CHAPTER 5

Navigating the Institutional Review Board

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■ Objectives:

- Explain the institutional review board (IRB) procedures to protect human subjects.
- Identify ethical principles that are foundational to the IRB process.
- Describe the link between research and quality improvement (QI) as they relate to the IRB process.
- Describe the types of IRB reviews.

■ Introduction

The purpose of this chapter is to establish insight into the IRB and describe the basic process of reviewing research in regard to the protection of human subjects and the necessity of connecting these with the safeguards and structures of an IRB application. Inherent in the processes of IRB review is the counterbalancing of the power differential that has been at the center of atrocities. Thus, the development of independent review has sought to have a single body to protect the rights and welfare of humans in this process (Tappen, 2011). The ethics of research are usually ensured through an IRB review. Most universities and healthcare agencies have their own IRB committees; however commercial IRBs also exist. Researchers must have their research projects (protocols) and informed consent forms reviewed by the requisite body, which may include both university and agency committees (Steneck, 2007).

Despite revelations of atrocities in clinical research that alarmed the international community during the post–World War II Nuremburg Trials, Dr. Henry K. Beecher brought to light multiple research violations in the United States scientific community in his publication "Ethics in Clinical Research" (1966). This publication led to the 1974 National Research Act and the 1974 Belmont Report. Federal regulations are established by Congress

and are disseminated to the public as law in the Code of Federal Regulations (CFR). In 1991, the Federal Policy for the Protection of Human Subjects, or "Common Rule," was codified as 45 CFR part 46, subpart A. This required the establishment of IRBs to review all research in agencies receiving any federal funding. The Common Rule applies to all federally funded research conducted both intramurally and extramurally. The rule directs a research institution to assure the federal government that it will provide and enforce protections for the human subjects of research conducted under its auspices. These institutional assurances constitute the basic framework within which federal protections are affected. Local research institutions remain largely responsible for carrying out the specific directives of the Common Rule. They must assess research proposals in terms of their risks to subjects and their potential benefits, and they must see that the Common Rule's requirements for selecting subjects and obtaining informed consent are met (U.S. Department of Health & Human Services [DHHS], 2011b, 2012c).

Other parts of the Common Rule recognized the need for increased protections for vulnerable populations including children, pregnant women, and prisoners. The IRB has complete authority to review, approve, require modifications for, or disapprove of a study (DHHS, 2012c). See **Table 5-1** for a list of regulations pertaining to human subject research. These regulations may be obtained from the DHHS website ecfr.gov.

In the late 1990s, as human subject research expanded to international and low-resource countries, the U.S. Department of Health and Human Services, Office for Human Research Protections (OHRP) established requirements for federally funded institutions to register IRBs and to obtain a Federal-Wide Assurance (FWA) that ensures adherence to the Common Rule, Belmont, and the Declaration of Helsinki. Moreover, in another more recent example of the history of research ethics, the tragic death of Jesse Gelsinger in 1999, an investigator-initiated gene therapy

Table 5-1 U.S. Department of Health and Human Services and Food and Drug Administration Regulations

Regulation Topic	*Citation*
Common Rule (IRBs, Informed Consent, Vulnerable Subjects, Registration to clinicaltrials.gov)	45 CFR Part 46
Informed Consent	21 CFR Part 50
IRBs (and Registration to clinicaltrials.gov)	21 CFR Part 56
Conflict of Interest	21 CFR Part 54
Electronic Records and Signatures	21 CFR Part 11
Investigational New Drug Applications	21 CFR 312
Investigational Device Exemption	21 CFR 812

Setting Off on the Road to Responsible Conduct of Research

Source: Illustration by David Zinn, © 2011, www.zinnart.com

study, revealed the need for more extensive review in the areas of financial conflict of interest. Failure to disclose new findings could affect an IRB's willingness to consent to the study and also violates participants' true informed consent (Steinbrook, 2008). Current IRB procedures require review related to financial conflict of interest, stringent adverse event reporting, and disclosure of new research findings in the processes of protocol review and informed consent. In 2001, an accreditation process for IRBs was launched by the Association for Accreditation of Human Research Protection Programs (AAHRPP). This accreditation is now the accepted standard for IRBs regardless of funding sources. Additionally, clinical research regulations expanded requirements to include the registration of clinical trials (and soon, behavioral studies) into clinicaltrials.gov. The reason is to ensure that results of research are shared and that negative findings are not hidden or prohibited from being published.

Definition of Research

Research is defined as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge" (DHHS, 2010a, 45 CFR 46.102[d]).

An investigation must meet certain principles to be classified as research. A research study involves an organized, logical investigation that can range from a scientific inquiry to a qualitative research study of a specified group. It may be local or multilocational. Research development, measurement, and assessment (e.g., literature review, pilot study, feasibility study, or preclinical study) must be included before a study is considered true research. Also, an investigator must design the protocol, data management plans, and data collection tools to collect reliable data or reduce threats to validity that will improve or supply generalizable information, experience, or understanding (Polit & Beck, 2012).

When an investigation meets the criteria for being defined as research with *human subjects,* the proposal and procedures require IRB review and approval. A *human subject* is defined as "a living individual about whom an investigator (whether professional or student) conducting research obtains" (DHHS, 2010a, 25 CFR 46.102(f). Examples of data from human subjects are (a) data either by involvement or interaction of any kind (e.g., email, observation), not necessarily face-to-face; or (b) data that distinguish one person from another (e.g., behaviors in specific places or times when the person is unaware; data collected for certain reasons when the participant counts on that data not becoming public). All human subject research requires IRB approval; however, procedures and activities that include contact with human participants and even data collection may not meet all the criteria for research that demand an IRB review. Some research activities, such as those designed as in-house QI, may be exempt from IRB review (Polit & Beck, 2012; Wilfond, 2013). It is important to consult with the IRB to determine the type of IRB review needed for a study.

Purpose of an Institutional Review Board

IRBs or ethics committees (ECs) are locally managed committees that are given the responsibility to assess research proposals that include human participation. The IRB has federal mandates if the research being reviewed is funded by a U.S. federal agency or is under the auspices of the Food and Drug Administration (FDA) (45 CFR 46.501, Subpart E; 21 CFR 56.106). Both the IRB process and the research involving human participants have received intensified examination by not only lawmakers, but also the general public because some participants have been harmed in the process of taking part in the research study (Beh, 2002; Oakes, 2002). This intensified inspection has had an impact on the IRB process and the IRB evaluators. Evaluators are now expected to know and understand both state and federal rules when assessing research procedures in *biomedical, behavioral, and social science* areas. IRB officials must train local evaluators and IRB members to such a level that the evaluators can even describe what many people might deem an insignificant risk to human participants. These new demands upon IRB members may cause conflict among the evaluators, their supervisors, and the researchers (Eissenburg et al., 2004).

Because the function of the IRB is to protect the public's health, IRB members include the representative public, in addition to scientific experts. The federal government set forth regulations in the Common Rule for determining membership criteria for an IRB (DHHS, 2012c). An IRB ordinarily involves persons from the following areas: (a) faculty who are not only associated with the institution but also represent multidisciplinary academic areas that are characteristically involved in research that includes human participants; (b) faculty who are associated with the institution but who would be classified as nonscientific faculty; (c) impartial delegates to represent the concerns of the community who have no official relationship with the institution but do live in the local area; and (d) local members whose primary responsibility would be to protect the rights of prisoners (e.g., lawyers or prisoner advocates), if the IRB examines research involving prisoners (DHHS, 2012b).

IRB members also must have a membership that includes adequate proficiency, or they must search for subject experts if members of the board are unfamiliar with a specified methodology or population being measured. Collectively, the IRB must have the knowledge, skill, and professional proficiency needed to accurately assess research activities often performed by their institution. Although IRBs serve their institutions, they do not represent the interests of their institutions. Federal regulations forbid institutional officials from overturning an IRB censure of a research proposal (DHHS, 2010a).

No research procedures, including screening for potential participants, may commence until the IRB has examined, evaluated, and agreed to approve the research. Even after the research process has begun, the investigator remains responsible for unceasingly safeguarding human participants; therefore, the IRB evaluates continuing research at least once per year. Also, if the investigator desires to make any changes in research procedures, the IRB must be notified and approve any modifications

before the investigator executes the changes. The investigator can expect to receive immunity from this rule if a modification to an agreed-upon course of action was the result of an unforeseen danger to the human subject and the situation demanded an immediate response for the health and well-being of the participants. The IRB must immediately be made aware of any changes made in response to these circumstances; the investigator may not wait until the research is finished. Federal mandates give the IRB complete power to defer or completely withdraw all approval for research to be conducted if the IRB discovers the research procedures are not in accordance with their approved conditions or that some unforeseen harm may come to human subjects (DHHS, 2010b). Researchers must relate to IRBs and be both knowledgeable about and effective in their response. This demands an understanding of the history, principles, and procedures of the ethics review process (Polit & Beck, 2012).

Ethics and the Institutional Review Board

Beginning with the Declaration of Helsinki, the well-being of the individual research subject has been recognized as taking precedence over all other interests (World Medical Association, 2013).

The Belmont Report

The Belmont Report was written in 1979 and forms the conceptual background for the regulations governing research and scientific studies involving human participants. The Belmont Report identifies three primary principles: beneficence or nonmaleficence, respect for persons, and justice or equality of burden. The first principle, *beneficence*, ensures that the study benefits the participants and does not produce harm; although there may be some risks or inconvenience, precautions have been taken to minimize these. The second, *respect for persons*, ensures that a person's agreement to be part of a study is voluntary, based on a process of informed consent with a reasonable description of risks and benefits, and includes the right to withdraw; they are not a "means to an end." The third, *justice*, is reflected in the potential for all persons to be considered for inclusion—that no single group, especially a vulnerable population such as prisoners, is singled out to bear the burden or risks of participation, such as the testing of an experimental drug (Polit & Beck, 2012). In addition, The Belmont Report obligates the investigator to (a) acquire and give proof of informed consent; (b) ensure and value the privacy of human subjects; and (c) include further protection for human participants with inadequate self-sufficiency (The Commission, 1979).

The investigator must be aware of the ethical dichotomies in the research plan. In controlled (randomized) research studies, equipoise should exist, meaning that there is equality in the value of treatment A versus treatment B. IRBs will be called upon to evaluate this along with undue risks. Another issue is therapeutic misconception, which can occur when individuals believe that their participation will ensure a cure or health improvement, despite informed consent that does not support that belief. Research has shown that 40–80% of subjects showed basic misunderstandings of research trial design

(Appelbaum, Roth, & Lidz, 1987), and that as many as 70% have some sort of therapeutic misconception (Appelbaum, 2002). Moreover, the investigator must be aware that there are other human participants who may be subject to *coercion* (e.g., employees, students) or *undue influence* (e.g., low socioeconomic status) (Polit & Beck, 2012). For example, a grade should not be withheld or altered because of failure to participate in research. An alternative educational experience should be approved if the research participation is part of an academic course. An employee should not have to fear losing his or her job for failure to participate in an employer-sanctioned study. These situations often require additional protections. For example, a list of participants should not be shared with supervisors because that would affect voluntary participation. The investigator is obligated to endeavor to protect these at-risk participants (Polit & Beck, 2012).

To adhere to Belmont principles, the investigator is required to detail how beneficence will be ensured in the research procedures in the following five major areas:

- Procedures are being used that will cause minimal possibility of jeopardy or danger to human subjects even with responses to research questions.
- Data will be collected from present events or endeavors for any purposes unrelated to research.
- Any risk to human participants must be practical because it may correlate to any advantage to the participants and also to any anticipated research significance.
- Anonymity and privacy will be guaranteed and upheld.
- Data will be supervised to establish and ascertain participant privacy (The Commission, 1979).

Investigators navigating the IRB process must be certain that all human participants are equally considered for participation in the research, requiring honest and equitable treatment, without favoritism. Any research inconveniences and obligations must be distributed impartially. Moreover, investigators must plan research in a way that ensures that all human participants will share any advantages, help, or profit that arise from the research process. Investigators must explain how they will meet two primary conditions that are established on justice: (a) participants were chosen fairly and impartially, and (b) vulnerable human subjects or *population of convenience* were not taken advantage of or abused (The Commission, 1979).

Research Ethics Education

An investigator involved in research at any level will be required to complete basic training in the protection of human subjects. In this advanced, complex biomedical environment is not uncommon to care for or work with a patient who is also receiving experimental treatment. Therefore, today's healthcare provider must be aware of the principles of responsible conduct of research (RCR). With the breadth of scholarly work in health care, a clear understanding of these principles is mandatory for all professionals, regardless of whether they are working as a member of the research

team (Polit & Beck, 2012). Basic training in the protection of human subjects may be obtained through the National Institutes of Health (NIH) or the Collaborative Institutional Training Initiative (CITI) modules (CITI, 2016; NIH, 2015).

Link Between Research and Quality Improvement Related to the Institutional Review Board Process

Multidisciplinary contexts demand that healthcare professionals understand the relationships among types of projects and innovations and the criteria for pursuing IRB approval. QI projects are those developed to test the efficiency and effectiveness of translating research into practice or evaluate the effects of intervention improvement (Polit & Beck, 2012). Confusion exists about which projects may or may not require IRB approval; regardless of professional opinions, IRBs reserve the right and the federally mandated responsibility to protect all human participants (The Commission, 1979).

Investigators who are conducting a QI project may have questions about their project meeting the definition applied to *research* and why they should submit their proposal to IRB for review. The DHHS (2010d) has responded to this concern. For example, an investigator wondered if his project could be classified as research, because there was an intention to publish a QI project. The answer from DHHS (2010c) was no. The plan to publish the project is not an adequate measure of establishing that a QI project involved research (DHHS, 2010d).

It is important for investigators to know that there are types of QI projects that do meet the definition of research; therefore, these projects are not exempt from IRB review and are held accountable to DHHS human subject rules (DHHS, 2010c). The DHHS gave an example of a QI project in which a clinical intervention is implemented untested. The purpose of the project was care improvement and data collection concerning patient effect to determine scientific confirmation about how the intervention accomplished its projected results. In this QI project example, the project met nonexempt human subjects research (DHHS, 2010c). The decision-points about clinical research versus QI studies have undergone bioethical debate (Wilfond, 2013).

QI can be both prospective and reflective. QI encourages healthcare clinicians to think out of the box and develop innovative ways to improve healthcare systems. It can be employed as a strategy to prevent errors or ensure that standards of care are being met (Duke University Medical Center, 2005). Because QI processes are significant contributors to the advancement of evidence-based practice (EBP), they may be disseminated through presentations and publications. These processes then become contributors to the general knowledge and now meet the criteria for review (McNett & Lawry, 2009).

Types of Institutional Review Board Reviews

The IRB is an independent body whose sole purpose is the protection of human subjects. In the IRB guidelines, this board is a local board with authority for approving or withholding approval (Fain, 2009). The IRB review is structured in three

levels: (a) full board review, (b) expedited, and (c) exempt (Polit & Beck, 2012). Investigators need to know which type of review their research project requires.

Full review applications are evaluated by a convened board that includes scientific, nonscientific, and community members. Typically, a primary and secondary reviewer is designated for protocol review; however, all members read, consider, question, and vote to approve, modify, or disapprove the protocol. After IRB review and approval, responsibility of the conduct of research resides with the principal investigator (Polit & Beck, 2012). Full IRB review is usually reserved for studies with inherent risk, such as drug studies, studies on sensitive topics such as sexual behavior, and studies with vulnerable populations.

Expedited review is a lower IRB review level for research that poses nothing more than what is known as minimal risk to the participant. Minimal risk means that the participant can expect no more harm or accident to come to them than could be expected in just living everyday life. The research is entitled to an expedited review if it meets the minimal risk definition and all proposed activities meet the eligibility requirements as set forth in the Common Rule 45 CFR Part 46.1110 (Polit & Beck, 2012).

QI projects with minimal risks are often reviewed through *expedited* procedures. They are often reviewed by either the IRB chairperson or one or more individuals on the IRB designated by the IRB chairperson. Reviewers may deem the study as higher risk and require it be returned to the investigator for revision or submission as full review (Nerenz, 2009).

Finally, there is a category of *Exempt Review,* meaning the research does not involve human participants and human subjects are at no risk. This includes studies done in which the subjects cannot be identified, including the usual practice of education (educational tests), collecting existing data, observations of public behavior, and anonymous surveys (DHHS, 2010a).

The final determination of the type of IRB review required rests with the IRB chairperson and is not determined by the investigator.

Protection of Vulnerable Populations

Vulnerable populations are those with factors that would impair their ability to give voluntary consent. These include those with mental impairment, limitations of developmental status (children, developmentally disabled individuals), and special conditions, such as those incarcerated (prisoners). It also includes pregnant women because of the particular vulnerability of the developing fetus (45 CFR Part 46, Subparts B, C, and D, 2016).

The technical definition does not include other groups that could be considered vulnerable and susceptible to coercion, such as decision-impaired students or employees; however, studies or projects involving these groups may be required to include special safeguards, such as assurance that supervisors will not be notified of participation or answers and that grades will not be affected.

The special case of precautions and protections is that of child assent. For minors, parental consent is required, with the number of signatures depending on the level of

risk. Higher risk may require both parents to sign. In addition, the evaluation of risk in children was redefined to be activities in the usual course of day-to-day living, or the "healthy child" criterion, meaning that investigators could not subject a child to higher level risk because the child's illness was life-threatening. In developing assent documents, a child-friendly language has been developed to read in ways understandable to a child aged 7–14 years. After age 14, a minor may be given an adult-type form for assent or a combined consent/assent form with signatures from both parent and child. The concept of emancipated minor may not apply to pregnant minors who do not have authority to consent for research even though they are legally able to give consent for care for themselves and their child. Thus, the parental standard for consent usually must be met or waived by the IRB (Polit & Beck, 2012).

Waiver of written informed consent may be approved if the creation of a signed consent document could link the participant to the study findings or individual data in ways that result in a loss of privacy. For example, if a woman is responding to a survey in a clinic treating sexually transmitted illnesses, a breach of confidentiality could cause psychosocial harm. This risk may argue for waiver of signed documentation of consent. It does not change the need for informed consent, and the investigator may prepare for this by drafting an information sheet for use in the consent process (DHHS, 2012b).

Another example of modifications for groups that do not technically meet the criterion of vulnerability but warrant special protections involves those with low literacy. The investigator may prepare low literacy consent (Flesch-Kincaid reading level of 7.0; see **Box 5-1**) and include a protocol provision to read the consent out loud. All protocols require an opportunity for the potential participant to ask questions and have them answered. Other modifications include large font size (14 or 16 points) for elders or those with lower visual acuity (Agency for Healthcare Research and Quality, 2009).

Protection of Human Rights

Human rights include privileges and demands and have been validated by the perceptiveness of a person or a group of persons. Human rights are applicable to all individuals involved in a research project, including (a) the team conducting the project, (b) the healthcare providers practicing in the project setting, and (c) the participants enrolled in the project. Prior to receiving approval to conduct a project, the human rights concerns must be resolved (Haber, 2010).

Elements of Institutional Review Board Application
Protocol Review and Consent

In preparing a protocol and IRB application for expedited or full review, there are key concepts of participant protection that must be ensured. Protocols may be submitted online through a program such as IRBNet, which is "a web based interface for the submission, correspondence, and monitoring of protocols" that makes the process paperless and also tracks the process through multiple review agencies and stages (see **Figure 5-1** IRBNet, 2012; University of South Alabama, 2011).

Box 5-1 Example of Flesch-Kincaid Reading Level of 7.0

Heart Health Study Information Sheet

You are invited to participate in a research study about your heart health. You may choose to be in the study or not. Dr. Linda Roussel is in charge of this study. She is a faculty member at the University of South Alabama (USA). She also runs Our Neighborhood Healthcare Clinic and outreach programs.

If you are in the study, you will be asked to answer questions from several surveys. We will take your blood pressure, height, weight, waist circumference, and basic laboratory values (such as cholesterol and blood sugar). These will be repeated approximately every 3–6 months. You have the right to skip any questions that you do not wish to answer. There are no known risks for you to participate in this study other than the usual risks of having your laboratory values and blood pressure taken. The laboratory values will be measured from a finger stick, which may cause slight discomfort and could cause a bruise.

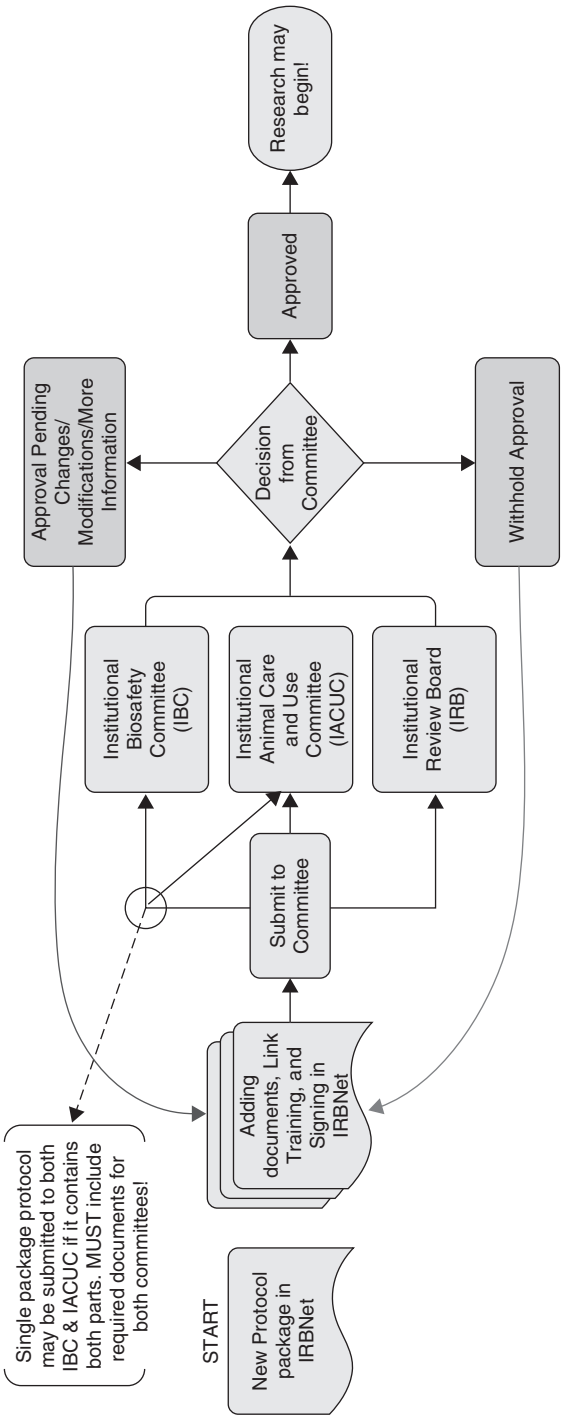
There will be no payment, but healthy snacks will be given during the sessions. There will be no costs to you. You may benefit by receiving help from the outreach program. If you have *any* questions about the research, Dr. Linda Roussel or another member of the research team will be glad to answer these; her phone number is 251-609-1585. If you have questions about your rights or any complaints about the research, you may contact the staff at the Office of the USA IRB for Human Use at University Boulevard at 251-445-5678.

Your Personal Health Information (PHI) is protected by law. Under these laws, your health information cannot be used or given out to the research team without your permission. All records will be kept confidential. The results of this study might be published, but no information that identifies you will ever be given out. The following individuals will be able to see the research records to be sure the research is being done correctly—the research staff, the USA Research Compliance and Assurance Office, and the USA IRB. All information will be entered into a computer without names. Information stored on the computer will be password protected. Information stored in files will be stored in locked files.

Your permission does not run out. You may quit the study at any time. If you wish to quit, please contact any research team member or call Dr. Roussel at the number mentioned above. If you quit, you will be removed from the study. However, information already gathered may be used to complete the study.

You are not giving up any legal rights by agreeing to participate in this research. If you agree to be in the study, it means that you understand everything that has been explained to you. Feel free to ask about anything that is unclear at this time.

Thank you!



■ **Figure 5-1** Diagram of Process Overview of the Steps of Protocol Submission Through IRBNet
Courtesy of Michael Housley, II, Office of Research Compliance and Assurance, University of South Alabama.

Privacy, anonymity, and confidentiality refer to protections of identity. Consent and assent refer to basic willingness and voluntary participation. Data management includes understanding of the level of protection in different types of data collection as well as techniques for data to remain unidentifiable, cleaned, and stored. Procedures may be specified for screening and recruitment, and specific instructions may be developed for use of questionnaires, interviews or focus groups, obtaining physical data, or secondary analysis of clinical data records (Polit & Beck, 2012).

Key Elements of Informed Consent

Provision of informed consent is a process for participants in research or QI. It is an essential process that includes the conveying of information and the expectation of adequate understanding. There is increasing concern for low literacy and the need to keep the consent document at an appropriate reading level. In some cases, IRBs will approve low-literacy consent to be read aloud to potential participants. Sufficient time and opportunity for consideration of the decision and receiving input from others must be provided. To meet this requirement, some investigators mail consent forms to prospective subjects and review these prior to arrival at the study site. The participant may want to consult family, clergy, or other individual resources prior to agreeing. The provision of 24 hours for consent may be waived in minimal-risk studies but always should be a consideration as part of the process (DHHS, 2012b; Polit & Beck, 2012).

Many university IRB websites have provided comprehensive information on (1) how to submit studies for review and (2) regulatory requirements related to the Health Insurance Portability and Accountability Act (HIPAA), the Family Educational Rights and Privacy Act (FERPA), and the Genetic Information Nondiscrimination Act (GINA). In the consent process and through written informed consent, an individual may authorize the investigator's use of medical information or records. This is called a HIPAA authorization or waiver. Likewise, a student may authorize access to educational records protected by FERPA (DHHS, 2008; DHHS, 2012a).

■ The Consent Form

Human subjects should sign an informed consent form before participating in research. Even if the participant's only interaction with the investigator is an interview, the participant should sign a consent form. Often researchers employ checklists and comprehension checks for ensuring adequate informed consent (Kripalani, Bengtzen, Henderson, & Jacobson, 2008). Special methods can be used to enhance informed consent, including Patient Information Sheets, eConsent, Gamefication, Video Consenting, and websites (Hoffner, et al., 2012; Tait, Voepel-Lewis, Levine, 2015). All materials and methods used for the informed consent form or process require IRB approval. Recruitment materials also must be IRB approved before implementing a study, including materials that use media, bulletin boards, fliers, posters, verbal scripts, letters, social media, email, or referrals. Ensuring the readability and comprehension of informed consent forms requires that scientific language and reading

levels be reduced. Research on the informed consent process and documents often reveal issues in complexity in the informed consent document (Reinert et al., 2014). Documentation of the recruitment and informed consent process must be thorough, prior to commencing research and at all subsequent visits. The adage, *"if it is not documented, it was not done"* applies to informed consent as well as other clinical activities.

The IRB can determine to put aside the necessity for getting informed consent when (a) the risk to human subjects is negligible; (b) human participants' rights will not be harmfully influenced by not requiring participants to sign; (c) if performing the research without the waiver is not realistic; and (d) if significant, participants will be allowed to obtain more applicable information after they take part (DHHS, 2011a).

Before investigators submit to the IRB, the informed consent form should include the following:

- What the participants will be requested to do, who will ask them, and what the purpose is for doing what they will do
- Identification of the investigator and contact information for participants if they have questions they want answered
- Contact information of investigator and the IRB
- Advising participants of possible risks they may encounter if they participate in the research
- Alerting participants of their rights (e.g., right to examine data; right to abandon the research)
- Indicating if participants' names or any names will be used in the process or what substitutions for names will be made
- How the research results will be distributed and if participants will profit in any way from research participation
- That participants may withdraw from the research with no bias against them
- The understanding that a legal guardian must sign for a minor child to be able to participate
- Writing the consent form in the second person [e.g., *"You have the right . . ."*] (DHHS, 1998)

Investigators have the responsibility to acquaint the potential participants with any new findings that would affect their willingness to continue. Participants also must be given information on any alternative treatments they may consider in making their decision. A checklist of consent elements is presented in **Box 5-2** (DHHS, 1998). At the University of South Alabama, a subjects' bill of rights (see **Box 5-3**) accompanies the informed consent process (University of South Alabama, 2004).

Privacy refers to how one approaches the potential participant. It requires, in most cases, that the researcher not approach a person in any way that would identify the potential participant as having particular characteristics. It would also require some type of permission to contact a patient who could be eligible to participate. Privacy refers to the right of an individual to control what other people know about him or her.

Box 5-2 Informed Consent Checklist

Basic Elements

- A statement that the study involves research
- An explanation of the purposes of the research
- The expected duration of the subject's participation
- A description of the procedures to be followed
- Identification of any procedures that are experimental
- A description of any reasonably foreseeable risks or discomforts to the subject
- A description of any benefits to the subject or to others that may reasonably be expected from the research
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
- For research involving more than minimal risk, an explanation as to whether any compensation or medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject
- A statement that participation is voluntary and that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled

Additional Elements as Appropriate

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus if the subject is or may become pregnant) that are currently unforeseeable
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
- Any additional costs to the subject that may result from participation in the research
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject
- A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject
- The approximate number of subjects involved in the study

Data from U.S. Department of Health & Human Services, http://www.hhs.gov/ohrp/policy/consentckls

Box 5-3 University of South Alabama Medical Research Subject's Bill of Rights

If you are invited to participate as a subject in a medical research study or are asked to consent on behalf of another, you have the right to:

1. Be informed of the purpose of the research.
2. Be given an explanation of the procedures to be followed in the research protocol and of any drug or device to be used.
3. Be given a description of any discomfort, risk, or potential medical complication that reasonably could be expected to occur as a consequence of participation in the research study.
4. Be advised of any potential benefits from your participation in the research, if applicable.
5. Be informed of any procedures, drugs, or devices that might be of help to you and provide an alternative to participation in the research.
6. Be informed of the process required to receive medical treatment promptly should complications arise as a result of your participation in the research.
7. Be given an opportunity to ask any questions concerning the research.
8. Be instructed that you may discontinue your participation in the research study at any time without jeopardizing the future medical care you receive at USA.
9. Be given a copy of a signed and dated written consent form, whenever written consent is required.
10. Be given the opportunity to decide freely and without undue pressure from others whether or not to participate in the research.

Data from University of South Alabama Office of Research Compliance and Assurance.

This right is limited in that no person can completely control what other people know about him or her if that knowledge is based on the individual's public speech, actions, or location. Informed consent is not required for research projects that monitor unidentified subjects' public behavior. However, when information that individuals would normally control is collected, informed consent indicates that the participant has voluntarily chosen to disclose certain information to investigators (Polit & Beck, 2012; University of Montana with Office of Research Integrity, 2002).

Anonymity is met if a study participant cannot be identified, such as by a survey with no names. A data set with matched Time 1 and Time 2 data is not anonymous because it has been collected in such a way as to be sure that the two times match; thus, at some point, the participant was identified. Anonymity is not the same as a de-identified data set and occurs only when there are no identifiers collected at all (Polit & Beck, 2012).

Confidentiality means that the identity of participants is not released and identity is protected. It can be maintained through code numbers on surveys and many

precautions that ensure safe storage. Confidentiality is required in interviews in which the researcher clearly knows the participant. It can be encouraged but not ensured in focus groups. A breach of confidentiality is often considered a risk in any study, and some IRBs require all investigators to list it on the consent form. Any person engaged in research in which sensitive information is gathered from human subject participants (or any person who intends to engage in such research) may apply for a Certificate of Confidentiality (DHHS, 2011c; Office for Human Research Protections [OHRP], 2003; Polit & Beck, 2012). A Certificate of Confidentiality helps researchers protect the privacy of human research participants enrolled in biomedical, behavioral, clinical, and other forms of sensitive research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant (OHRP, 2003; Polit & Beck, 2012).

Consent is agreeing to participate as an adult or providing permission for one's minor child to participate. It must be voluntary, obtained without coercion or undue influence, and follow a process of adequately informing the potential participant to make a reasoned decision whether to participate. Consent may be given by a guardian or a legally designated caregiver who is acting as a legal authorized representative for a participant (DHHS, 2010a; Polit & Beck, 2012).

Assent is agreement by a child, generally between the ages of 7 and 18, to participate in the research. Child assent must be accompanied by parental or guardian consent. Because children are not competent to give informed consent, informed consent of children's parents or legal guardians must be obtained. The age of majority varies from state to state, with most being 18 years but some being 19 or 21. Assent has been referred to as an affirmative agreement to participate (Polit & Beck, 2012).

Vulnerable populations refers to specific classes of persons who may be incapable of giving fully informed consent (e.g., developmentally delayed people) or may be at risk for unintended side effects because of their circumstance (e.g., fetuses, neonates, children, pregnant women, and prisoners) (DHHS, 2010a).

Incentives are reasonable compensations for participation. Most incentives provide for expenses to participate, such as travel, and may compensate someone for his or her time (Tomlinson, 2011). For the majority of the time, using incentives for recruitment and retention for research participants is innocuous. However, there are times when this is not the case. The responsibility related to ethics to advance health care must be balanced against the charge that participants are autonomous persons who deserve respect. Therefore, the ethical use of incentives can be significant in meeting that balance (Grant & Sugarman, 2004). Example incentives are a $25 gift card (adult), a movie pass or music download (adolescent), crayons (child), or discount coupons for baby supplies (pregnant woman, parent). Incentives must be given throughout the study, but a proportion may be reserved for study completion (Frederick, 2009).

Benefits refers to actual direct benefits the participant may expect to receive and the global benefits to society. A benefit could potentially be helpful to the participant

(e.g., an intervention that may not be accessible to the participant otherwise, discussing their issue with an unbiased individual, and/or incentives). A risk-benefit assessment should be conducted (Polit & Beck, 2012).

Risks are included with every research study; however, risk can be minimal. *Minimal risk* is not larger than the risk an individual would come upon daily or during a routine procedure. If a risk is more than minimal, caution must be taken and a process must be followed to decrease risk and maximize the benefits. The possible risks to participating in the study should be shared with participants (e.g., physical harm, psychological distress, stigma, privacy, financial). The study should be restructured if the anticipated risks are greater than the anticipated study benefits (Polit & Beck, 2012).

Community-Based Participatory Research and Institutional Review Boards

Community-based participatory research is a research method that engages community and academic partnerships (Flicker, Travers, Guta, McDonald, & Meagher, 2007). Communities are recognized as more than a grouping of persons in a neighborhood. A better description of communities might be social networks that create subcultures with greater diversity. For example, people who reside in an urban center are likely to have higher rates of health and psychosocial problems compared to people living in rural areas (Flicker, Skinner, & Veinot, 2005). Community partners offer an opportunity to increase communication with academics using a research paradigm. Specific research questions can be created that reflect health issues of real concern to community partners. This collaboration would improve the researchers' ability to obtain informed consent and design a study to benefit the community (Minkler, 2005). New ethical concerns surface that traditional ethical review boards have not been required to consider in the past (Flicker et al., 2007). For example, how does the community interpret the research question(s)? Have community leaders contributed to the questions and design? This is particularly vital for the recruitment and retention of participants. IRB forms may favor traditional biomedical research methodology. This may unintentionally harm community-based research (Flicker et al., 2007). Members of the community should be included in all meetings related to research studies or QI initiatives. If these collaborative meetings do not occur, the perception might be lack of equality in terms of the cost-benefit of the scholarly work. The ethical component of all projects must be discussed before submitting the IRB application.

■ Conclusion

In any venue for dissemination—both presentations and publications—investigators are being asked to verify the review and approvals that were done with the initiation of the research. In an international survey of journal reviewers, Broome, Dougherty, Freda, Kearney, and Baggs (2010) found that the most commonly reported concern was inadequate protection of human research participants. Recently, some journals

have required documentation of the IRB protocol number and approval date for submission of manuscripts to peer-reviewed journals. It is important that healthcare providers recognize this as a required element in the evaluation or critical appraisal of the work as they draw implications for practice. However, professionals are also in key positions to provide oversight for protection of human participants and patients who may be invited to participate or who may be involved without adequate attention to these safeguards. In many cases, whistleblowers have been individuals who identified serious omissions in these safety measures. Knowledge is power, and comprehension of the necessity of IRB and ethical review can only strengthen our multidisciplinary healthcare environments. In all of these, the focus is on issues of protection of human subjects and building structures and processes that strengthen relationships with the providers and public.

■ Case Studies in Institutional Review Board and Informed Consent Requirements

It is important to be able to apply the principles of human subject research protections as it relates to IRB approvals and informed consent. On initial review of these principles, it initially appears clear cut and intuitive. However, as human subject research opportunities present themselves, the lines related to regulatory requirements for studies can become blurred. Using the resources in this chapter, look at four examples or research to gain clarity about different types of requirements for IRB review and approval and for informed consenting.

Example 1

Cynthia is a nurse manager for a team of infusion nurses at an oncology practice that has two office locations. Each office location has an infusion team of four registered nurses (RNs). The physicians in the practice admit patients to two local hospitals that are designated as regional medical centers that have 400 and 620 beds, respectively. The oncology referral for breast cancer patients is robust, and the infusion clinic is busy. Cynthia and one of the physicians have learned about a novel new head-cooling device that is being developed by a local company. The "device" company (sponsor) representative has asked if the group would consider "trying it out" by participating in a small study of the device. The company has agreed to provide the device and instructions for the device (company generated study protocol) and is asking that it be studied in 15 cases of patients beginning initial chemotherapy treatment for stage 1 to 2 breast cancer. This oncology group does not have a clinical research staff, and Cynthia is navigating next steps.

It is important for nurses to understand the basics of clinical research regulations and human subject protections. Clinical trials take place in academic medical

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centers, private practices, and freestanding research companies. Nurses encounter varied opportunities to work on a clinical trial, either in a supportive role coordinating a study or in clinical role, caring for patients who happen to be enrolled in a study. Sometimes a clinical role can evolve into a study coordination role, either formally or ad hoc. Such opportunities, even unexpected ones, are more common than expected and present additional role requirements and role conflicts for nurses. Moreover, there renewed interest in clinical research ("moon-shot for cures for cancer") and those opportunities will continue to evolve. Moreover, nurses are key researchers on the process of clinical research, especially tool development and innovations in informed consenting.

In Example 1, the study is obviously a clinical trial of a device and would require full IRB review. While the study is an open-label study, which does not include a "comparator" device or double-blinding of the participant or research staff, it is still a clinical trial that is gathering safety and efficacy data on a new device. The company may or may not have submitted this study to the FDA as an investigational new device. Indeed, such a device may just as easily be an innovative product developed by a nurse! For now let's unpack what needs to be considered when moving ahead through the decision process of agreeing to participate in this project:

- What is the company's prior experience with this population and device?
- What does the "protocol" say?
- What is the specific population eligible for this study? New breast cancer, grade 1 to 2 is not specific enough. What if a relapsed patient wants to be in the study?
- What risks have been identified? How might the risks and benefits be articulated for potential participants and for the IRB?
- Which IRB will be used, because this is a private practice? What kind of IRB approval is needed?
- If the study is funded by a government agency, such as the NIH, what IRB requirements must be in place before it can review the study?
- Does the company provide an informed consent? How might the informed consent be reviewed and rewritten to conform to IRB policies and ensure it is in simple language? Are all of the elements of informed consent as described by regulations in place?
- The people will be participating in the study for multiple chemotherapy infusion visits. What are the implications for informed consent at each visit?
- How is informed consent documented? What if English is not a first language for some of the patients?
- Who will be listed as the investigator and sub-investigators?
- Is there a project contract and budget? What indemnifications will be in place? Will the product sponsor reimburse participants' if there is injury?
- What attendance is required by the IRB of the physician taking part in the study?
- What is the role of the nurse manager and staff in this study?

- How will taking part in this study enhance the practice and care of patients in the practice?
- Should this study be registered with clinicaltrials.gov?

Example 2

The community oncology practice described in Example 1 is using a new FDA-approved chilled cap to prevent hair loss in breast cancer patients on chemotherapy called Dignicaps®. The caps have circulating liquid that is kept at a steady cooling temperature (32°F) and are worn prior to, during, and after chemotherapy. Cynthia is considering several nursing research questions related to alopecia in chemotherapy patients as part of her Doctor of Nursing Practice (DNP) degree pursuits. Because the use of the caps prolongs the time requirement for patients to be in the infusion chairs (before and after infusion), Cynthia wants to use audioguided meditations and electric blankets to increase comfort and satisfaction of patients using this device. She also wants to include the use of a portable, disposable cooling cap to be worn home, because during the summer, a sharp contrast from cooling temperature to home transportation could possibly affect the efficacy of the cooling cap. What are the regulatory considerations for these study questions?

The use of cooling caps for the prevention of alopecia in chemotherapy patients existed in Europe prior to the United States and only gained FDA approval by Dignitana AB in 2013 (Dignicaps®). It is becoming incorporated as optimal care for avoiding alopecia for breast cancer chemotherapy patients; however, as with any newly approved device or medical treatment, third-party payers are slow to approve as standard of care and more readily and affordably accessible. Nursing care of patients using new treatments or medicines offer opportunities for innovative nursing research questions and quality improvement. In fact, nursing studies can enhance the case for third-party payer acceptance and policy decisions. In case Example 2, Cynthia is posing multiple questions and should focus a study plan that aims to measure comfort and satisfaction. Moreover, she is posing a new intervention that could measure efficacy.

- *What classification of device is Dignicaps®? Does that matter?*
- *Are these two different studies or one single study? Can those study questions be combined?*
- *What tools will Cynthia use to measure comfort and satisfaction?*
- *Will the guided meditations and electric blankets be standardized (same used for all?). What settings will be used for the electric blankets and when would the electric blanket be used and for how long?*
- *What risks are associated with the use of electric blankets and in the satisfaction and comfort measurements?*
- *What would be included in the informed consent form?*
- *What kind of IRB approval is needed and which IRB will be used?*

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- *If Cynthia wants to introduce an alternative cooling system for the ride home, what is planned and how will that be standardized to ensure it is used similarly for all cases? What will this cost?*

Example 3

Cynthia determines that she does not have the resources available at the time to develop a portable cap to be used on the way home; however, she is going to investigate that for a later nursing research project. Moreover, she decides that she first needs to focus on piloting a tool to measure satisfaction and comfort for patients using cooling caps. Some patients already bring portable audio and blankets with them; and sometimes the clinic warmed blankets are available; however, those interventions are varied, and the use of comfort measures will be assessed generally in the survey as descriptive data, but will not be compared to satisfaction results. Cynthia is going to use existing tools (previously studied for reliability and validity) to measure patient comfort and satisfaction and has created a SurveyMonkey® survey (surveymonkey.com). *Eligible patients will be asked to complete an anonymous survey using an Internet link generated by SurveyMonkey®. Patients without Internet connections will be allowed to complete the survey at subsequent clinic visits using a study iPad. No patient identifiers are collected in the study.*

Because this study is measuring satisfaction and comfort, is anonymous, and poses no significant risk to the participants, full IRB review is not required; however, the study still requires IRB approval, but likely will only need expedited review. Consider these additional questions as you apply the principles in this chapter:

- *Who ultimately decides whether a study requires full review or expedited review?*
- *What will Cynthia need to do to prepare an expedited IRB submission?*
- *What elements will be required for the informed consent for this study? Is face-to-face informed consent required? Can survey URLs be sent out with an invitation letter and information sheet only? Who determines these requirements?*
- *Should Cynthia include patients in the development of the survey?*
- *How will Cynthia report findings to patients?*
- *How does SurveyMonkey® ensure privacy of participants?*
- *Will Cynthia disseminate her findings beyond the local clinic? Does this make a difference?*

Example 4

Cynthia notes that several patients are complaining that they are experiencing varied levels of alopecia despite the use of cooling caps at the clinic. After investigating these cases, it is difficult to ascertain the consistency of cooling cap usage, because of varied charting practices. Moreover, she also observes that during busy infusion days, some patients are not wearing the infusion caps long enough prior to the

initiation of infusion, and, in some cases, there are more patients than cooling caps. She determines that a standard operating procedure (SOP) needs to be developed to improve the quality of care in patients using the cooling caps, as well as new training to ensure consistency in practice. She initiates a checklist and audit practice to instill quality control and quality assurance. Moreover, she uses staff and patient input when developing the SOP. After implementation, she will survey patients for their satisfaction and to measure if there are any improvements in rates of alopecia.

As presented in this chapter, the spirit of inquiry should be present for all levels of care and includes measuring quality indicators for patient care, safety, and satisfaction. There can be a fine line between quality improvement studies and research studies. What should be considered when developing research questions that are aimed at quality improvement?

- What kind of IRB approval is needed to measure the effectiveness of or adherence to a new SOP? Is Example 4 a research study or a quality improvement study?
- Is informed consent needed for this study?
- Should a study plan (study protocol) be developed for this QI study?
- Cynthia realizes that the SOP she developed could help other community cancer centers and submits an abstract of her results to a national nursing convention. She also plans to write a manuscript of her process, SOP, survey, and findings. Does this make a difference in categorizing this as research or quality improvement?

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Reflective Activities

1. Review an informed consent document and evaluate the elements.
2. Review a research proposal that has had a full review and justify the review by the IRB.
3. Describe three different populations considered to be vulnerable according to the descriptions in this chapter. What are the appropriate IRB procedures for protecting these human subjects?
4. Describe the differences between the elements of a research study proposal and a QI proposal in regard to the IRB.
5. Attend an IRB meeting or interview and IRB member.
6. Volunteer to participate in a research study.
7. Compare and contrast informed consent for a research study to informed consent for a medical procedure.
8. Obtain Human Subject Protections Certification from NIH or CITI

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