

Working with the institutional review board

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The Nuremberg Doctor's Trial that occurred at the end of World War II is generally cited as the event that drew attention to the need for a formal system for the protection of individuals who participate in research studies. The conduct of human experimentation described at the Nuremberg Trial, in addition to the final judgment, resulted in a set of standards for the conduct of human research known as the Nuremberg Code.^{1,2} The Nuremberg Code was followed by the development of other ethical standards for human research, such as the Declaration of Helsinki and the International Ethical Guidelines for Biomedical Research Involving Human Subjects.^{3,4} Unfortunately, the Nuremberg Code was also followed by further cases of disregard for the protection of research subjects, such as cancer experiments at the Jewish Chronic Disease Hospital, hepatitis experiments at the Willowbrook State Hospital, and radiation experiments at the University of Cincinnati.^{5,6} However, in 1972, the exposure of what has become known as the Tuskegee Syphilis Study led to the establishment of the current U.S. regulatory standards for the conduct of human research.⁷ The Tuskegee Syphilis Study began in 1932, by the U.S. Public Health Service, in order to study the natural

Purpose. Working with an institutional review board (IRB) to ensure compliance and ethical conduct of research involving human subjects is discussed.

Summary. The Department of Health and Human Services (DHHS) and Food and Drug Administration regulations for the conduct of human research are grounded in the principles of the Belmont Report. By establishing the requirements for the function and operation of the IRB, the criteria needed for the review and approval of research, and the requirements for obtaining and documenting informed consent, the federal regulations help ensure the safety, rights and welfare of subjects. In developing research protocols and submissions to the IRB, the investigator should include clear, detailed information that addresses the regulatory requirements for the review and approval of research. Before starting a research study, review and approval by the IRB is required unless the study is determined to be minimal risk and fits one of the defined categories. Some research projects involving observation of public

behavior, collection of anonymous surveys of nonvulnerable individuals in which the information is not considered sensitive, and evaluation of standard education practices may be exempt from DHHS regulations. Informed consent is central to the protection of human subjects and is required unless the IRB allows a waiver or alteration of informed consent. Once the study is approved, the investigator must conduct the study as approved by the IRB and continue to meet the regulatory requirements related to modifications, reporting unanticipated events, and continuing review.

Conclusion. IRB review is integral to ensuring regulatory compliance and ethical conduct of research involving human subjects. Working closely with the IRB or colleagues who have had experience with the IRB will help junior investigators better understand the IRB submission and review process.

Index terms: Clinical studies; Compliance; Ethics; Institutional review boards; Methodology

Am J Health-Syst Pharm. 2009; 66:176-84

history of syphilis. Despite the development of treatments for syphilis, subjects remained untreated and continued to be followed until 1972 when the study was exposed. In addition to remaining untreated, the study participants were not afforded an adequate opportunity to make fully informed initial or continu-

ing decisions about taking part in the study. The revelation of the Tuskegee Syphilis Study led to the National Research Act of 1974, which requires regulatory protection for human subjects, and to the creation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

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The author has declared no potential conflicts of interest.

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The Research Fundamentals section comprises a series of articles on important topics in pharmacy research. These include valid research design, appropriate data collection and analysis, application of research findings in practice, and publication of research results. Articles in this series have been solicited and reviewed by guest editors Lee Vermeulen, M.S., and Almut Winterstein, Ph.D.

In April of 1979, this commission issued the Belmont Report, which established the ethical principle for the treatment of research subjects in the United States.⁸ The Belmont Report established three ethical principles to guide the conduct of research involving human subjects—respect for persons, beneficence, and justice. The Belmont Report also distinguished research from medical practice (treatment) and placed the responsibility on the investigator to submit research activity for review by an institutional review board (IRB).

Based on the principles set forth in the Belmont Report, the Department of Health and Human Services (DHHS), in 1981, codified regulations for the protection of human research subjects. This regulation governs research sponsored or funded by any of the 17 signatory federal agencies and has become known as the Common Rule.⁹ Food and Drug Administration (FDA) regulations for the protection of human subjects and the use of IRBs were codified in 1980¹⁰ and 1981.¹¹ These regulations govern research involving FDA-regulated products (e.g., drugs, devices, biologicals, dietary supplements). The main elements of both the DHHS and FDA regulations are to establish requirements for

- Compliance with the regulations,
- Obtaining and documenting informed consent from all study participants,
- IRB membership, function, operations, and review of research and
- Record keeping.

In addition to the general provisions, the regulations contain several subparts that provide protections for certain vulnerable research subjects (e.g., pregnant women, prisoners, children). These regulations are not the only ones that impact the conduct of human research. While outside the scope of this article, other federal regulations, such as those related to electronic records, financial disclosure, drug or device approval, and patient privacy, Veterans Affairs facilities and many individual state regulations also contain provisions related to human research. When applicable to a specific study, the IRB will consider these requirements.

IRB function and jurisdiction

The Common Rule and FDA regulations establish specific requirements for the conduct of human research. The Common Rule defines a human subject as “a living individual about whom an investigator obtains data through intervention or interaction or obtains identifiable private information” and research as “a systematic investigation designed to develop or contribute to generalizable knowledge.”⁹ FDA regulations define a human subject as “an individual, either a healthy individual or a patient, who is or becomes a participant in research, either as a recipient of the test article or as a control.” Reflecting the focus on drug and device approval, FDA regulations use the term “clinical investigation” rather than research. A clinical investigation is defined as “any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration.”^{10,11} Both definitions must be considered when determining whether a project is research and whether any of the regulatory provisions unique to DHHS or FDA regulations apply. Pharmacists should work with their IRB or a member of their department who is familiar

with the regulations regarding the distinction between the two sets of regulations and how they impact specific research studies.

These regulations do not apply to providing medical care. Medical care encompasses activities such as diagnosis, treatment, and therapy designed to enhance the well-being of an individual patient with a reasonable expectation of success. However, if a project involves gathering or using specimens, tissue, cells, data, documents, or information about or derived from humans for purposes other than medical care, it is important to determine whether the definition of human subjects research is being met and, if so, what regulations apply. In determining whether an activity is human research, DHHS regulations focus on the type of information and the manner in which it is collected, the procedures that guide the collection of the information, and how the information will be shared. FDA regulations center on the use of FDA-controlled material and the use of the information for regulatory purposes. If there is any doubt about whether a project is classified as human subject research, it should be discussed with the IRB. Investigators can also refer to DHHS decision charts for guidance in determining whether an activity is human research.¹²

Quality-improvement (QI) and quality-assurance (QA) projects and assessments present specific challenges to investigators and institutions as to whether these projects meet the definition of human subject research; therefore, falling under federal regulations and requiring IRB review. QI projects are small-scale cycles of interventions linked to assessments, and the goal is to improve the process, outcome, and efficiency of complex systems of health care. QA initiatives are designed to assess the adequacy of a current practice or process within a specific organization.¹³ Both QA and QI projects can

resemble classical research studies in their use of private, confidential health information and observational or experimental designs. However, these projects use data that are part of usual care, lack protocol-directed interventions or interactions, and focus on assessment of implementation or changes to processes or interventions that have already been demonstrated to be potentially effective. For these reasons, QI and QA projects are often cited as being different from research.¹³⁻¹⁵ The final assessment of whether QI and QA projects require IRB approval is often determined by institutional policy and, if in doubt, the IRB should be consulted. Investigators must remember that even if a project does not fall under IRB jurisdiction, they are still responsible for its ethical conduct and for the safety, rights, and welfare of all those involved.

IRB members and their responsibilities

The IRB is composed of a mix of individuals with diversity in experience, perspective, gender, and, if possible, race and ethnicity. An IRB must have a minimum of five members including a scientist, a nonscientist, and at least one person who is not affiliated (e.g., employment, family relationship) with the IRB's supporting institution.^{9,11} While these are the minimum requirements, the number and diversity of IRB members are typically determined by the volume of research and the need to ensure adequate expertise.

The IRB will rarely be as intimately familiar with a study as the investigator, even though its members have broad knowledge in study design and conduct and have or obtain scientific expertise in the areas of research that are presented for review. When preparing materials for IRB submission, it is important to write for the reviewers. Materials typically provided to the IRB for review include an institution-specific submission

form, a research protocol, the full grant application (if one is available), the informed consent, and all subject recruitment materials. The submission must be understandable to both a sophisticated scientific reviewer and the nonscientist member. A submission that provides a clear, detailed justification and plan for the research will provide IRB members with the information they need to assess the risks and benefits of the study.^{16,17} A well-written submission also allows the IRB to determine whether a study raises any specific ethical concerns and, if so, how the investigator will address those issues. Submission of materials that lack specificity and detail, have gaps in the information, are missing information, or contain inconsistent information will lead to multiple questions that the investigator must address in order for the IRB to make a final determination. A scientifically rigorous, methodologically sound study protocol and detailed IRB submission allow IRB members to have a clear understanding of the proposed study and enable them to make the regulatory determinations required for approval (Appendix A). It is important to develop a protocol and submission method that are appropriate for the specific aims of the proposed study. Pharmacy practice research generally differs from that of randomized controlled clinical trials. Attempting to apply the methodology of a randomized controlled trial to a pharmacy practice research question often makes it difficult for the IRB to determine whether any research is actually being proposed and whether the project can be approved.

Investigators should remember that the IRB will consider both the ethics and science of proposed studies. The concept of equipoise requires that there be a state of genuine uncertainty regarding the comparative merits of each group in the study and that there is a valid research question that has a reasonable chance of being answered if the study is successful.¹⁸

A study that will be unable to reach valid conclusions because of flaws or shortcomings in design or that fails to identify how, if successfully concluded, it will advance scientific understanding can never be ethically justified.

Although the requirements for IRB review and approval of research are laid out in the regulatory requirements, the interpretation and application of those regulations occur at the local IRB level, which results in considerable variability in the review and approval process. This includes variation in review type (exempt, expedited, or full IRB review) and variation in the content of informed consent documents.¹⁹ The impact on investigators is confusion and frustration about how to meet regulatory requirements and delay in study approval. Engaging the IRB chair or administrator early in the study development process allows an investigator to craft a submission that addresses local IRB interpretation of regulations. Having a department member who serves on the IRB or who has experience with the submission process involved in developing the IRB submission will also help an investigator understand the local processes.

Exemption from IRB review

Even though a research study involves human subjects, it may be exempt from the DHHS regulations. Examples of such studies include the observation of public behavior, the collection of anonymous surveys of nonvulnerable individuals in which the information is not considered sensitive, and the evaluation of standard educational practices and analysis of existing nonidentifiable data.⁹ Any study involving prisoners and some studies involving children cannot be declared exempt because of the vulnerable status of these subjects, regardless of whether the study meets the other requirements for exemption. In addition, studies that

involve surveys, interviews, or observation of public behavior cannot be exempt if disclosure of the responses could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.⁹ The collection of some data, such as dates, in combination with any of the 18 identifiers specified by the Health Insurance Portability and Accountability Act (HIPAA) may also preclude an exempt determination. DHHS decision charts can help guide investigators in determining whether a particular study is exempt.¹² Because slight variations in how a study is conducted and what data are collected can impact whether a study is exempt, many institutions do not allow individual investigators to make this determination and instead require some level of IRB review.

Because FDA regulations are based on the use of FDA-regulated material, they do not contain analogous criteria for exemption.² Exemption from FDA regulation is possible if the use meets criteria for specific emergency-use situations.¹¹ While DHHS regulations do contain some provisions for emergency use, they do not encompass all the uses specified in FDA regulations. If an investigator anticipates involvement in emergency-use situations, he or she should work with the IRB in advance to understand the specific regulatory requirements and operational details rather than trying to figure them out when the situation arises. While outside the scope of this article, pharmacists should have an understanding of FDA emergency use regulations and their institution's policy for emergency use so they can facilitate the appropriate use of drugs or devices when emergency-use situations arise.

Exemption from the regulations does not necessarily mean IRB review is not required. Many institutions do not allow individual investigators to determine whether a study is exempt.

Institutional policy will often require the IRB to make this determination, although it is usually through a streamlined process. While some studies may qualify for exemption, an IRB can be more restrictive and can require whatever type of review it determines appropriate. Even if a study is exempt, investigators must continue to assess the study—especially if any changes are made—to ensure that it continues to meet the criteria of exemption. An investigator should always check institutional policy regarding who is allowed to determine if a study is exempt and consult with the IRB if there is any question as to whether an ongoing study continues to qualify for exempt status.

Expedited IRB review

Research that does not qualify for exemption but poses minimal risk and fits at least one of the defined allowable categories may be reviewed by expedited procedures.²⁰ For a study to be minimal risk, it cannot present any risk greater than risks experienced in daily living or routine physical or psychological examinations; cannot place the subjects at risk of criminal or civil liability; and cannot be damaging to the subjects' financial standing, employability, or reputation. Categories of research that qualify for expedited review include drugs or devices where an investigational new drug application or investigational device exemption is not required; defined quantities of blood in healthy or nonhealthy subjects; collection of biological specimens for research purposes by noninvasive means; noninvasive clinical procedures that do not involve general anesthesia, sedation, or radiation; data, documents, and records collected for nonresearch purposes; voice, video, and image recordings made for research purposes; and surveys, interviews, or focus groups of individual or group behavior or characteristics. Pharmacy practice studies that involve the re-

view of medical records and surveys of pharmacists, physicians, nurses, or patients are types of research studies that may meet the requirements for review by expedited procedures. In addition, minor changes to approved studies and continuing review of specific types of approved studies may be reviewed using expedited procedures.^{20,21}

The use of the term "expedite" to define a specific type of IRB review should not be confused with "to go faster," the more common definition. Expedited review procedures allow the chair or an experienced IRB member to review and approve a study rather than requiring review by the full IRB, but the extent and depth of the review are the same. The reviewer must still make and document the same determinations required when the full IRB reviews a study. Issues that need to be determined include whether the study is no more than minimal risk and meets one of the expedited categories and whether the informed consent is appropriate or can be waived or altered.^{17,20} The material submitted for expedited review must be as well written as the material submitted for review by the full IRB in order to allow the reviewer to determine the approvability of a study. Because these types of studies do not involve the type of risk or the level of subject intervention or interaction as studies reviewed by the full IRB, there is a tendency to feel that the protocol and submission do not require the same attention to describing methodology or discussing subject risk. However, it is precisely because of this difference that a thorough discussion of methods and risks, such as confidentiality and privacy, is needed. Working with a colleague or mentor who is familiar with the methodological and ethical issues of studies that can typically be reviewed through expedited procedures can help in the development of studies that the IRB will find acceptable. Under expedited review proce-

dures, the study may be approved or require modification or clarification. After receiving written notice of approval, the investigator may begin the study. If modification or clarification is required, the investigator should provide a prompt and complete response to avoid delaying a final determination. If it is determined that a study cannot be approved using expedited procedures, it is referred to the full IRB for review.

Full IRB review

Research studies that do not meet the criteria for exemption or cannot be reviewed and approved through expedited procedures require review by the full IRB. Review occurs at a convened meeting of the IRB with a majority of members in attendance, including at least one member who is a nonscientist. Members review the submission form, protocol, informed consent, relevant grant applications or investigator's brochures (if applicable), and any recruitment material.²² Materials must be provided to members far enough in advance of the meeting to allow them to review the materials. Investigators should consult their IRB's policies and determine what material must be provided, the number of copies, and when materials must be received.

Following review and discussion, the IRB will vote to approve, disapprove, or require modifications for each study. If the study is approved, the investigator will receive written notification of the approval, at which time the study can begin unless additional institutional approval is required.^{9,11,22} An investigator should not begin research until he or she has written approval from the IRB in hand. If the study is disapproved, the investigator will receive written notice of the disapproval that includes the reasons for disapproval. The investigator should take the opportunity to meet with the IRB to discuss the disapproval. If the IRB requires modifications to the study or

has unresolved questions, these will be communicated to the investigator in writing. The investigator should provide a complete and prompt response. If the investigator is unclear about how to respond or what modifications are required, contacting the IRB for assistance and guidance and working with a colleague or mentor who has experience with the IRB and the type of research being proposed will greatly help in developing a response. Failing to provide a prompt, complete, detailed response will likely result in the IRB having additional questions and requiring additional modifications, which could delay the approval and start of the study.

Procedures for making changes

The study can begin once it is approved through expedited procedures or by the full IRB. It is important that the study is conducted exactly as described in the IRB-approved protocol. Any changes to the protocol, informed consent, recruitment material, or any other material or documents must be reviewed by the IRB and approved before the changes are implemented. The only exception is an immediate change that is required to eliminate an apparent immediate hazard to research subjects.^{9,11,22} If this occurs, the investigator should be in contact with the IRB as soon as possible. Repeated protocol deviations may cause the IRB to question the appropriateness of the study or the investigator's ability to conduct the research. Once a study is approved, if the need to collect additional data, the need to alter for certain evaluations or events, or any other changes arise, the protocol should be modified and the modifications approved by the IRB. Failure to strictly follow the IRB-approved protocol or use only the most recently approved version of the informed consent represents a serious departure from ethical standards and regulatory requirements, which may result in investigator

sanctions and suspension of the study by the IRB.

Unanticipated problems

In addition to modifications, investigators are required to report any unanticipated problems involving risk to subjects or others to the IRB, appropriate institutional officials, and any supporting department or agency head.^{9,11} Although the phrase "unanticipated problems involving risk to subjects or others" appears in both DHHS and FDA regulations, it is undefined. Recent guidance indicates that DHHS intends to consider this phrase to include any incident, experience, or outcome that meets all of the following criteria²³:

1. Unexpected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document, and the characteristics of the subject population being studied,
2. Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research), and
3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

FDA has recently issued similar guidance in draft form.²⁴

Investigators should appreciate that the terms "unanticipated problems" and "adverse events" are not synonymous. Adverse events are thought of most often in the context of biomedical research and apply to physical and psychological harm. Unanticipated problems represent a larger universe of events.²³ Examples

of unanticipated problems that are not adverse events, but would need to be reported, include the loss of an unencrypted laptop containing sensitive identifiable research subject information and a dosing error with the potential for toxicity even if there was no detectable subject harm. Investigators should also be aware that other FDA regulations contain additional sponsor reporting requirements for adverse events and for reporting adverse events related to gene therapy. Multicenter studies, such as those sponsored by the National Cancer Institute, may also have their own event-reporting requirements. Most IRBs will also have their own local requirements for reporting unanticipated problems and adverse events. When conducting or participating in research studies, investigators will need to meet all applicable event-reporting requirements. Developing a study-specific operating procedure or flow chart will help to ensure that events are reported in a timely and appropriate manner. The requirements for reporting unanticipated events and adverse events are continuing to evolve. If an investigator is unclear on exactly what to report or how to report, he or she should discuss the reporting requirements with the IRB and study sponsor.

Length of IRB approval

All studies are subject to continuing review by the IRB at least once a year.^{9,11,25} When approving a study, the IRB will establish the duration of approval. The degree of risk posed by the study determines the length of IRB approval and when the IRB will conduct continuing review of the study. Continuing review must occur at least annually but may be more frequent. Continuing review must occur at a convened IRB meeting unless the IRB determines the continuing review can be conducted using expedited procedures. To conduct continuing review, IRB members

should receive and review a protocol summary and a study progress report (Appendix B).²⁵ It is important for an investigator to know the information required for continuing review, the local IRB continuing review policy, and the format of local IRB continuing review forms so that study procedures can be implemented at the start of the study to make sure the required information is collected and available at the time of continuing review. Most IRBs will require submission of continuing review material well in advance of the date that the continuing review is actually due. This is necessary to allow distribution of material to IRB members and to schedule the continuing review for an IRB meeting or for expedited review. While most IRBs provide notices and reminders, it is ultimately the responsibility of the investigator to make sure that he or she submits the study for continuing review and receives approval to continue the study. If the IRB requires any modifications or has any questions regarding the study, the investigator should address these as quickly as possible to prevent any lapse in study approval. If the IRB has not reviewed and approved a study by the continuing review date specified by the IRB, all aspects of the research must stop, including data analysis. The only exception is if the IRB finds that continuation of study interventions or interactions is in the best interest of individual subjects. The IRB—not the investigator—must make this determination.

IRB requirements for informed consent

Informed consent is central to the protection of human subjects.^{2,17} It is both a process and a procedure. The process of informed consent is the exchange of information that takes place between the subject and the investigator and study staff before, during, and after the study. The procedure of informed consent includes developing the consent form

and obtaining subjects' signatures. The informed consent process and procedure are equally important and necessary to ensure the protection of human subjects; both are considered by the IRB when reviewing a study.

The person obtaining consent must communicate openly and honestly and present information about the study in a manner that allows a subject to make an informed, voluntary decision about taking part in the study.¹⁷ This includes addressing any questions or concerns a subject may have about the study. Providing subjects adequate time to consider participation and an opportunity to discuss participation with their spouse, family, or friends is also important to ensure informed, voluntary consent. This should not be a one-time event. The investigator and other members of the study team should continue to explain the study and make sure of a subject's continued willingness to participate across the duration of the study. The discussions should always be conducted in a way that protects the subject's privacy and ensures confidentiality. For participants who do not speak English, simply having a translated copy of the informed consent is insufficient. Unless the exclusion of non-English-speaking subjects can be adequately justified, the investigator should include a plan on how informed consent will be obtained from these subjects.

By signing a consent form, a subject is indicating and documenting his or her willingness to be part of the study.¹⁷ Regulations provide the required and optional elements to include in a consent form (Appendix C).^{9,10} When developing an informed consent document, an investigator must make sure the information is understandable to the subject. Technical language should be avoided, and any unfamiliar terms should be defined in lay language. The use of short, direct sentences

and brief paragraphs will help make the document easier to read. The consent form must be an accurate representation of the study protocol. Inconsistency between the consent form and protocol or omission of important information that is present in the protocol will result in questions from the IRB and the need for revisions and will delay the approval of the study. Having colleagues and subjects (similar to those you plan to enroll) read and critique the consent form will help in developing an understandable document.

Whether the consent form must be signed and dated depends on specific DHHS, FDA, HIPAA, or other regulations that apply to the study. The IRB will often have institutional policy that provides guidance. All regulations require that each subject must be given a copy of the consent form.

When preparing a submission for the IRB, the investigator should indicate who will obtain consent. The investigator must make sure that everyone who obtains consent is knowledgeable about the study and understands the regulatory and ethical requirements. Where and when consent will be obtained should also be described, along with a plan on how the impact of any unusual or stressful conditions that might affect the ability to make an informed, voluntary decision will be minimized. The consent form should be developed carefully and proofread. Misspelling and grammatical errors make the information difficult to understand and will delay study approval. The investigator should have someone who is not familiar with the study review the consent form to help assess whether it is understandable. Because the consent form may be modified as the study progresses, the investigator must have a procedure in place to ensure that subjects sign the most current IRB-approved version. The signed consent form for each subject must be retained by

the investigator. A good practice is to confirm that a subject has a current signed consent form on file at the start of any study interventions or interactions. To assess the subject's level of understanding of the study and the information in the consent form, the investigator should consider using open-ended questions and statements such as

- In your own words, describe the purpose of the study.
- What more would you like to know?
- Explain to me what you think we are going to ask you to do.
- What are your concerns?

Waiver or alteration of informed consent

Although a signed consent is the default standard, there are instances when the IRB may waive or alter the requirement for the consent process.^{9,10} One or more elements of informed consent can be waived or altered if the IRB determines that the research involves no more than minimal risk to the subjects, the waiver or alteration will not adversely affect the rights and welfare of the subjects, the research could not practicably be carried out without the waiver or alteration, and, whenever appropriate, the subjects will be provided with additional pertinent information after participation.⁹ In a minimal-risk behavioral research study, where disclosing every detail of the study may alter the behavior under study and make the study scientifically unsound, the IRB may require a signed consent form but allow the investigator to leave some information out as long as he or she debriefs the subjects after their part in the study is complete. In a retrospective review of medical records, the IRB may waive the requirement for informed consent altogether.¹⁷ The investigator must provide sufficient justification for the waiver or alteration in the consent procedure. Simply because it is difficult, time-consuming, or

costly does not make it impractical to obtain consent.

There may be times where providing all or some of the elements of consent is appropriate but it may not be necessary to obtain a signed consent form.⁹ By linking a subject to a particular study, it may create a risk that would not otherwise exist. An example would be a minimal-risk study documenting an illegal behavior in which a signed consent form may put the subject and researcher at risk for criminal or civil liability.¹⁷ The IRB may also waive the requirement for signed, informed consent when the study presents no more than minimal risk of harm and when it does not involve procedures for which written consent is normally required outside of the research context. However, the IRB may still require the investigator to provide subjects with information about the research.⁹ A phone survey where the researcher and subject do not otherwise directly interact is an example of this type of waiver.¹⁷ These situations apply only to a waiver or alteration of informed consent under DHHS regulation. FDA regulations differ and only allow the waiver of informed consent in certain emergency situations.^{2,10,11} While both DHHS and FDA regulations allow for waiver or alteration of the requirements for informed consent, the investigator should always assume that obtaining signed consent is the standard for all studies and should provide clear, detailed justification for why the IRB should consider waiving this requirement.

Conclusion

IRB review is integral to ensuring regulatory compliance and ethical conduct of research involving human subjects. Working closely with the IRB or colleagues who have had experience with the IRB will help junior investigators better understand the IRB submission and review process.

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- Selection of subjects is equitable, taking into account the purposes of the research and the setting in which the research will be conducted, being particularly cognizant of the special problems of research that involves vulnerable populations, such as children, prisoners, pregnant women, mentally disable persons, and economically or educationally disadvantaged persons.
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative as required by regulation.
- Informed consent will be appropriately documented as required by regulation.
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Appendix B—Elements required for the continuing review progress report²⁵

- The number of subjects accrued
- A summary of any unanticipated problems and available information regarding adverse events
- A summary of any withdrawal of subjects from the research since the last institutional review board (IRB) review
- A summary of any complaints about the research since the last IRB review
- A summary of any recent literature that may be relevant to the research and any amendments or modifications to the research since the last IRB review
- Any relevant multicenter trial reports
- Any other relevant information, especially information about risks associated with the research
- A copy of the current informed consent document and any newly-proposed consent document

Appendix C—Elements of written informed consent^{9,10}

Required

Appendix A—Criteria for institutional review board approval of research^{9,11}

- Purpose of the research
- Description of procedures, identifying those that are experimental
- Description of risk
- Description of benefit
- Disclosure of alternatives
- Extent confidentiality will be maintained
- If compensation and treatment from injury are available
- Contact for research, subjects' rights, and adverse-event issues
- Participation is voluntary, refusal to participate will involve no penalty or loss of benefit
- Risks to subjects are minimized by using procedures that are consistent with sound research design, do not unnecessarily expose subjects to risk, and, whenever appropriate, use procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may reasonably be expected.

fits 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

- 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 unforeseeable
- Anticipated circumstance 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 that 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