this as role confusion or as posing unnecessary risks to privacy and confidentiality for research participants. Thus employment of participating community members as recruiters or data collectors will not occur in all partnerships. When community members serve as recruiters or data collectors, it is important that there is ongoing oversight to ensure ongoing compliance with HSP requirements.

HSP training should address the risks that may accrue due to the fact that the community is a research partner. These risks include concerns about privacy and confidentiality both in data collection and storage as well as risks to the community as a community because of its participation or because of the data findings. There are also threats to agency: threats that individual community members may feel pressured to participate and threats to the community as a structured entity if the academic partners do not respect the community’s self-governance and decision making authority.

**POINTS TO CONSIDER**
- Are the training methods culturally sensitive and comprehensible to the community research partners who may not have prior research experience or familiarity with medical terminology?
- What additional risks need to be incorporated into training of research personnel when the community is a research partner?

**Concluding Thoughts**

Risks to research participants can be focused at the level of the individual, of the individual as a member of a group, or at the level of the group. These risks include process, outcome and agency risks, risks that may be dynamic over the course of a partnership. To ensure that the rights and safety of all subjects are promoted, and that the benefit: risk ratio is favorable, a variety of HSP mechanisms exist. Protection is best achieved if these mechanisms are coordinated. While some overlap is to be expected and may even be desirable, coordination can serve to minimize unnecessary redundancy, ensure that no gaps exist, and to provide checks and balances between the different sources of HSP and the nine functions that they must realize.

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References


