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Points to Consider:

The Research Ethics Consultation Service and the IRB

Laura M. Beskow, MPH, PhD [Assistant Professor],

Duke Institute for Genome Sciences and Policy, Duke University, Durham, NC

Christine Grady, MSN, PhD [Head],

Section on Human Subjects, Department of Bioethics, National Institutes of Health Clinical Center, Bethesda, MD

Ana S. Iltis, PhD [Associate Professor],

Department of Health Care Ethics, Saint Louis University, Saint Louis, MO

John Z. Sadler, MD [Professor and Chief], and

Division of Ethics and Health Policy, Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, TX

Benjamin S. Wilfond, MD [Professor and Head]

Division of Bioethics, Department of Pediatrics, University of Washington School of Medicine, and Director, Treuman Katz Center for Pediatric Bioethics, Seattle Children's Research Institute, Seattle, WA.

Research ethics consultation was first mentioned in the published literature nearly 20 years ago when Singer and colleagues described a collaborative process between clinical investigators and ethicists to analyze the ethics of liver transplants using living donors.¹ Today, such consultation is increasingly recognized as a potentially valuable mechanism for addressing the depth and breadth of ethical issues that arise in research related to human health and well-being, including biomedical, clinical, translational, behavioral, and social science research. Representatives from academic institutions, including Johns Hopkins Bloomberg School of Public Health,² Stanford University,³ University of Texas Medical Branch,⁴ and Weill Cornell Medical College,⁵ as well as government agencies such as the National Institute of Environmental Health Sciences,⁶ have recently written about their research ethics consultation services. Further, the National Institutes of Health's Clinical and Translational Science Awards (CTSA) program, an initiative that aims to “transform the local, regional, and national environment for clinical and translational science,” encourages applicants to develop innovative research programs “that bridge clinical research ethics with other CTSA activities.”⁷ This language has generally been interpreted as encouraging something like research ethics consultation, and many of the institutions receiving a CTSA have developed or will be developing such a service.⁸

In addition to generating significant interest, the concept and emerging practice of research ethics consultation has generated lively debate,⁹ and fundamental questions remain: What is research ethics consultation? And what value does this activity provide beyond what existing institutional entities already offer?

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In this paper we examine how a research ethics consultation service may differ from and complement the role of an institutional review board (IRB). We offer a definition of research ethics consultation and explore the potential scope of a research ethics consultation service in terms of types of clients served, questions addressed, and assistance provided at various stages of the research process. We then consider the relationship between a research ethics consultation service and an IRB and the issues that may arise in this relationship, including possible conflicts of interest and problems with how to evaluate a research ethics consultation service.

We recognize that research ethics consultation services and IRBs are not homogeneous entities. Depending on the expertise available, resource constraints, and the kinds of research conducted at an institution, the purpose, composition, and function of a research ethics consultation service may vary considerably across institutions. Additionally, IRBs and/or individual IRB members can and sometimes do provide ethics consultation. Our goal is to describe a comprehensive range of research ethics consultation activities and to delineate the rationale for offering such consultation, while recognizing that a variety of models may be used. Regardless of the model adopted, a research ethics consultation service should be synergistic with the IRB in facilitating the ethical design and conduct of quality research.

IRBs and Research Ethics Consultation

The landmark Belmont Report¹⁰ identified three principles supporting ethical practices in the conduct of research, setting the stage for what are now considered the twin pillars of protection for human research subjects: informed consent and independent review of the risks and benefits of research.¹¹ These principles and protections form the core of federal policy governing human subjects research, codified at 45 CFR 46 and known as the Common Rule.¹²

According to the Common Rule, an IRB's mandate is to review proposed research to ascertain its acceptability in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. In order to approve a research project, the IRB must determine that risks to subjects are necessary, minimized, and reasonable in relation to anticipated benefits; selection of subjects is equitable; informed consent is obtained and documented appropriately (when required); and when appropriate, the research plan makes adequate provision for monitoring the data collected to ensure subjects' safety, protect their privacy, and maintain the confidentiality of data.

Over the past 25 years, transformations in the research enterprise and weaknesses in the current system of oversight have magnified and complicated IRBs' responsibilities.¹³ Commentators have questioned whether IRBs have sufficient time to reflect on the ethical issues that research protocols may raise given the administrative and regulatory requirements they have to follow¹⁴ and the fact that their members are not required to have ethics expertise or training in ethical analysis. The Common Rule requires only that an IRB has members with "varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution" and diversity in terms of race, gender, and cultural background.¹⁵ Although some IRBs do include ethicists among their members,¹⁶ ethical deliberation beyond regulatory requirements is sometimes seen as beyond the scope of the IRB.¹⁷

Concerned about whether scrupulous adherence to procedural elements of review actually enhances protection of research participants, MacKay highlighted the possible role of ethics consultation in research, calling it "an area of enormous potential to be developed to ensure substantive gains in safeguarding the right of individuals who become involved as subjects in research."¹⁸ He further suggested that the goal of research ethics consultation is to

“enhance the substantive deliberations and determinations of IRBs and to assist clinical researchers in carrying out their research.”¹⁹ Here, we expand this idea to encompass a general pursuit of ethical values in research and use it as a basis for defining research ethics consultation as:

an *advisory* activity available *throughout the lifecycle of a study*. It involves interaction between *researchers or other stakeholders* in the research enterprise and one or more individuals knowledgeable about the ethical considerations in research, regarding an ethical question related to *any aspect* of planning, conducting, interpreting, or disseminating results of research related to human health and well being. The purpose of the interaction is to provide information; identify, analyze, and/or deliberate about ethical issues; and recommend a course of action.

Potential Scope of a Research Ethics Consultation Service

Here we examine four aspects of a comprehensive research ethics consultation service—the clients who might use it, the research phases during which consultation might be sought, the issues and questions that might be explored, and the nature of the assistance provided—and compare and contrast the roles of a consultation service to those of the IRB.

Types of Clients

A research ethics consultation service should be created with the understanding that it serves the entire research enterprise, rather than a particular stakeholder. Thus, a consultation service can be made available to a variety of clients, including investigators, IRB members and staff, other institutional agents and committees, research participants, and research sponsors (see Table 1).

Investigators can seek a research ethics consultation throughout the lifecycle of their projects. They can also receive valuable assistance from an IRB, although not necessarily at every research stage. For example, due to resource constraints, some IRBs do not engage in extensive discussion of a study with investigators who have not yet submitted their protocol to the IRB.

The IRB or the IRB's representatives may seek a research ethics consultation in the context of reviewing a specific protocol, developing policy or guidelines, or in anticipation of reviewing a particular type of study. For example, faced with a scientifically important but ethically complex protocol, an IRB might request a consultation with experts who have specialized training—expertise that may not exist among its own members or staff— or simply to get a second opinion about the issues under review. Other institutional committees and agents, such as a conflict of interest committee or research integrity officer, could engage the research ethics consultation service to help develop or revise policies or for input about how best to handle particularly challenging cases. These entities could also confer with the IRB; however, their relationship with the IRB would involve shared authority over final decisions, whereas a research ethics consultation service plays strictly an advisory role.

Research participants (or parents/guardians/legally authorized representatives) could seek a consultation, although this may occur relatively infrequently because participants are instructed during the informed consent process to contact the IRB with any concerns they might have about the study. Nevertheless, a research team might occasionally direct a research participant to the consultation service, and some commentators have suggested that a research ethics consultation service be explicitly extended to research participants.²⁰

Finally, research sponsors—including biotechnology and pharmaceutical companies, as well as nonprofit organizations and community-based groups—might seek advice about a

particular study or type of research. Research ethics consultations may be especially appropriate when sponsors are collaborating with university investigators. However, concerns about conflict of interest and academic freedom may arise when an industry sponsor seeks a consultation, particularly when financial payments and/or nondisclosure agreements are involved.²¹

Research Phase

A research ethics consultation may be initiated at one or more times during the life-cycle of a study, as well as outside the context of any particular study (see Table 2). During the study design phase, investigators could request a research ethics consultation to help anticipate and explore ethical issues that might arise and to identify possible options to address these issues. Consultation during the design phase provides maximum flexibility for addressing potential ethical concerns and allows investigators to request the funding that might be necessary to address them.

In the absence of a research ethics consultation service, an investigator might be able to seek assistance during the design phase from an IRB member or staff person, or from someone familiar with ethical issues in research. However, when such individuals are not available or cannot undertake the kind of analysis needed, a consultation service could fill this void. For example, an IRB member contacted by an investigator to discuss a future study may not have time to conduct literature searches, gather expert input, or carry out other tasks that might be necessary to explore an issue fully. In addition, at institutions that use an external IRB, investigators may not have access to an IRB early in the process of designing their study.

During the phase of applying to a sponsor for funding or to an IRB for approval to conduct a study, a research ethics consultation service could help the investigator develop and explain the rationale for particular aspects of the study. This might include citing examples of other relevant research practices or explaining how a particular approach best fulfills the relevant ethical and regulatory requirements for human research. A consultation service could also help develop certain parts of the application, such as consent documents, recruitment materials, or supplemental educational information.

During the review process, the IRB might find it beneficial to initiate a consultation to discuss ethical issues associated with certain protocols, such as those involving novel technologies or a population of participants not often involved in research.

After the sponsor or IRB reviews the protocol, a research ethics consultation service may help when the sponsor and/or IRB raised ethical concerns and asked the investigator to justify an aspect of the study or to make changes to the protocol. In some cases, the IRB might give specific instructions about the changes needed, or an IRB representative might be available to discuss changes with the investigator. But in particularly complicated cases, research ethics consultation may be of value not merely to help the investigator formulate a response that would satisfy the IRB, but to understand fully the issues underlying the IRB's concern and to explore potential solutions. The investigator could initiate the consultation, or the IRB could specifically request that the investigator utilize the consultation service for this purpose.

When the research study is underway, a research ethics consultation service can assist with concerns that might arise, such as difficulties recruiting or retaining research participants, the behavior of research participants, unexpected research findings, and the disclosure of interim findings. Sometimes these concerns can be addressed simply by speaking with an IRB member or staff person, and any changes made to the protocol in response to these

types of issues would have to be approved by an IRB. However, if the issues are particularly novel or complex, research ethics consultation may be beneficial to investigators, participants, and/or the IRB.

After a study concludes, investigators might request a consultation about issues such as whether and how to disseminate research results that could be potentially stigmatizing to certain populations. These issues are sometimes addressed prior to initiating a study, but unexpected findings may lead to new questions and concerns. A research ethics consultation service might also help identify ways to communicate research results to participants and/or communities, or help sort out the thorny issues related to posttrial access to interventions. In addition, investigators, IRBs, other institutional entities, or research participants could use a consultation service to explore issues that emerged during the study that might influence future research. For instance, investigators might have encountered recruitment or retention problems during a study and may seek help to identify ethically appropriate alternatives to avoid these issues in the future.

Outside the context of a particular study, investigators, an IRB, or other institutional entities might request an ethics consultation—for example, when planning to embark on a new area of research or when developing or revising institutional guidelines.

Substantive Focus

Even when a study meets regulatory requirements, ethical issues and concerns can remain for which research ethics consultation may be especially useful. A research ethics consultation might address questions about study design, whether the inclusion and exclusion criteria are appropriate, and about the mechanisms for recruiting appropriately diverse participants. Other issues that might be addressed include identifying and assessing a study's risks and potential benefits, identifying ways to minimize risk and increase benefits, and exploring issues pertaining to the relationship between researchers and participants and between research and clinical care. Some studies may be more likely candidates for research ethics consultation because the issues involved are more complex. These include studies that involve the initial application of a technology or first-in-human trials, studies that pose significant risk of harm with little or no potential benefit to participants, and studies that raise ethical questions for which there is no authoritative consensus (see Table 3).²²

In some cases, investigators or others may seek information and assistance concerning ethical issues beyond the scope of IRB review, such as those surrounding research that does not involve human subjects (e.g., certain research using stored biospecimens and data) and questions about the potential societal implications and long-range effects of contemplated or ongoing human subjects research.

Nature of Assistance Provided

Research ethics consultants offer information, advice, and/or analysis in response to issues presented. Importantly, a consultation service provides nonbinding advice to clients; it is not imbued with the regulatory authority of an IRB or with the institutional authority of a committee whose decisions are binding. The assistance offered falls along a continuum of informal to formal. Informal assistance may be as straightforward as directing someone to existing institutional guidance about payment to research participants or how to request that the IRB waive the requirement for informed consent. IRB members and/or IRB staff also regularly provide this kind of information.

A more formal research ethics consultation may involve in-depth exploration of what the ethical conduct of a particular proposal or type of research might require, including advising on areas where existing guidance, regulations, or standards are silent, vague, or evolving. In

conducting such an analysis, the consultant would rely on broad ethical principles, ethical reasoning, and published literature related to the issue at hand and would generally provide the person requesting consultation with a written analysis of the issues and pertinent recommendations. In some cases, especially when there are novel or unsettled issues at stake, the consultation service may work with the requester to promote public discussion and debate, convene experts or consult others outside the institution, investigate the views of the relevant community (e.g., patients, investigators, or policy-makers), or conduct other appropriate empirical research on the issue. The results of these activities would then be used as the basis for assisting clients to determine how to move forward. These activities could lead to development of new policies or guidance, and/or broader dissemination or publication of the consultative findings.

In order to provide this range of assistance, consultants should have training or expertise in research ethics and ethical analysis, and the necessary time, skills, and institutional support to engage in analysis, investigation, and related activities. (Although beyond our scope here, defining specific competencies for research ethics consultants is an important issue.) While one or more members of an IRB sometimes have similar expertise or training, their role as IRB members does not always lend itself to in-depth analysis or planning and conducting community discussion or investigation. For instance, because IRBs are established in accord with and for the purposes described in the Common Rule, their primary goal is to interpret and apply the regulations. Thus, to some extent IRB deliberations are constrained by the need to comply with regulatory provisions. Typically, an IRB uses its limited resources to review research protocols and inform investigators about the outcome of its review, rather than to consider how its decisions might be used to guide the future conduct of research.

Models for a Research Ethics Consultation Service

Based on the similarities, differences, and potential areas of overlap in the roles of a research ethics consultation service and an IRB, three models exemplify the possible membership of a research ethics consultation service and its relationship to the IRB.

The Research Ethics Consultation Service and the IRB Are the Same Entity

In this model, there is no separate consultation service; consultation to investigators or institutional officials or others is available as needed from the IRB. This model is based on the premise that ethics consultation can and should be an integral and essential part of an IRB, not something outside of it. To some extent, this model has existed since the establishment of IRBs, although the role of IRB members as consultants has been hampered by limited resources, time, and sometimes expertise. When the IRB provides research ethics consultation, information about this service should be widely disseminated to investigators so they are aware of its availability and how and when to access it. This model would not work for institutions that rely on external IRBs.

The Research Ethics Consultation Service and the IRB Are Separate and Distinct Entities

In this model, individuals can serve on the IRB or the consultation service, but not on both. This intentional separation of membership serves to reduce conflicts of interest and to ensure that the independence and fairness of the IRB protocol review process is not compromised. For example, Cho and colleagues²³ describe the deliberate separation of the research ethics consultation service and the IRB at Stanford University as a way to minimize potential conflicts of interest. Although this approach may be feasible at some institutions, others will not have the resources to provide an adequate number of members for both entities. If individuals with ethics expertise are not on the IRB because they are members of the consultation service, the IRB would be deprived of their participation and thoughtful

contributions to IRB deliberations. When the two entities are distinct, there should be clear guidance for investigators and institutional officials about who to call for advice about different kinds of questions.

Distinct Entities with Considerable Overlap

In this model, there are specified divisions of labor between the research ethics consultation service and the IRB, but individuals can be members of both entities. Overlapping models can take various forms but are characterized by a decision that the consultation service and the IRB will have some members in common and will work together on certain issues. Sharing common members is seen as enhancing the activities of both entities and allowing for ethical synergy. There is evidence that several research ethics consultation services have adopted the overlap model.²⁴ The possibility clearly exists, however, for the intersection between consultation services and IRBs to be problematic, especially when a member of a consultation service is also an IRB member or is also the chair of the IRB. As discussed in the next section, communication between the two entities should be transparent, and rules should be established for the review of protocols when there is overlapping membership on the IRB and the ethics consultation service.

Boundary Issues

Because IRBs have regulatory and decision-making authority and the consultation service is designed to provide nonbinding advice to the requester, the potential exists for morally problematic situations when a research ethics consultant is also an IRB member. For example, should consultants who are also IRB members participate in the subsequent IRB review of a study on which they provided consultation? One concern is that the consultant will function as—or will be perceived to be functioning as—an advocate for the investigator's viewpoint. In such cases, the consultant/IRB member should ensure that the IRB is aware of his or her dual role. The consultant/IRB member could recuse him- or herself from IRB voting, from any IRB discussion of that particular study, or perhaps from both. Arguably, it may be appropriate for the IRB to ask the consultant to explain the recommendations he or she made to the investigator—somewhat comparable to asking the investigator or any other expert to discuss the study with the IRB.

It is worth noting that the concern about a consultant/IRB member being seen in the conflicted position of advocating for the investigator's viewpoint assumes that the investigator took the consultant's advice. It is entirely possible that the investigator chose not to follow the proffered advice, in which case it might be important that the consultant at least raise those concerns with the IRB. The risk in this course of action is that investigators may come to view the consultation service not as an independent source of assistance but rather as a policing agent that reports to and possibly biases the decision-making of the IRB.

Another question concerning the boundary between the research ethics consultation service and the IRB is whether consultants should advocate for an investigator's viewpoint even when the consultant is not a member of the IRB. If the consultant stresses concurrence with shared ethical principals among the interested parties and draws conclusions based on those principals, he or she can argue in favor of a particular decision in a specific case. This approach, constrained by procedural rules governing IRB meetings, seems a good use of a consultant's expertise. Again, however, the consultant's discretion and professionalism is essential to avoid the perception that he or she is a “hired gun” for the investigator.

Confidentiality in the consultative relationship could raise conflicts relative to the IRB. For example, a consultant might become privy to research information that is pertinent to IRB review, yet not routinely detected in continuing review of ongoing protocols or even in

audits of ongoing and closed studies. If the person requesting a consultation was promised confidentiality, the consultant could face a dilemma about whether to report the information to the IRB, especially if there is substantive potential for altering the risk-benefit equation for the research. Our presumption is that the consultant should respect the confidentiality of the requester, although we appreciate that there are justifiable limits to such promises. Although beyond the scope of this paper, we believe a thorough discussion of this issue is one worthy of its own treatment in a separate paper.

These issues suggest that potential conflicts regarding the roles of research ethics consultants and IRB members require careful attention. We offer several general recommendations based on the recognition of the problems and of the lost opportunities that could result by excluding consultants from the IRB setting:

- When developing a research ethics consultation service, establish a basic set of operating principles and policies regarding the relationship between the consultation service and the IRB, the management of potential conflicts of interests, and the reporting lines of authority for each entity.
- Consider establishing a default policy that prohibits a consultant who is also an IRB member from voting on a protocol for which he or she provided a consultation, but that permits the consultant's participation in IRB discussion of the protocol after disclosing the consultative role. Because each situation is different, permit exceptions to the default policy if both the consultation service and the IRB agree. Such exceptions might take into consideration appointing an acting chair when the consultant is also the chair of the IRB.
- If the consultation service and the IRB disagree about whether an exception should be made to a default policy, the decision should be made at a higher level within the institution (e.g., by the agents to whom the IRB and consultation service report, such as a dean or the administrator responsible for research oversight).

Evaluating the Research Ethics Consultation Service

Another important consideration in the relationship between the research ethics consultation service and the IRB is how a consultation service should be evaluated. Potentially appropriate metrics might include requester satisfaction, requester response to consultants' assistance, level of consultation activity, the frequency of identifying broader system or policy issues, and perhaps even the frequency of collaborations between clinical investigators and consultants. However, because evaluation metrics are value-laden, their final selection should be approached with caution. Consider, for example, a research ethics consultation metric that compares how often the IRB sent a protocol back to the investigator to make substantial changes for studies in which an ethics consultation was provided and for those for which no consultation was provided. If the consultant was also an IRB member, such a metric might create an inappropriate incentive for the IRB to make decisions that reflect favorably on the consultation service. More subtly, this metric might create an incentive for the IRB to review less thoroughly a protocol for which there was an ethics consultation under the assumption that the ethical issues had been vetted by another entity.

Assessing the effect a consultation has on the time from protocol submission to the IRB to the IRB's decision on that protocol is also problematic. A short IRB turnaround time may be of limited value as a metric if all it reflects is that conscientious investigators are more inclined to use the ethics consultation service and that doing so produces better protocols that move quickly through the IRB review process. This is a methodological problem, however, not an ethical one. More ethically problematic would be the consultant who is also

an IRB chair and who, in the latter role, influences turnaround time to improve the performance of the research ethics consultation service.

Another problematic metric is evaluating the research ethics consultation service against the frequency of IRB audits or problem reports from the Office for Human Research Protections or the Food and Drug Administration. This metric conflates the regulatory role of the IRB and the advisory role of the consultation service. Moreover, consultants do not control investigator behavior, nor do they have authority over or responsibility for day-to-day research operations. Neither the research ethics consultation service's responsibility to offer sound and justified advice nor the IRB's responsibility to provide a careful and thoughtful review of research protocols releases investigators from their responsibility to comply with regulatory and ethical requirements for research.

An appropriate metric to evaluate the success of a research ethics consultation service ultimately turns on the goals and objectives of the service—that is, on the aims of the consultation enterprise and the means used to accomplish those aims. It is not surprising that there is uncertainty about how one should measure success in this arena, much like there is uncertainty about how to measure the success of a clinical ethics consultation²⁵ service and of the IRB's review of research protocols.

Conclusion

A research ethics consultation service and an IRB are similar in a number of ways. Members of both entities are familiar with regulations and guidance governing research with humans, they exercise judgment in applying the regulatory provisions and guidance to specific situations, they work with investigators and others to promote the ethical conduct of research, and they play a role in supporting the research enterprise at their institutions. However, these entities are also different. Whereas the IRB's primary purpose is to interpret and apply federal regulations in order to protect human subjects, research ethics consultation goes beyond regulations when it engages in ethical exploration. An IRB has a diverse membership of scientists and others who have varying familiarity with ethical principles and ethical analysis. A consultation service usually comprises a smaller group of people with less diverse backgrounds, all of whom are trained in the ethics of research. The scope of a consultation service's involvement could include every stage of the research process and may span the range of considerations for evaluating the ethics of research.²⁶ Generally, IRBs have limited resources to provide services beyond their essential mission of reviewing research protocols to determine if they are ethically acceptable and meet regulatory requirements. Ideally, consultation services are established with the resources, time, and local support to engage in complex ethical analysis.

An overarching consideration regarding the relationship between a research ethics consultation service and an IRB is the overall goals of each entity and, by association, whose “agent” the research ethics consultation service might be. Some might consider the IRB to be primarily accountable to the institution, since it helps ensure that the institution complies with the Common Rule. Others might consider the IRB to be primarily accountable to research participants and thus would expect the IRB to give priority to the needs of research participants over those of the institution. We suggest that a research ethics consultation service has a more general “pursuit of the research good” as its primary interest. In other words, the goal of research ethics consultation should be to explore and identify the best ethical strategies to promote and balance mutually held interests related to the rights and welfare of research participants, the social value of research, and the integrity of the research enterprise. Thus, a consultation service should consider and weigh a range of values and interests that interact with the research enterprise and help identify ethically justifiable

approaches to pursuing a research project or program that considers and balances these interests. Although one could argue that an IRB should do this, IRBs are not explicitly designed for this purpose and may not have the expertise or resources necessary to offer research ethics consultation. Thus, the value that a research ethics consultation service adds over and above that offered by an IRB may include:

- service to a wider variety of stakeholders, including the IRB itself;
- analysis and advice throughout the lifecycle of a particular project, but most importantly during early design stages, as well as outside the context of a particular study;
- assistance by those with training and expertise in ethical analysis to address complex issues for which no consensus exists; and
- assistance that goes beyond existing guidance and regulations and is based on detailed ethical analysis, careful review of the literature, consultation with the public or experts, and the gathering of empirical data.

The emerging practice of research ethics consultation raises numerous other issues and questions that merit further dialogue and deliberation, such as the relationship between a research ethics consultation service and other entities related to research ethics (e.g., clinical ethics consultation, office of research integrity, research subject advocates); the types of expertise and competencies needed to provide research ethics consultation; the identification of valid metrics to systematically assess consultation service performance and outcomes; and sources of funding support for research ethics consultation.

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Table 1

Examples of Research Ethics Consultation “Clients”

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- **Investigators:** An investigator receives comments from a manuscript reviewer who suggests that her research methods were not ethical. The study involved a social networking analysis of alcohol use, and the IRB determined that it was exempt from the requirements of the Common Rule. The investigator is seeking an assessment of whether her study was unethical.
 - **IRB:** Investigators propose a study about posttraumatic stress disorder. Potential participants to recruit would be identified from publicly available records of serious automobile accidents. The IRB had rejected this proposal on several occasions because of the recruitment method, but now requests input from the research ethics consultation service about ethical issues related to recruitment and privacy.
 - **Sponsor:** A research sponsor is developing a new drug that would be used for a disease that primarily affects infants. The IRB is reluctant to approve the study because it believes further efficacy data from adults is necessary before approving a study involving infants. The sponsors want to understand the ethical issues involved in order to decide how to respond.
 - **Research participant:** A 50-year-old man enrolled in a study of pulmonary fibrosis was informed that he had a hereditary form of the disease, and thus his children were at increased risk. The man had given up his daughter for adoption when she was an infant and, as an adult, she had requested that he not contact her again. He is unsure whether or how to communicate with her about her risk of developing the disease and the possible influence of certain behaviors, such as smoking.
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Table 2

Examples of Consultation during Different Research Phases

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- **Study design:** A group of investigators are working on grant and IRB proposals for testing a new tumor biomarker in humans. The biomarker predicts tumor recurrence weeks to months before recurrence is detected by current technologies in animal studies, but has never been tested in humans. The research team seeks research ethics consultation because they are concerned about the ethics involved in disclosing the results of the biomarker study to research participants.
 - **Research review:** Investigators propose to establish a biobank using biospecimens obtained from pediatric patients admitted to a children's hospital. The IRB reviewing the protocol asks the research ethics consultation service for advice concerning the level of risk involved and the safeguards that should be employed.
 - **Study implementation:** Investigators conducting a study for a vaccine for children seek advice about how to approach the matter of obtaining assent from children who have not been told they are HIV positive.
 - **Poststudy:** The IRB and research integrity officer learn after a study is completed that part of the grant application for the study was plagiarized. The study had significant findings that may be important to clinicians. The IRB and research integrity officer seek research ethics consultation to explore the ethical issues involved in the decisions they must make about whether and how the data may be used, as well as options for sanctioning the investigator who submitted the proposal.
 - **Outside a particular study:** An investigator maintains an extensive collection of blood and tissue samples collected for her research in transfusion typing and cross-matching. After an outbreak of a new and serious blood-borne viral illness, she believes she can identify the virus proliferation in her old samples as well as currently banked blood at her institution. She seeks research ethics consultation because she is not sure about whether a "lookback" at her samples and blood supply constitutes research or quality assurance, and she is also concerned about the potential issues around privacy and disclosure of her findings.
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Table 3

Examples of Research Ethics Consultation Questions

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- **First-in-human studies:** Investigators want to inject phage libraries into humans to map their distribution. Based on extensive preclinical work, they hypothesize that phage could be engineered to home in to specific targets, with the future potential of serving as therapy delivery systems. They initially considered a traditional phase I population but decided that the risk of diminishing quality of life was too high. They seek research ethics consultation to help them find, if possible, a suitable and ethically appropriate research population.
 - **Studies that pose significant risk of harm:** Investigators propose a phase I surgical trial that poses significant risks in people who have progressive neurological disease, characterized by communication difficulties and declines in cognition. They request advice from the research ethics consultation service about how to ensure that participants understand they will not benefit from the study.
 - **Studies that raise ethical questions on which there is no consensus:** A researcher conducts clinical trials with depressed children and adolescents. One of the difficulties is that new drugs for the treatment of adult depression quickly become used for off-label treatment of pediatric patients without solid empirical evidence. His new study involves comparing a new antidepressant drug to a standard drug and a placebo. All subjects are followed for suicidal ideation and withdrawn from the study if suicidal potential is evident. He argues a placebo control is required in order to answer the scientific question about the efficacy of the new drug. The IRB deferred his study by a narrow vote because it disagreed about the need for a placebo. The IRB recommended a research ethics consultation to address the issue.
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