Institutional Review Boards

Everything community cancer centers need to know

by Kathleen M. Neill, DNSc, RN

Over the past decade, many clinical research studies have moved from traditional academic healthcare centers to primary healthcare settings. During this time, the percentage of clinical trials in the academic setting has dropped from 80 percent to 44 percent.[1] While community cancer centers have been conducting cutting-edge clinical cancer trials for many years, these practice-based research centers often encounter unique issues meeting the regulatory requirements for the review and the protection of human subjects.[2] Challenges include: 1) ensuring compliance with federal regulations across practice sites, 2) assuring privacy and confidentiality of records, especially electronic records, and 3) special recruitment and consent issues.

Institutional Review Boards: 101

An institutional review board (IRB) is formally defined as the administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the institution with which it is affiliated.[3] Under this definition, "research" is considered to be any systematic investigation designed to develop or contribute to generalizable knowledge from data or identifiable private information through an intervention or interaction with a human subject. The IRB's primary charge is two-fold: review whether the benefits of the proposed research project outweigh the risks to the potential subject and make certain that investigators have explained all the relevant issues so as to secure the subjects' informed consent.

IRBs must have a minimum of five members. These individuals should be of varying backgrounds with sufficient experience, expertise, and diversity of racial and cultural heritages, as well as sensitivity to community attitudes. IRB members should also have knowledge of institutional commitments and regulations, applicable law, and professional conduct. At least one IRB member should have a scientific background, one member should come with a non-science background, and one member should have no connection to the institution or not be closely related to anyone who is connected with the institution. Both genders must be represented in the IRB.

A 2002 survey of IRB administrators in the United States revealed the following picture.[4] IRBs were understaffed, with an average of 1.8 fulltime staff persons (Range = 0 to 20). Approximately 77 percent of respondents indicated that a professional ethicist was not part of their committee. The average number of IRB members was 13 with the majority of members being scientists. The study authors concluded that IRBs needed more non-affiliated and non-scientist members since such lay members have demonstrated an ability to improve readability of consent forms and explanations of risks and benefits.[5]

Traditionally, local IRBs are the predominant type of IRB found in the United States. The average review time of a local review is estimated to be 46 to 102 days; however, one study reported a median time of 104.5 days (range 31-346) for a local IRB review.[6]

Partly in an effort to expedite the review process, other IRB configurations have been developed.[7] For example, commercial IRBs are freestanding (not affiliated with a specific institution) commercial committees established to review protocols for compliance with ethical and regulatory standards. Commercial IRBs are often referred to as non-institutional review boards (NIRBs) or independent review boards. These IRBs claim an average review time of 10 to 11 days with a minimum of 5 days at an average cost of $1,300 for a new protocol.[7]

Commercial IRBs claim their reviews are speedy and efficient, their members are experienced, and their customers (hospitals and practices) are satisfied with their services. Commercial IRBs also claim the ability to provide potential subjects with complete information on readable forms. Some commercial IRBs function as part of a contract research organization (CRO); others are supported by the pharmaceutical industry. Proprietary commercial IRBs have a troublesome conflict of interest if they review research sponsored by the company that supports them.

A second alternative IRB configuration is the National Cancer Institute's central IRB mechanism (CIRB), which meets monthly and expedites multi-site studies. CIRB also provides an expert pre-review of NCI-sponsored trials at the national level prior to a local IRB review. CIRB's pre-review mechanism facilitates the local IRB process by avoiding duplication and waste. These pre-reviews can usually be obtained in 5 to 14 hours.[7] The American Academy

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of Pediatrics also has its own national IRB that provides similar services.

IRBs can also function as part of a consortium that is based upon cooperative agreements among several research ethics review boards.[7] Usually, one IRB assumes primary responsibility for review and monitoring on an ongoing basis. Reciprocity within these cooperative IRBs may be broad or more limited. Two examples include the Multicenter Academic Clinical Research Organization (MACRO), an alliance of the University Alabama at Birmingham, the University of Pennsylvania School of Medicine, Vanderbilt, and Washington University School of Medicine; and the Biomedical Research Alliance of New York (BRANY).

A recent study of IRBs in the Veteran Affairs (VA) system showed that the unadjusted average cost per IRB action was significantly related to the volume of actions and whether the actions were initial review, continuing review, review of amendments, or reporting of adverse events.[8, p. 818] "…The cost of operating the IRB was calculated as the sum of 1) personnel costs, 2) space costs, 3) supplies, and 4) education and training costs." The total costs also varied by IRB size, with larger IRBs being more costly. Interestingly, the study found that small IRBs used more institutional resources than large IRBs to complete the same amount of work. The number of actions per year that was the point at which the economies of scale started to level off was 150. The VA study was limited by two factors, however. First, proxy measures were used as outcomes. And second, the study excluded the time IRB members spent reviewing proposals outside of the committee meeting.[9]

The IRB Review

The basic components in an IRB review include: 1) a risk/benefit analysis of the trial design and protocol, 2) an appraisal of the consent form, 3) an evaluation of the procedures for recruitment and selection of subjects, and 4) an examination of the privacy and confidentiality mechanisms.[10] All four components must be present for a complete review. Community cancer centers that consistently

and systematically appraise these basic components will usually obtain a thorough review and a confident approval.

Benefit and risk analysis. The benefit of the research project to the individual subject cannot be overstated. Risks are classified as physical, psychological, social, and economic in nature.[11] Minimal risk has been described as the probability and magnitude of harm or discomfort not greater than that encountered in daily life or in the performance of routine physical and psychological examinations. While some health professionals believe that risk can be estimated by a thoughtful projection of oneself as a potential subject, others argue that IRBs are applying the federal risk standard too cautiously.[12]

Generally, IRBs review "less risky" studies annually, while higher risk studies are reviewed more frequently. For these higher risk trials, data safety and monitoring boards (DSMBs) are established to review data as it comes in at predetermined intervals. After review, DSMBs are required to report their decisions and findings to the IRB.

IRB consent issues. IRBs determine whether eight required elements are included in the consent form (see Table 1).[13] In addition to adequate content, IRBs examine the clarity of language used in the consent forms and the comprehensiveness of documentation. Informed consent as an ongoing process is not measured solely by the printed form and signature. IRBs use other devices, such as consent monitors, videotaping of the signing interaction, post consent interviews and quizzes, subject group discussions, and consent aids (e.g., computer programs) to improve and evaluate the consent process.[14]

Recruitment and selection of subjects. If a potential subject is considered to be "vulnerable," IRBs require an ethical justification for including the individual in research.[15] Vulnerability is defined as a "distinctive precariousness in the condition of the potential subject" that affects an informed, understood, and voluntary consent.[16, p.G-5] In addition to the Federal Common Rule[13] that attributed vulnerability to children, prisoners, fetuses, and pregnant women, additional categories of persons have since been added as vulnerable populations. These categories include persons with mental disabilities and economically or educationally disadvantaged persons. The definition of "vulnerable" can vary from institution to institution. For example, some groups also consider students, employees, and critically or terminally-ill patients to be vulnerable. In Table 2, researcher Kenneth Kipnis describes six types of vulnerability.[16]

Before vulnerable persons may participate in clinical research, four criteria must be met. First, the research could not have been reasonably carried out with less vulnerable subjects. Second, the research project must provide some benefit to the vulnerable group who will then have access

Table 1: IRB Consent Form Determinations

1. Explanation of the purpose of study, including expected duration of a subject's participation, procedures to be followed, and identification of any experimental interventions
2. Foreseeable risks
3. Reasonable benefits to participant or to others
4. Disclosure of alternative treatments
5. Confidentiality procedures
6. Compensation plan if more than minimal risk
7. Contact information in the case of questions or injuries
8. Emphasis on voluntariness of participation.

Barriers to Clinical Trials

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Excerpts from "Improving Clinical Trial Accrual in Community Cancer Centers," a roundtable discussion at ACCC's 22nd National Oncology Economics Conference

Participant 1: I see time as the number one barrier to clinical trial accrual. Some patients don't want to invest the time, and busy clinicians can also have difficulty finding the time to participate in clinical research efforts. You also have the challenges of data management and reimbursement. Our practice does some drug company protocols. We also participate in ECOG and RTOG, which we do through one of the large hospitals in our area. We see patients in our office and do a good amount of the work related to the clinical trial, but only the hospital is reimbursed. Our practice met with the hospital to discuss this issue, but it was a stalemate. The hospital wanted more patients accrued to trials; our practice wanted to be reimbursed for its costs.

Moderator: Doesn't the hospital do all the data management related to the clinical trials?

Participant 1: The hospital does do the data management, but our practice still has to gather and send all the information to the hospital. That's nurse staff time our practice can't really afford to lose.

Moderator: My practice does its data management in-house, and the process is pretty seamless. Plus, I think we accrue patients to trials much better having it all in-house.

Table 2: Six Types of Vulnerability with Regard to Clinical Research Participation

1. Cognitively vulnerable subjects cannot deliberate and decide whether or not to participate in a research study.
2. Juridically vulnerable subjects are under the authority of others who may have an independent interest in that participation.
3. Deferentially vulnerable subjects display deferential behavior that may disguise a reservation about participation.
4. Medically vulnerable subjects have a serious health problem.
5. Allocationally vulnerable subjects lack necessities that will be provided as part of the research project.
6. Infrastructurally vulnerable subjects are involved in a study, which lacks sufficient resources to support the conduct of the study.

SOURCE: Kipnis K. Vulnerability in research subjects: A bioethical taxonomy. In: National Bioethics Advisory Committee. *Ethical and Policy Issues in Research Involving Human Participants, vol. II.* Bethesda, MD. 2001:G-1 – G-13.

to research findings. Third, if an individual vulnerable subject will not benefit from the research, the research must involve only minimal risk for the participant. Finally, proxy consent of a guardian or duly authorized individual must be obtained.

IRBs carefully scrutinize all patient recruitment and selection procedures for every approved study. If more than basic trial information is provided in advertisements and/or on websites, IRBs are also required to review the ads and websites. Basic trial information consists of the title, study purpose, protocol summary, eligibility criteria, study site locations, and contact information.[17]

Recruitment of ethnically diverse and under-represented subjects for research generally involves a more elaborate strategy. These methods may involve media campaigns of various sizes, mailings, involvement of community leaders, one-on-one education, and personal invitations.[18-21] Additional tactics include enhancing access to healthcare for the research population and developing health services within a community after the research is finished.

Privacy and confidentiality. Due to the increased use of electronic health records and electronic medical records (EMRs), privacy and confidentiality of private health information are becoming important concerns for researchers and regulators. IRBs at community cancer centers must carefully examine their method of storing long-term data and ensure that this information is well guarded from non-authorized use. In addition to the trial information itself, IRBs are expected to provide a privacy review of prescreening procedures for trials in which identifiable data is stored.[17] This review requires practice-based researchers to provide increased security measures for data.

In addition to the four factors listed above, IRBs also consider the *ethical justification of the proposed project*. To do so, IRBs review: 1) the competence of the research team, 2) the power of the trial design to detect significant change, 3) the protection plan for vulnerable subjects, and 4) the scheme to monitor safety and compliance, among other criteria. Emanuel and colleagues[22] propose an ethical framework for evaluating research that determines the:

- Social or scientific value of the project
- Scientific validity of the project
- Fairness of subject selection
- Favorability of the risk-benefit ratio
- Presence of an independent review

The research nurses are there. The data people are there. People are put on the trials quickly. Patients don't have to go to three different places to get the necessary paperwork completed.

PARTICIPANT 2: What about the issue of competing trials. How do you pick between a SWOG trial that's got this wonderful science involved but pays nothing, and a competing pharmaceutical trial that is looking to treat the same condition using a drug?

PARTICIPANT 3: One issue that plagues our program is insurance reimbursement. We pre-authorize every patient we put on a clinical trial, but it takes time. How do you help the insurance companies understand the importance of clinical trials? It's hard to just find a person who will look beyond the "script" the insurance companies use.

PARTICIPANT 4: You have to reach the right person. And it's not the assistant; it's usually the medical director or the senior health benefits person.

In Michigan, we were dealing with some of these same barriers. Eventually, we were able to leverage our legislators. We found a "friend" in the state capitol who convened a group that said, "*We're going to mandate coverage of clinical trials unless stakeholders are able to come together and reach a consensus.*" We were lucky to get the right people at the table: the Michigan State Oncology Society, the major Michigan payers, purchasers of healthcare, the automobile industry, and the unions. And these groups came because they were afraid *not* to be there—not because they had a great interest in the science.

But the effort required a great deal of education to challenge the assumptions that payers—and even providers—make. As a provider, I learned about the obligations insurance companies have to their clients (patients and employers), and about some of the futile care they've paid for. In our case, we were able to come to a consensus: clinical trials in Phase II or better would be covered.

MODERATOR: You have to come at payers with a stick—not a carrot. And whether that's done legislatively or through other means, the state medical oncology societies are a great resource. We've had similar issues in Indiana, and were also able to solve them through legislative channels.

- Informed consent process
- Evidence of respect for potential and enrolled subjects.

In order to minimize exploitation, Emmanuel's framework also includes a criterion of collaborative partnership among researchers, health policy makers, and the community.[23]

The Investigator-IRB Partnership

The IRB role as "gatekeeper" for human research participant protection continues to evolve—especially after a number of tragic and fatal mistakes in recent research projects.[3] Community cancer centers and other practice-based research sites are also facing new challenges as they attempt to develop efficient and practical ways to respond to increasing demands in the IRB approval and monitoring processes. While these changes and challenges can add stress to the investigator-IRB partnership, investigators at community cancer centers should view the IRBs careful review of the proposed research project as supportive of investigative efforts. After all, patient safety and welfare is of utmost concern to *both* parties.

One step towards enhancing the working relationship between investigators at community cancer centers and the IRB is for investigators to be more acutely aware of federal regulations and what they expect of investigators—particularly with regards to the protection of human research subjects.[3] For example, investigators are obligated to fully disclose the required elements of the consent form (Table 1) to all potential research subjects.

Today's complex research environment requires a

Physician Buy-in

Excerpts from "Improving Clinical Trial Accrual in Community Cancer Centers," a roundtable discussion at ACCC's 22nd National Economics Conference

Participant 1: Does anyone have any ideas for reaching out and educating referring physicians?

Moderator: Primary physicians are inundated with educational pieces from all sectors: oncology, cardiology, neurology. Our practice holds a quarterly educational meeting for primary care physicians. Usually, it's dinner followed by a talk about a topic relevant to oncology and hematology. But it's difficult even getting physicians to attend.

Participant 2: Our hospital-based clinic invited primary care physicians to a meeting and no one showed up. Our take—primary care physicians rely on oncologists to refer patients to clinical trials.

Participant 1: We don't expect primary physicians to refer patients to clinical trials. We simply want them to be supportive and to provide some buy-in that clinical trials advance cancer care.

Participant 3: Here's something that's created some skepticism in our referring physicians: patients who've been told they're going to get better follow-up if they're put on a clinical trial. There are many reasons to be on a clinical research trial, but getting "better" medical care is not the message we should be sending.

Participant 4: I've had patients told they are going to be followed "more closely" while enrolled in a clinical trial. What my patients are *not* told is that it's the Fellow that's going to see them—rarely the attending [physician]. On nights and weekends, my patients may be seen by house staff.

Participant 1: How do you get the subspecialties—like the surgical subspecialties—to come around?

Participant 2: Our practice distributes brief newsletters throughout the hospital when we have trials open for patient accrual. For example, we've focused heavily on trials for prostate cancer. And guess what? Our practice is starting to see an increase in prostate cancer patients.

Moderator: Our practice goes a step further by holding educational sessions where we ask urologists and medical oncologists to speak as part of a combined program. If the urologist is speaking, physicians are more likely to come and be interested in research-related partnerships. These sessions help make the primary care physicians feel like part of the cancer care team.

Participant 5: Our practice has been very successful with an annual fall "Get-Together." It started out primarily as a venue for our oncologists to discuss clinical guidelines, but evolved into an event where we target about three disease states. We invite referring physicians and surgeons. We usually hold the event at a ski resort, and participants bring their families. Our physicians look forward to the event, and it has enhanced communication between surgeons, referring physicians, and our oncologists.

Moderator: And it's well-attended?

Participant 5: To the point where next year we're looking at offering continuing education units and opening the event to people outside of our state.

Moderator: Perhaps an annual event is better or more convenient than a quarterly or monthly meeting.

Participant 5: Maybe. But within our practice, our physicians meet once a month. And a standing item at that meeting is clinical trials accrual. Each physician is given a sheet outlining how many patients have been screened and how many

multifaceted and interconnected system of protection.[3] Community cancer centers and IRBs *both* benefit from the support of an expanded institutional infrastructure.[1] New institutional roles, such as research subject advocates, are improving human subject protection in many research-intensive settings.[24]

Investigators and IRBs can learn from each other. In fact, Green and colleagues suggest that practice-based research networks maintain, as a critical element of their own infrastructure, "a detailed database of IRB procedures and contact information, a collection of their forms, and at least one person experienced in working with [the IRB]."[25, p. S8] Such an infrastructure could also be helpful to larger research centers and programs. The success of the investigator-IRB partnership is intrinsically linked to the success of the cancer center's research program.

Opportunities and Challenges

Practice-based research centers offer both opportunities and challenges for research and the protection of human subjects. Research programs at community cancer centers operate at the interface between research and quality improvement,[26] facilitating the quick translation of research into practice and providing multiple occasions for clinician learning in an evidence-based context.[27] Multiple sites also support the generalizability of research findings by enrolling sufficient numbers of subjects to power studies.

On the other hand, multiple sites can create a nested design where the site itself becomes part of the research and investigators become subjects whose privacy needs to be protected.[28] A nested design implies that the unique context of each research site is itself a variable that could influence the outcome variables and should be addressed in the

patients were actually accrued to each trial.

Moderator: So we've circled back to physician buy-in. In my 15-physician practice, probably only 7 or 8 physicians actually accrue patients to clinical trial. How do you get the others interested? You mentioned a monthly tally. Does everyone participate?

Participant 5: Our practice has a lead physician who is the president of the group. If we identify a specific problem or trend, he'll go directly to the appropriate physician. Our practice does have small satellite offices that are only open a few days a week, so support can be an issue. But most of our doctors are committed to clinical research.

Participant 6: Physicians have a certain focus in their professional career. Some physicians like to do clinical trials and some don't. But our practice doesn't penalize these physicians.

Participant 7: Generally, what reasons do your physicians give for not participating in clinical trials?

Participant 6: I've been in cancer care for 18 years, and I haven't been able to pinpoint the problem. Two physicians out of five accrue a great number of patients to clinical trials. One physician does a little accrual. The other two physicians just don't have much interest in clinical research trials.

Participant 8: Time is almost always an issue, in addition to the level of physician interest.

Participant 6: One of our physicians is a specialist. So when a sarcoma trial comes up, he's very interested. Otherwise, he's just not. One of our other physicians has a special interest in prostate cancer. So again, if there's a prostate trial, he'll most likely accrue patients. But he has little interest in other clinical trials. I have two new physicians—fresh out of school and still quite interested in research—that may stir the pot.

Participant 8: The principal investigator at our program is getting ready to retire. None of the other partners wants to step up to the plate because of the time involvement. There's been some discussion about offering a financial incentive to the physician who takes on this role. How do others deal with this situation?

Participant 9: We assign different principal investigators to different disease sites—usually their area of interest or their specialty.

Participant 10: Principal investigator can be a difficult position to fill. The individual has to be interested in research—the actual science of the work. I work at an academic center, so all of our researchers are interested in the science of cancer treatment and prevention. We're reaching out to the surrounding communities to help them with patient accrual. Unfortunately, we run into a lot of financial issues. You can't pay to get patients on trials. And practices and some smaller hospital program are lucky if their clinical research program breaks-even.

Participant 8: Throughout most of the year, clinical research is *not* a break-even proposition for my practice because we're not receiving the funds on a regular basis. If we're lucky, at the end of the year we may break-even.

Participant 10: We tell practices that there's not a lot of money in clinical research. Clinical trial participation is *not* going to help your bottom line, but it *will* help advance the science and potentially help your patients. If a practice can focus on those benefits, fine. But if a practice can't afford to participate in clinical trials—for whatever reason—we understand.

Participant 11: Periodically, I have to cut back on new patients because I literally can't do all my schedules and follow-up visits. You want to make commitments to clinical research, but sometimes there are just not enough hours in a day. Our practice could probably accrue a good number of patients to clinical trials—*if* we had the staff and the time. It's called reality. If you've got a physician that really wants to champion clinical research, great! But if you're in a community where you're short on research staff and where you have more cancer patients than you have bodies, it's hard.

analysis plan. Often, clinicians and staff at practice-based research centers require additional training in the protection of human subjects, specifically the differences between treatment and research, informed consent issues, and confidentiality procedures.[28]

The Health Insurance Portability and Accountability Act (HIPAA) requires IRBs to pay special attention to protected health information (PHI) contained in research and health records.[29] Often practice-based research centers face challenges in ensuring the privacy and confidentiality of collected research data. Pace and colleagues[29] suggest five ways to use research data that comply with HIPAA regulations:[25]

1. Patient authorization through a consent process. (However, this traditional process is time consuming and difficult to accomplish after data have been gathered.)
2. Blanket authorization by patients for sharing private information for potential study recruitment.
3. Removal of identifying information and creating "de-identified" data for research purposes.
4. Establishment of data use agreements that limit the type and amount of available data for research purposes.
5. Explicit business agreements that blend quality improvement activities and research. (Business agreements permit a group of credentialed research assistants authority to abstract records across practices when an IRB approves a particular study.)

Today, technology can ease or minimize the challenges of multiple research sites.[30] For example, practice-based research centers now have access to notebook computers, tablet computers, personal digital assistants, and browser-based systems. Whatever electronic tool is selected to collect research data, the tool should ensure complete, accurate, and timely transmission of data—without being overly burdensome to research participants. The choice will usually depend on several factors: who will gather the data, and where the data is gathered, verified, transmitted, and secured. In the IRB application, practice-based research centers must include a detailed description of their privacy protection program.[17]

Probably the biggest challenge to research programs at community cancer centers is the consent form itself. Oncology consent forms are usually long and complicated due to the nature of the treatments themselves. A recent example of a simplified oncology form reduced the consent form from 4,126 words on 11 pages to 1,319 words on 3 pages.[31] For example, the long form stated outcomes as, "…interaction between such things as your lifestyle habits, medication

Recruiting and Retaining Research Staff

Excerpts from "Improving Clinical Trial Accrual in Community Cancer Centers," a roundtable discussion at ACCC's 22nd National Economics Conference

Participant 1: Our practice would love to hire a research nurse so we could get involved in some pharmaceutical trials, but we simply can't find qualified staff. I'm amazed at what our practice has offered and *still* not been able to hire qualified staff. Any suggestions or resources for recruiting qualified research staff?

Moderator: At our practice, it's often an in-house promotion. We've had several OCN-certified nurses who wanted to try something new and different—outside of direct patient care.

Participant 2: Our office contracted with a CRA [clinical research associate] from our local CCOP. She comes to the office and looks at new patient data *prior* to the patient arriving at our office. After she reviews the new patient data, she notifies the physician of anyone who might qualify for a trial before the physician even sees the patient. And our practice has good accrual to clinical trials. Each week, the CRA also spends a few hours with us working on pharmaceutical trials. Maybe one option would be to hire a clinical research coordinator to get your clinical trials program up and going. And you could probably hire a clinical research coordinator for less than a nurse.

Moderator: Our practice had a very skilled research nurse who was hired away by a research company. Pharmaceutical companies hire away qualified staff as well. For others, perhaps the job turns out to be not quite what they were expecting. Certainly, there's some tedium that goes along with research documentation. Anecdotally, I've heard of nurses who go into research, find it's not quite what they expected or get tired of it after a certain amount of time, and end up returning to patient care. Research staff tends to have a higher burnout rate compared to other positions.

Participant 3: Do you think we overburden research staff with the number of trials we ask them to handle? I hear that research staff doesn't realize the amount and intensity of the work involved.

Moderator: It's probably not the two or three trials they're managing; it's the 16 patients that you're referring to each trial. And certainly, as physicians, we expect research nurses to know the inclusion and exclusion criteria, as well as all of the side effects. We demand and ask a lot of our research staff, and that can lead to the burnout.

Participant 4: It's been really hard for us to find qualified staff; and—once we find them—to get them trained. The research nurses seem to be pulled in all different directions. But we do try to assign only three or four studies to each research nurse. One nurse is doing GI trials. Two or three of the nurses

use or dietary patterns and the molecular markers contained within your tumor…" The revised form described, "…How do your habits, like smoking and eating, affect your cancer…"[31, p. 319] Flory recommends "avoiding digression, unnecessary background information, boilerplate language, and repetition and remembering also to write the consent form from the reader's perspective."[31, p. 316]

In terms of the challenge posed by vulnerable subjects, practice-based research centers can address the special needs of the vulnerable subject by including specific remedies, including:[16]

- Plain language consent forms
- Advance directives
- Supplementary educational measures
- Surrogates and advocates who can work with cognitively vulnerable subjects.

If there is a concern about undue influence from authority figures, these persons should be excluded from any recruitment sessions. Including an ombudsman in the consent process may be necessary. Recruiters who are trained to be sensitive to cultural norms can approach potential subjects who are considered to be deferential.

Subjects with specific conditions can be treated with respect and justice if the research design is considered with the fair distribution of benefits and risks. In addition, the efficacy of treatment cohorts is determined first in terms of the subject rather than the study goals. For example, if a double dose of a drug works better, then testing a standard dose cannot be justified ethically.

Going Forward

Investigators have the opportunity to educate IRB chairs and members about the special challenges faced by community cancer centers, such as the multiple site nested design issue mentioned previously. Investigators can also discuss concerns regarding the protection of human subjects in practice settings, such as the privacy of records issue, and invite IRB chairs and members to participate in practice-based human subject training sessions.[28] Both of these procedures will enhance the partnership between the community cancer center, its research investigators, and the IRB.

A research program adds credibility to a clinical care program.[1] An exemplary research program requires attention to the ethical principles of respect for persons, justice, and beneficence, all of which provide the foundation for the protection of human subjects. If an IRB is to facilitate the strategic role of compliance with federal standards for the protection of human subjects then the institution in question must provide for continuing education of clinician inves-

are doing breast trials. And the nurses communicate back and forth with each other constantly. But there's always the days when you're trying to recruit someone to a GI trial, and the GI nurse isn't there. Then the work falls back onto those other nurses, and they don't know that particular trial as well. Those days are frustrating for *everyone*.

Participant 5: My program has seen a fair amount of turnover in our research department; we're constantly looking for new people. We've started looking at the different trials we participate in—some are more labor intensive than others—and making choices based on that information. For our program, pharmaceutical clinical trials tend to be a little bit easier to manage, and they help pay for other trials. We try to offer a good cross-section of trials for the different disease states: colon, prostate, breast. We balance our research program that way.

Participant 6: Any thoughts as to how many pharmaceutical protocols a practice goes with, since they're a little more lucrative and a little easier to administer than others?

Moderator: It depends on the practice and the practice's financial situation. Physicians and administrators should look at their patient mix and the available research protocols to make rational decisions about what clinical trials to offer.

Participant 5: Early on, a practice might do more pharmaceutical trials because it's trying to get a revenue stream to support its research efforts. As the research program becomes more stable and staff more skilled, the practice would probably want to transition to a research program that offers more choices.

Participant 7: Our physicians first look at a trial to see if it's one they would even be interested in offering to patients. Any research trial that passes physician scrutiny is then sent to our nurses to see how much work is *really* involved. Still, I'm not sure pharmaceutical trials are a way to make money with the amount of time they take. You have to look at pharmaceutical trials very carefully before signing on the dotted line. Our practice was burned on one pharmaceutical trial because of some very stringent data management.

Moderator: Our practice had a similar experience. Sometimes the fees are higher from the pharmaceutical companies, but it's because the trials usually have more requirements. And we've had some clinical trials request information that wasn't asked for when we signed on to participate.

Participant 7: The idea is to have different eyes looking at each clinical trial protocol from different angles. Sometimes the physicians aren't looking at exactly *how* the work will be carried out, what kind of data are required, and how time-consuming it will be to staff—all things nurses look at. If our nurses say, "*This particular trial is going to be too time consuming*," our physicians accept that analysis and most often the decision is made not to participate in that particular trial.

Participant 8: When your practice negotiates contract terms with the pharmaceutical company, I would suggest that you incorporate start-up expenses so you get paid for the work your practice does even *before* one patient is accrued. A practice can do a lot of work—preparation and staff training—and receive no money until the first patient is accrued.

tigators, examination of the flow of information through the organization, and infrastructure assessment. Working in partnerships with IRBs in this fashion, community cancer centers have the opportunity to become institutions of renown in comprehensive patient care by participating in research that leads increasingly to enhanced evidence-based standards for medical care.

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Informed Consent in Clinical Trials

Excerpts from "Improving Clinical Trial Accrual in Community Cancer Centers," a roundtable discussion at ACCC's 22nd National Economics Conference

Participant 1: Our practice doesn't have trouble introducing or "selling" clinical trials to patients. Our problem starts and ends with informed consent. When our patients see the informed consent [forms], they quit. It's multi-page and multi-institution.

Moderator: That's why it's important that an experienced staff member sit down with patients and go through all the steps involved in the clinical trial. Our practice often refers to informed consent as the "scare sheet," outlining every side effect known to man. I'm a firm believer in informed consent, but it's laborious and takes a huge amount of time.

Participant 2: Our program often does informed consent in two or three visits. The first visit is, "*We're going to read this through with you.*" We ask patients to go home, review their notes, and come up with any questions they'd like answered in the next visit. It may be the second or third visit before the patient signs the informed consent.

Participant 3: Our private practice uses a clinical research associate, who also happens to be an oncology-certified nurse. And we use basically the same system. At the first visit, our physician presents the clinical trial to the patient and provides a copy of the informed consent to take home and review. Then we give them our CRA's phone number and tell them to call with any questions. At the second visit, our physicians answer questions and give patients another opportunity to discuss the trial before actually signing the informed consent. It's been very successful for our practice.

Participant 4: Our practice did a PowerPoint presentation that went along with the informed consent. It got really good feedback from our patients. Patients said they were able to better understand the informed consent when the information was broken down slide by slide. Patients take notes during the presentation and then come back and talk to the nurse at the next appointment.

Participant 1: Does a staff member present the PowerPoint slides to patients?

Participant 4: We email the presentation to patients. Most of our patients come from out of state, so it's more convenient.

Moderator: From my experience with clinical trial accrual, probably 25 percent of patients drop out after going through the informed consent. And maybe you just have to accept it. It's scary for patients to think about a clinical trial and to read about the risks on paper. But in the end, 75 percent of patients will sign on to the trial and go from there.

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Increasing Patient Accrual

Excerpts from "Improving Clinical Trial Accrual in Community Cancer Centers," a roundtable discussion at ACCC's 22nd National Economics Conference

Participant 1: Here's one way our program was able to increase patient accrual. When patients come in to see their doctor, we hand them a questionnaire that asks questions such as, "*Do you ever have trouble sleeping? Are you receiving chemotherapy and have these symptoms*? *Do you have numbness or tingling in your fingers or toes?*" Patients just check "yes" or "no" and hand the piece of paper back to the physician. Not only does this information help our doctors see if there's an area that maybe needs to be presented, but every question is related to a clinical research trial. Using this tool, we've been able to refer a lot of patients to supportive care clinical trials.

Participant 2: Our program does a good job of educating nursing staff about the different clinical research trials. Our nurses often flag patients whose disease is changing or advancing and who may now be eligible for a clinical trial.

Participant 3: What methods do you use to educate nursing staff? Annual meetings? In-service trainings? What types of activities can our program do to get our nurses on board with clinical trials?

Participant 2: Our cancer program holds monthly nursing meetings geared toward different topics. About once a quarter this meeting covers clinical trials, educating our nurses about what trials are available and open for accrual.

Participant 4: Our program has a website for staff to know which clinical trials are open and which have closed. And for every open protocol a research nurse gives staff in-service training on the drugs, potential side effects, and documentation needs. We also assign one infusion nurse to each trial, so the research nurse has a contact person within the infusion center. We started that about six months ago, and it's been very effective.

Participant 3: How exactly does that work?

Participant 4: Our program has about six nurses. At any given time we're probably referring patients to between 12 and 15 active trials, so our nurses usually end up with one or two [trials] apiece. We've set it up so that even when the research nurse isn't available, we have our "primary" nurses and infusion nurses that can talk about the clinical trial—even if it's not at the research nurse's level of expertise.

Participant 3: From my perspective, more patients are accrued when an onsite nurse is available to enroll patients that day. Not too many patients want to go to the hospital or another location. Then again, our practice has trouble even staffing a nurse at each of our practice sites. And when there isn't a nurse, there aren't any accruals.

Moderator: Obviously, we've come up with two relatively simple ways to increase accrual: adequate and educated staff and a streamlined enrollment process for patients.