Navigating the Institutional Review Board (IRB) Process for Pharmacy-Related Research

Marjorie Shaw Phillips, MS, RPh, FASHP^{,†}; Osama Abdelghany, PharmD, BCOP[‡];
Susan Johnston, PharmD[§]; Rachel Rarus, PharmD, BCPS[¶];
Jennifer Austin-Szwak, PharmD, BCPS^{**}; and Craig Kirkwood, PharmD^{**}*

ABSTRACT

Pharmacists' specialized training and knowledge qualify them to lead and engage in research pertaining to optimal medication use. Performing research promotes pharmacy professionalism and fosters interdisciplinary collaboration. To conduct research appropriately, one must have thorough knowledge of when institutional review board (IRB) approval is required and how to successfully navigate IRB processes. The overarching mission of the IRB overseeing research at an organization per federal guidelines is to protect the rights and welfare of human subjects participating in research. This article discusses the following general pharmacy practice-based considerations relating to IRB processes: strategies for developing research projects, key distinctions between quality improvement and research, practical considerations for submitting IRB applications and documentation, different categories of IRB submission, informed consent and conditions for waivers or alterations of consent, and principal investigator obligations for approved research. Pharmacists should also account for organization-specific IRB processes when designing, submitting, and implementing research projects.

Key Words— institutional review board, IRB, pharmacy research, pharmacy residents

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Pharmacists have special expertise and unique knowledge that make them particularly suited for participation and leadership in research related to safe and effective medication use and enhanced medication processes.¹ Pharmacy practice-based research is not solely the domain of those in academia, therefore, it is important for all pharmacists to know when institutional review board (IRB) approval is required for a project they plan to initiate and how to successfully navigate the IRB process. All research involving patients (as well as other human subjects) should be reviewed and approved, before initiation, by an IRB. However, not all pharmacy proj-

ects are considered human subjects research requiring the oversight of an IRB. Making the determination about whether a proposed project is research or performance improvement/quality improvement (QI), which could be exempt from IRB review, is an important first step because biomedical journals commonly require evidence of IRB approval or review as part of the publication process.²

Completing a “research” project has long been a rite of passage for pharmacy residents. Although the requirement for a project is unchanged from the 2005 standard, guidance supporting the new (2014)

^{*}Pharmacy Manager, Clinical Research and Education, Augusta University Medical Center, Augusta, Georgia; [†]Clinical Professor of Pharmacy Practice, University of Georgia College of Pharmacy, Augusta, Georgia; [‡]Manager Oncology Pharmacy Services, Yale-New Haven Hospital, New Haven, Connecticut; [§]Manager, Pharmaceutical Research Center, University of Wisconsin Hospital and Clinics, Madison, Wisconsin; [¶]Clinical Research Pharmacist and Medication Safety Officer, University of Toledo Medical Center, Toledo, Ohio; ^{**}Clinical Pharmacist Specialist, Internal Medicine, University of Chicago Medicine, Chicago, Illinois; ^{††}Assistant Director for Pharmacotherapy Services, VCU Medical Center, Richmond, Virginia. Corresponding author: Marjorie Shaw Phillips, MS, RPh, FASHP, AU Medical Center at Augusta University, 1120 15th Street, BI-2101, Augusta, GA 30912; phone: 706-721-0802; e-mail: mshillip@augusta.edu

American Society of Health-System Pharmacists (ASHP) postgraduate year 1 (PGY1) pharmacy residency accreditation standard makes clear that the resident's major project does not necessarily have to be research, specifically (Goal R2.2): "[residents] should have sole responsibility for, present, and prepare a manuscript for one major project to be completed during the residency. The major project could address quality improvement, a practice problem, or a research question."³ Pharmacy research is considered an elective competency area with Goal E1.1 to "conduct and analyze results of pharmacy research." Similarly, the ASHP accreditation standard for postgraduate year 2 (PGY2) pharmacy residency programs simply refers to residents' "projects" rather than research.⁴

Participating in practice-based research and completing other projects is one way that residency preceptors can demonstrate "ongoing professionalism, including a personal commitment to advancing the profession" (Standard 4.8.f).⁵ In order for pharmacists to be effective in initiating practice-based research and key contributors in collaborative health care research, they must understand the role of the IRB in human subjects protection, comprehend the organization's IRB policies and procedures, and be able to apply federal regulations for study conduct, informed consent, patient privacy, and data security to the project.

CHARTER AND MANDATE FOR THE IRB

An IRB is a body that oversees research and clinical investigation at an organization in order to ensure that all regulatory and ethical standards are met. The role of the IRB is to protect the rights and welfare of human subjects (participants) in research, and this obligation must take precedence over the interests of any researcher or organization. Documents submitted to the IRB should provide justification for the research and a plan for the conduct of research. The IRB provides oversight of research during the life of a protocol to confirm that the benefits continue to outweigh the risks, that the risks are minimized, and that the project should continue (continuing review).

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research⁶ issued the Belmont Report in 1979 and established 3 basic ethical principles of human subject research – respect of persons, beneficence, and justice.⁷ The Department of Health and

Human Services (DHHS) regulates the protection of human research subjects in order to limit harm to participants in what has become known as the Common Rule.^{8,9}

PROJECT DEVELOPMENT

Designing a research project can be a challenging task for residents, students, and practitioners. Fortunately, several review articles and resources are available to guide research novices through this process.^{2,10} The ASHP Research and Education Foundation has compiled a list of resources to support researchers with topics covering the continuum from establishing timelines at project initiation to submitting the manuscript.¹¹ The key components of project development are identifying a problem and formulating a research question, methods and project implementation, outcomes and data analysis, and presentation and publication of the results. Close attention to every step and careful planning will lead to successful implementation of the project and will enhance the quality of the results.

Idea generation is the first step in conducting a research project. Pharmacists should identify a broad area of interest, search the existing literature, and then pinpoint areas where knowledge gaps exist. In general, projects should aim at creating new knowledge, improving patient care, or developing a new approach to a clinical or operational problem. The topic should be stimulating, relevant, and ideally be important to the profession, institution, or department of pharmacy. Pharmacists should be encouraged to discuss their ideas and concepts with colleagues and managers for input and feedback before embarking on a research project. A robust literature review is essential to identify current needs, avoid unnecessary duplication of projects that have been adequately conducted, and ultimately better refine and focus the research question.

The development of the research question is the most important aspect of a research project. The FINER criteria – feasible, interesting, novel, ethical, and relevant – outline the desirable properties of a research question and are often used to increase the chances of designing a successful project.¹²

It is critical to clearly define the scope of the project when developing the research question. The project aims need to be achievable and realistic. The scope of the project and the nature of data will guide the methodology and design selection process. Several elements should be considered during this stage

of project development: the need for IRB review and approval, inclusion/exclusion criteria, how the variables of interest will be measured, source(s) of data, data collection procedures, and timeline for project completion.¹³ It is helpful to think about the team and expertise required to complete the work and about endorsements and engagement needed from other health care providers and key stakeholders within the institution. Practitioners without working knowledge of statistics should involve and consult with a biostatistician at the beginning of the project regarding sample size, data collection, and data analysis.

The results of a well-designed study or project can have a positive impact on patient care within the institution. However, knowledge sharing and the dissemination of the research findings are equally important. Pharmacists and pharmacy students are encouraged to publish their results in peer-reviewed journals or through poster presentations. If a specific biomedical journal is being considered, the project team should be familiar with its submission requirements, including the need for IRB approval, before initiating the protocol. The journal may require written documentation supporting an author's contention that IRB oversight was not required for a project.

RESEARCH VERSUS QUALITY IMPROVEMENT

Many projects undertaken by pharmacists or pharmacy students are not research but fall into the quality improvement domain; however, misconceptions surrounding regulatory requirements persist. During planning, one should determine if a project contains elements of (human subjects) research, thus requiring IRB review, or whether it does not require IRB oversight. Accessing and/or collecting protected health information as part of the feasibility assessment or design stage of a research project is in itself a research activity requiring approval. As IRB approval cannot be retrospectively granted, it is imperative that a project be correctly characterized before its initiation.

The DHHS regulations, 45 Code of Federal Regulations (CFR) part 46, include 4 subparts: subpart A, also known as the Federal Policy or the "Common Rule"; subpart B, additional protections for pregnant women, human fetuses, and neonates; subpart C, additional protections for prisoners; and subpart D, additional protections for children. The Common Rule defines *research* as a "system-

atic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge" and a *human subject* as a living individual about whom an investigator (whether professional or student) conducting research obtains "1) data through intervention or interaction with the individual, or 2) identifiable private information."⁸ A project analyzing administrative data or using an anonymous database of health care information is research, but not human subjects research, and therefore is not under the purview of an IRB.

The US Food and Drug Administration (FDA) regulations define clinical investigations, or clinical research, more specifically in terms of an experiment involving a test article and one or more human subjects. *Human subject* is defined in these statutes as an individual (either a patient or a healthy human volunteer) who is or becomes a participant in research, either as a recipient of the test article or as a control.¹⁴ Research involving a drug, medical device, or biologic product – the test article – used in humans will therefore require IRB review and oversight. Clinical investigations of marketed drugs may be exempt from the Investigational New Drug (IND) application requirements,¹⁵ but still require IRB approval. Nonclinical laboratory studies are not considered clinical investigations.

Often the lines between research and quality improvement (QI) initiatives are less than clear. QI has many definitions depending upon the practice in which it is being applied. The term is perhaps best described by Batalden and Davidoff, who defined quality improvement as the combined and unceasing efforts of everyone – health care professionals, patients and their families, researchers, payers, planners, and educators – to make the changes that will lead to better patient outcomes (health), better system performance (care), and better professional development (learning).¹⁶ At a simple level, QI can involve current processes, practices, and outcomes. The intent to publish results is not sufficient to characterize a QI project as requiring IRB review. However, the implications for failing to properly characterize a project as research (and forgoing the required IRB review and approval) can be significant, resulting not only in the inability to publish or present the results but also in disciplinary action or academic sanctions at the institutional level (such as loss of the ability to conduct research).

QI and research occur along a continuum but contain identifiable elements in the intent, methods, risk, and applicability of results.¹⁷ Focus on and examination of these elements of a project may make the distinction clearer. Many tools and articles have been published in an effort to assist the reader in performing a careful evaluation of a project for elements of research or QI. **Table 1** contains many of the questions that can be applied to specific domains of a project, along with the assessment of whether it falls into the research or QI category.

Classification of a project as QI does not signal the end of required regulatory evaluation. Institutional policies vary; some IRBs require that all projects (even QI) be submitted for their review and a formal determination that a project does not involve human subjects research. In some cases, a posted IRB policy can be provided as documentation that IRB

review is not necessary. For example, an IRB may state that retrospective data collection for a case report or case series involving 1 to 3 patients does not require IRB review because the information would not be considered generalizable (not research). Other IRBs may provide decision support and documentation in an alternative manner to avoid the time-intensive and costly review of projects that do not meet the regulatory requirement for review. Some institutions may have multiple IRB pathways—specifically designed for human subjects research or for QI—that have different submission requirements and review processes. Investigators should contact their organization’s IRB with questions or for clarification of institutional policies to ensure they are in compliance.

Table 1. Differentiating between research and quality improvement projects^{16,17,39-41}

	Research	Quality improvement
Purpose	To generate generalizable knowledge Project seeks to develop new knowledge (new paradigms, previously untested methods, or new untested standards). Intervention, interaction, or use of information occurs outside of the usual clinician-patient therapeutic relationship.	Practice or process improvement Project seeks to implement existing knowledge to improve care. Intervention would be considered within the usual clinician-patient therapeutic relationship.
Starting point	Knowledge seeking is independent of routine care and intended to answer a question or hypothesis.	Knowledge seeking is integral to ongoing management system for delivering existing care.
Motivation or mandate	Individual professional goal	Institutional mandate
Design	Protocol defined criteria that are not flexible. May involve randomization to treatment assignments.	Expected to change over time (iterative) Typically does not involve randomization to different practices or processes.
Benefits	May or may not be direct benefit. If there is a benefit, it is delayed or incidental. Societal benefit	Participants should benefit directly from the change to the practice or process.
Results	Published Expected to generalize beyond the study population.	Often published Extrapolation of results to other settings is possible but not the main intent.
Participant obligation	None	Yes, as a component of standard care
Risk	May put subjects at risk.	Risk to privacy or confidentiality of data
Funding	Often has external funding, eg, through a research grant (but funding is not a requirement for human subjects research)	Unfunded (institutionally supported or departmentally funded)

EXEMPTION FROM IRB REVIEW

If determined to be research (or a QI project containing elements of research), a project may still be exempt from DHHS (Common Rule) regulations requiring IRB oversight. The regulations do not specify who at an institution may determine that research is exempt, but the Office for Human Research Protections (OHRP) recommends that investigators not be allowed to make that determination due to possible conflict of interest.¹⁸ Variations in how a study is conducted and what data are collected can impact whether a study is exempt, therefore many institutions do not allow individual investigators to make this determination and require some level of IRB review.¹⁹ Despite the fact that researchers will not be making the exemption decision, it is important for them to understand the categories of research that may be exempt and how they can be applied. Investigators must take into consideration that these exemptions may not apply to research involving vulnerable populations such as children and prisoners.

There are 6 categories of research that may qualify for exemption from IRB review as defined in the Common Rule:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
 - a. information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
 - b. any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under 45 CFR 46.101 (b)(2), if:
 - a. the human subjects are elected or appointed public officials or candidates for public office; or
 - b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
5. Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:
 - a. public benefit or service program;
 - b. procedures for obtaining benefits or services under those programs;
 - c. possible changes in or alternatives to those programs or procedures; or
 - d. possible changes in methods or levels of payment for benefits or services under those programs.
6. Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approve by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture (45 CFR 46.101 (b)(6) and 21 CFR 56.104 (d)).⁸

In addition, the OHRP has decision charts posted on their website that can be utilized to help distinguish what types of research are exempt from IRB review or oversight.²⁰ Regulations are complex and often subject to misinterpretation. Failure to abide by regulatory criteria may have serious consequences for both investigator and institution. For this reason, investigators are encouraged to contact their organization's IRB prior to project implementation. Most IRBs are available for consultation and are interested in fostering collaborative relationships with investigators.

Consultation should be made well in advance to allow sufficient time for a thorough review.

CONSIDERATIONS FOR PROJECTS REQUIRING IRB REVIEW

Once researchers have consulted the IRB and determined the project requires IRB oversight, the next step is to prepare an application packet and submit the research project to the IRB. The research team will identify who will be the principal investigator (PI); this individual will be ultimately responsible for the submission, reporting, conduct, and closure of the study.²¹ Some organizations, especially academic medical centers, require the PI to be a permanent employee of the organization (ie, faculty or staff); therefore, trainees in limited employment (eg, pharmacy or medical residents) may not be eligible.²²⁻²⁴ In some organizations, the resident may be allowed to enter, upload, or submit the study information as well as make required changes as needed on behalf of the PI (ie, be a submission “editor”), but the PI is ultimately responsible for all aspects of the study. In other academic settings, the trainee may be permitted to serve as the PI but a faculty advisor must provide oversight.²⁵

Each organization will have expectations of the research team members, particularly the PI. These expectations are delineated in the IRB’s policies and procedures. Therefore, the organization’s IRB Office or Research Administration web page should be reviewed early in the project development process. Many of the expectations will be consistent across organizations, particularly for training requirements and research conduct. Most organizations will require all investigators to complete research subjects training, most commonly through the Collaborative Institutional Training Initiative (CITI),²⁶ and confirm their understanding of the Health Insurance Portability and Accountability Act (HIPAA) or the Privacy Act (this is often done through the organization).²⁷ Other training requirements may be modules for Good Clinical Practices (GCP)²⁸ and research ethics or multiculturalism, either prepared at the institution or from a commercial vendor. Some organizations may require the PI to have more comprehensive training than the other investigators. Organizations typically require the PI and other key research team members to substantiate their preparedness for their research roles by completing a form and/or submitting their curriculum vitae. Additionally, investigators (especially PIs) may be expected to report potential

conflicts of interest or financial interests prior to the submission of the actual research project. As a quality check, sign-off or administrative approval by the department chair or director of the PI is often required prior to IRB review.

Academic medical centers often will have more than one IRB. For example, a medical center may have multiple IRBs with one or more of the following roles: an IRB for exempt research review; one for bio-behavioral (as opposed to biomedical) studies; an external, contracted IRB for multicenter, industry-sponsored research; an external, contracted IRB for National Cancer Institute–based oncology group studies; and/or an IRB with a focus on research in a specialty area (clinical or vulnerable population). The number and characteristics of multiple IRBs are determined by the research enterprise to best meet the needs of the organization and are reviewed by DHHS/OHRP relative to the organization’s approved plan for IRB review of research, called the federal-wide assurance for the protection of human subjects, or FWA.²⁹ For efficient IRB approval, if the organization has multiple IRBs, the researcher should review their organization’s IRB web site and policy information to determine which IRB is most aligned with, and best suited to receive, their research proposal.

The IRB submission may be paper or electronic and either process may require “registration” with the IRB as a potential researcher and prerequisite completion of training. Electronic submission, which will reduce the paper burden but may present an unanticipated learning curve, is gaining adoption.³⁰ Software platforms used for electronic submission, subsequent communication, amendment, and continuing review submission will vary from organization to organization. Thus training and skill for one IRB software platform may not be applicable to others; however, the concepts should be similar since the processes within IRBs are common.

Informed Consent

Written consent documentation may be required for a research project that involves direct interactions with human subjects. The informed consent document must provide a thorough, albeit not comprehensive, presentation of the research benefits and risks to the subject/participant.³¹ Consents may follow either a paragraph or a question/answer format, provided that all elements are included. OHRP provides an overview of content to be included in an informed consent document,³² and the FDA has

issued guidance for electronic informed consent documentation.³³ Examples of different informed consent documents are available on the internet; however, one must ensure that format and content are optimal for the research project's subject population and meet institutional IRB requirements. Many studies have shown that informed consent documents have mistakenly been written at a reading level well above the general research subject population (eg, 8th grade), so the use of reading assessment tools in creating the document (including Flesch-Kincaid available in Word) is highly recommended.^{34,35} Informed consent is more than getting a signature on paper; it is an entire process intended to ensure that potential human subjects understand what their participation involves. In addition, special consent processes may need to be developed for those potential subjects who lack the capacity to provide consent, who are illiterate, and who have limited English-speaking skills.

Waiver or Alternation of the Consent Process

Obtaining the informed consent of research participants prior to their participation is considered a cornerstone for the ethical conduct of research and a key protection for subject's rights. Justification must be provided and IRB approval obtained if the PI does not feel it is necessary or appropriate to obtain the consent of subjects through signature on an informed consent document. A waiver of informed consent (typical for retrospective chart review studies) or an alteration in the requirements to obtain consent can be requested if certain criteria are met according the HHS regulations at 45 CFR 46.116(d):

- (1) The research involves no more than minimal risk to the subjects;
- (2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- (3) The research could not practicably be carried out without the waiver or alteration; and
- (4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.³²

Some university hospitals notify all incoming patients that their records may be reviewed for research purposes, whereas others provide patients with an opportunity to consent (or refuse to consent) to such use.

One commonly approved alteration of the consent process is to waive written documentation of

consent. In such a case, the IRB may require a written information statement (or invitation letter) that provides some or all of the elements that would be included in an informed consent document. This approach is simple to justify when the participant's consent is obvious (such as by completing a survey), but it may be reasonable when a patient is asked to provide some data that is not of a sensitive nature for research purposes as part of what would otherwise be a standard of care interaction or when the only record linking the subject and the research is the consent document and the principal risk would be the potential harm resulting from breach of confidentiality.

When protected health information (PHI) is collected, a waiver of HIPAA authorization must be granted in conjunction with the waiver of consent. The following 3 criteria must be satisfied for an IRB or Privacy Board to approve a waiver of authorization under the Privacy Rule (45 CFR 164.501, 164.508, 164.512(i):

1. The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
 - an adequate plan to protect the identifiers from improper use and disclosure;
 - an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
 - adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;
2. The research could not practicably be conducted without the waiver or alteration; and
3. The research could not practicably be conducted without access to and use of the protected health information.²⁷

ADDITIONAL CONSIDERATIONS PRIOR TO IRB SUBMISSION

Once it is determined that IRB review is required, it is important to have realistic expectations about the time required for institutional approval. Although the time from initial submission to IRB approval can

vary widely, national benchmarking data show an average of 35 days for an expedited review protocol from submission to initial approval, with 40% of this time due to investigator errors, omissions, and time spent responding to committee decisions.³⁶

Project preparation activities may be done concurrently with IRB review; this will allow the project to start quickly after approval has been obtained. Some organizations may require a scientific review of the protocol and approval from a research committee prior to IRB submission, so the deadlines and timeframe for this review must to be factored in. Investigators should determine whether there is

a charge associated with IRB review. If an organization's (rather than a commercial) IRB is used, it may be possible to apply for a waiver of IRB fees for an unfunded resident or practitioner project. Researchers should not underestimate the importance of considering data security during protocol development and documenting the safeguards they will employ as part of the IRB application packet. The institutional Information Security Officer or Information Technology Office can be a valuable resource along with organizational policies, such as a prohibition against storing research data on portable media or computers without suitable encryption protocols. Because

Table 2. Institutional review board reviewer checklist: Questions to consider for protocol review ^a

1. Research design
 - Does the investigator provide sufficient information for the reviewers to understand the theoretical basis for this study?
 - Is the study design sound?
 - Is the experience of the participants clearly described?
 - Are all of the study materials attached, such as questionnaires, interview questions, data collection forms?
2. Subject selection
 - Is the subject population described in sufficient detail?
 - Does the researcher say how many participants he/she hopes to recruit?
 - Is the sample size justified (sufficient to answer research question)?
 - Are all recruitment materials included (eg, website posting, flyers, letters of introduction)?
 - If there are different experimental conditions, is it clear how participants will be assigned? Is assignment equitable?
3. Risks and benefits
 - Are there any foreseeable risks to the participants?
 - Are the risks minimized?
 - Are foreseeable risks reasonable in relation to anticipated benefits?
 - If no benefits to individual participants are likely, are the benefits to society at large or to the field of study described?
4. Confidentiality
 - Have all direct and indirect identifiers to be collected been described?
 - If relevant, has the plan for protecting the confidentiality of the data been described, including storage (location, duration) of the data and access by others?
 - If identifiable data about illegal activities are to be collected, does the researcher intend to secure a Certificate of Confidentiality?
 - If participants are to be videotaped, photographed, or audiotaped and the recordings will be made publicly accessible, is a release form provided? (Does not apply in public settings.)
 - If the data are to be collected and stored via the internet, is the confidentiality protection plan technologically sound? (This may signal the need for review by the computer security consultant.)
 - Are there any limits to the confidentiality that the researcher can provide, eg, the requirement to report suspected child abuse? HIV status?
5. Compensation (if applicable)
 - Is the compensation commensurate with the level of respondent effort?
 - Is the compensation offered appropriate for the study?
6. Informed consent process (separate checklist for process, documentation, consent itself)
 - If any of the elements of informed consent are waived or modified, see checklist with criteria for waiver (all 4 must be met).
7. Protected health information (PHI) (if applicable)
 - If researchers access or collect PHI, is a HIPAA authorization signed by the participant or has a waiver of authorization been requested (all four criteria for waiver must be met)?

^aAdapted in part from Duke University's IRB Reviewer Checklist. <http://www.ors.duke.edu/researcher/reviewer-checklist%20http://www.ors.duke.edu/researcher/reviewer-checklist%20>. Accessed July 26, 2011.

breaches in research data and health information in general are common and newsworthy, the IRB will scrutinize the management plan for both electronic and paper data as yet another means of minimizing the risks to research participants.

When writing an IRB application, it is important to consider the reader. Protocols requiring full convened IRB review will be discussed by a panel of 5 or more individuals (and often as many as 24) from a variety of scientific and nonscientific backgrounds. Expedited review protocols are typically scrutinized by the IRB chair or a single expedited reviewer, who may not be familiar with health system processes or contemporary pharmacy practice. Identifying and contacting the reviewer or an administrative staff member in the IRB office could open important lines of communication and avoid unnecessary delay due to insufficient detail in the research submission. The IRB reviewer will use the following criteria to evaluate the protocol submission: risk mitigation, risk versus benefit ratio, and the process of fair and equitable subject selection. In addition, the IRB reviewer will assess the proposed process for informed consent, any privacy protections, data safety monitoring, and additional safeguards for vulnerable subjects. It would be beneficial to use the organization's IRB reviewer checklist as a resource while reviewing and editing the IRB application packet (see **Table 2**).

The IRB may conduct an initial administrative review and contact the study team with items that must be addressed or clarified prior to forwarding the protocol to the expedited reviewer, chair, or full committee. Responses to feedback or questions from the IRB should be prompt and submitted formally. Each IRB may have a specific format for the response, which should be carefully followed. The research project cannot start until a letter confirming final IRB approval is received and any other institutional approvals (if applicable) have been granted.

PRINCIPAL INVESTIGATOR OBLIGATIONS FOR APPROVED RESEARCH

After a research study has received initial approval by the IRB, the PI has continued responsibilities including reporting to the IRB to ensure the appropriate and safe conduct of research studies. First, adverse events must be monitored and reported in accordance with IRB policies. Written procedures for each IRB will vary with regard to which adverse events to report. In general, however, federal regulations mandate that the IRB is promptly informed

of any unanticipated problems (UAP) involving risks to human subjects.²¹ UAP encompass a wide scope of unexpected incidents, experiences, or outcomes beyond simply an injury or side effect in a participant; one example is a stolen laptop that could represent a data breach.

As research proceeds under an approved IRB protocol, a continuing review report must be submitted to the IRB. At a minimum, continuing review of IRB-approved research is done on an annual basis, although the duration of the review period is contingent on the level of risk associated with the research. In accordance with the Code of Federal Regulations on IRB functions and operations, an IRB may determine that some research projects require review more frequently than annually. Approval documents issued by the local IRB will specify the approval period of the study. Studies that are initially approved by the expedited mechanism are reviewed again annually as expedited. Studies that were previously approved by the convened route (full committee review) may be submitted for a continuing review through the expedited procedure if certain conditions apply, such as a full IRB committee determination that the protocol is minimal risk or the intervention phase of the study is complete and remaining activities are limited to data analysis.

Changes to an IRB-approved research protocol may not be initiated without IRB review and approval, other than in circumstances of immediate hazard to the participants. Amendments may be submitted to the IRB for changes in research protocol, safety information, informed consent updates, and addition or deletion of approved study personnel. The expedited review procedure can be utilized for reviewing minor changes in an IRB-approved protocol during the study's authorized approval period. For example, an IRB may permit a personnel change amendment (other than a change in principal investigator) to be submitted for expedited review.¹⁴ Changes that adversely alter the overall risk-benefit or that could potentially affect willingness to participate must be reviewed by the convened IRB.

HINTS AND TIPS

For successful navigation of the IRB process, it is prudent to utilize all resources that are available. This can begin with requesting a review of the study question or methodology from a peer, mentor, or research advisor. An individual who is intimately familiar with the study population and topic area may be able to

provide suggestions for endpoints or may help identify potential difficulties with data collection. A peer from a different specialty may detect areas that need additional attention prior to IRB submission. At some institutions, the IRB will offer presubmission consultations that can prevent delays and revisions in the committee review process. Additionally, statisticians can ensure sound methods are used, and informatics consultants may be able to assist with data collection techniques and resources.

It is of utmost importance to carefully review, understand, and follow the IRB application instructions. It is unfortunately common for protocol review to be delayed due to incomplete submissions (missing documents), failure to address questions, or lack of compliance with IRB procedure. Training required by the institution should be completed at the earliest opportunity to avoid delays in approval or release of the project. Once submission is completed, maintaining communication with the IRB office contact can help an investigator and project stay on track. The IRB should be kept up to date with any changes to the study and may offer advice for troubleshooting common problems. Most important, the PI and any research team members assisting with the IRB application must fully understand the study and the potential implications of the research project (desired outcomes, risks, benefits, and the possibility of unintended consequences). This will allow for a much smoother navigation process.

CONCLUSION

While many pharmacy practice-based projects are beyond the scope of the IRB, others require review. IRB process and roles are often not well understood. Because the lines between what constitutes human subject research (requiring IRB review) and QI (IRB review not required) may not be clear, it is important for the pharmacist to be aware of organization-specific processes to make that determination or to seek counsel of the IRB in a timely manner during the planning stages of a project. A detailed human subject protection plan, including the procedure for obtaining informed consent or justification for waiving or altering the informed consent process, and clear lines of communication with IRB officials and staff will greatly decrease the time required for IRB review and approval. Establishing a data security plan is essential to research project development. A data breach leading to unauthorized release of PHI or other confidential information is often the greatest potential

risk in minimal risk research such as medical record review projects. On September 8, 2015, a federal proposal was issued to revise the regulations governing the ethical conduct of research involving humans.³⁷ If they are ultimately adopted, some low-risk research and nonresearch activities may be excluded from the Common Rule, while other low-risk research may be exempted from certain requirements.³⁸ Pharmacists interested in practice-based research need to stay current as the regulations evolve.

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