

RESEARCH ETHICS CONSULTATION SERVICES: State of the field and current directions

Prepared for the National Center for Ethics in Health Care based on the
experience of the Consultation Working Group of the CTSA Clinical
Research Ethics Key Function Committee

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PREFACE

This report was written at the request of the National Center for Ethics in Health Care, U.S. Department of Veterans Affairs (VA), to describe the state of the field about research ethics consultation. Robert Pearlman specifically asked that the following issues be addressed in this report:

- History of ethics consultation pertaining to research
- Characterization of the types and frequency of issues addressed through ethics consultations pertaining to research
- Characterization of who is involved in providing ethics consultations and how they occur
- The relationship between ethics consultation in research and (a) clinical consultation service activity, and (b) leadership
- The relationship between ethics consultations and IRBs and/or IRB functions
- Insights based on trends over time and experience, including success factors
- Caveats and anticipated future challenges

This report was written by Ben Wilfond and Elizabeth Dorfman. Ben Wilfond is a professor of pediatrics at the University of Washington (UW) School of Medicine and is currently the chair of the Consultation Working Group (CWG) of the Clinical Research Ethics Key Function Committee (CRE KFC) of the Clinical and Translational Science Awards (CTSA) consortium. Dr Wilfond has served as an IRB member on five IRBs over 18 years, has served as a bioethics consultant at seven institutions over 24 years, including 14 years providing research ethics consultations at the NIH Clinical Center and the UW. Lizzie Dorfman is a PhD student at the UW Institute for Public Health Genetics and is doing an independent study with Dr Wilfond on ethical and organizational issues related to data-sharing of research bioethics consultation, which includes participation in the CWG activities.

This report is based on Dr Wilfond's experiences and knowledge from his role as the CWG chair and on a review of the literature and of current websites by Ms Dorfman. The authors had access to three manuscripts in preparation by the CWG, 1. a paper describing the results of a 2010 survey of CTSA's, 2. a paper discussing the ethical issues facing consultants related to competing commitments towards requesters and institutions, and 3. a paper proposing a standard approach for data collection and data sharing. Additionally, Dr Wilfond and Ms Dorfman had access to proofs of the forthcoming research ethics consultation case-book by Danis et al. from the NIH Clinical Center. This report contains information from these manuscripts as well as insights based on workshops, meetings, and conference calls organized by the CWG.

The CWG currently includes approximately 50 members from 40 CTSA institutions who have some interest in these issues. The group published a manuscript on the relationships between IRBs and research ethics consult services in 2009 and conducted a survey of consultation services at the 46 CTSA institutions in 2010. A four-hour workshop at the 2010 American Society of Bioethics Humanities (ASBH) Annual Meeting was conducted for ASBH members who were interested in establishing such services, which allowed us to engage with non-CTSA institutions, as well as biotechnology companies, who are interested in establishing such services. In 2010, the working group received a one year supplemental award from the National Center for Research Resources (now the National Center for Advancing Translational Sciences) for a data-sharing and standardization project whose objective is to advance two important milestones towards the long-term goal of creating a system for CTSA's to share research bioethics consult data across institutions in a database for research, quality improvement and education. The project aims were:

1. Develop standard data collection practices and policies for research bioethics consultation at CTSAs that are requisite to creating feasible methods for data sharing between CTSAs.
2. Advance the development of informatics systems and policies that are requisite to sharing bioethics consult data between CTSAs.

The project coordinating committee included H. Taylor (Johns Hopkins), M. Danis (NIH Clinical Center), M. Cho (Stanford), J. McCormick (Mayo), R. Sharp (Cleveland Clinic), N. Anderson (UW), and B. Wilfond (UW/SCH). The coordinating committee shared responsibility for achieving the project aims and elicited further input by the establishment of workgroups that collectively included 24 members from 20 CTSAs and the project staff. These groups were the Descriptive Data Committee, Consult Process Policy Committee, Data Sharing Policy Committee, Informatics Strategies Committee, Productivity Committee, and the Software Development Group. One of the first activities for the project was the development of a discussion forum (www.ctsabiethicsconsult.org) to foster communication between CTSAs research ethics consultants.

The workgroups subsequently held monthly conference calls to develop recommendations that were presented at a project meeting (20 attendees) on June 7, 2011 in Cleveland, OH. At this meeting there was consensus that the informatics complexities and institutional concerns were significant barriers to the development of a prototype system for the sharing of *detailed narrative information* about research ethics consultation. It was agreed that these barriers would not be overcome during the project time frame. There was also a consensus that a more streamlined approach to a shared repository that would contain *minimal descriptive and narrative data* could be developed as a *functional* demonstration project. This approach would allow the participating consultants:

1. To use the repository to identify which consultants may have had similar issues in order to facilitate further “offline” discussion;
2. To better understand that range of research projects and the ethical issues that prompt research bioethics consultation; and
3. To determine if this approach is worth pursuing as a long-term CRE KFC project, with expanded scope and participation, and would justify the efforts expenses of addressing the noted barriers.

Over the summer and fall of 2011, the coordinating committee worked collectively, and through the specific workgroups, to define the structure and operating principles for the Repository. Eleven consult services agreed, in a memorandum of understanding (MOU), to participate in the Repository. The MOU reflected consensus decisions about managing confidentiality of the data, collaborative publication, and establishing a Repository Steering Committee of the 12 lead consultants. The participating institutions are Columbia University, Johns Hopkins University, Mayo Clinic, Medical University of South Carolina, National Institutes of Health Clinical Center, Ohio State University, Stanford University, University of Arkansas for Medical Sciences, University of California-Davis, University of Illinois at Chicago, University of Southern California, and University of Washington. Data collection began in January 2012.

The representatives of these 12 institutions and two other interested individuals comprise the CWG Steering Committee. While the CWG has been established within the CTSA consortium, the CWG steering committee is committed to underlying principles of open access and communication, and is motivated to explore how best to involve non-CTSA programs, such as the National Center for Ethics in Health Care.

INTRODUCTION

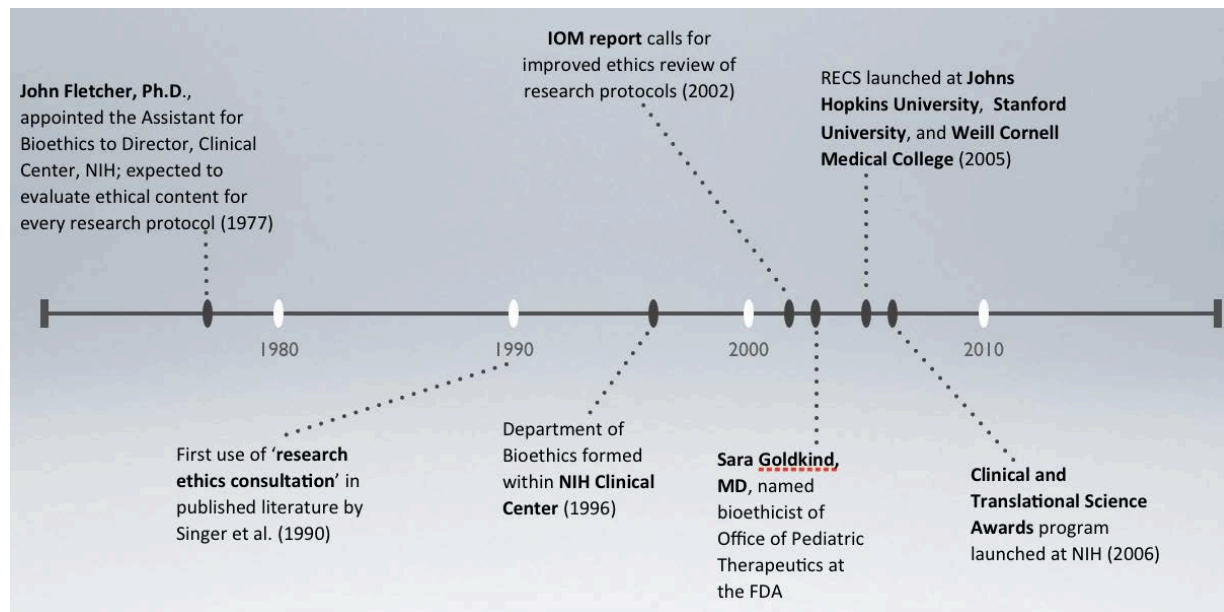
History

In contrast to many of the seminal documents, policies, and practices that serve to promote ethical research conduct, research ethics consultation (REC) was not born in the wake of violations, scandal, or public outrage. Instead, its origins were largely in the bioethics community's recognition that ethical challenges are common in many stages of the research process (McCormick et al. 2009), that some but not all ethical challenges can be anticipated (Danis et al. 2012, Cho et al. 2008), and that a focus on egregious unethical behavior neglects many interesting and important ethical issues that can occur in clinical research (Danis et al. 2012). Indeed the first instance of the term 'research ethics consultation' in the literature described an investigator-initiated process of incorporating ethical assessment into the clinical introduction an innovative therapy for liver disease (Singer et al. 1990).

In this same spirit of "going beyond the regulations," investigators have long sought informal guidance from ethicists to address challenging ethical questions related to their research (Fost and Farrell 1989). The first formal research ethics consultation service (RECS) was at the National Institutes of Health (NIH) Clinical Center, which in 1997 reorganized its clinical bioethics consult service to address the clinical ethical issues raised in the context of research and research participation (Emanuel 1998). Six years later, in response to the Best Pharmaceuticals for Children Act, the Office of Pediatric Therapeutics at the Food and Drug Administration (FDA) hired a bioethicist to provide ethics consultation, among other responsibilities (Franklin 2003). In 2005, amid mounting discussion of the insufficiency of IRBs for addressing complex ethical issues in some types of research (IOM 2002), a small number of academic medical centers also began to implement RECS. These included Johns Hopkins University, Stanford University, and Weill Cornell Medical College. The already growing interest was greatly intensified the following year with the launch of National Institutes of Health Clinical and Translational Science Awards

(CTSA) program. CTSA applicants were required to have procedures in place to address ethical concerns raised by their research, leading many applicants to develop RECS (Danis et al. 2012, McCormick et al. 2012). A 2010 survey of CTSA institutions found that 33 of the 46 institutions (70%) who had CTSA at that time had established a RECS (McCormick et al. 2012 draft). In 2012 the CTSA program had grown to 60 institutions, 44 of which (73%) have indicated the presence of a CTSA-related RECS or plans to create one. The number of RECS will likely continued to grow amidst continued and growing interest by the broader bioethics community.

Figure 1: Timeline of key events for RECS



It is important to note that while the development of RECS is relatively new and currently limited to a small number of institutions, many of the core activities have long been performed by individuals in other institutional roles. In some institutions, hospital ethics committees, institutional review boards (IRBs), research subject advocate programs, offices or research integrity, and others may offer advice about research ethics issues. The explicit “need” for organized RECS to address ethical issues related to

research remains an open question, and perhaps will depend on the ability of consultation services to demonstrate their value to requestors and the institutions.

Definitions

While there is no broad consensus regarding the definitions of research ethics consultation (REC) or research ethics consultation service (RECS), there have been efforts to describe and define the terms.

The first published reference to REC made no explicit attempt to define the term, but described collaboration between clinical investigators and clinical ethicists that the authors believed represented a prospective, public, and responsible attempt to address the ethical issues involved in the introduction of an innovative therapy (Singer et al. 1990).

Two definitions of REC have been published. Beskow and colleagues defined REC 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.” (emphasis in original) (Beskow et al. 2009). Danis and colleagues define REC as “a service provided by a team of consultants to assist clinical researchers, IRB members, research participants, and others involved in the research enterprise in understanding and addressing ethical issues raised by clinical research.” (Danis et al. 2012)

Only one definition of RECS has been published to date. McCormick and colleagues propose to define a RECS as “an individual or established group of individuals that is formally tasked with providing consultations to anyone involved in research activities who has research questions or concerns. Furthermore, an existing and publicized mechanism is in place by which investigators can contact a research ethics consultant in order to identify, analyze, and/or deliberate about ethical issues as well as to discuss a course of action.” (McCormick et al. 2012 draft)

Goals

There is wide spread agreement that the primary goal of REC/RECS is to promote ethical research conduct by providing real-time ethical guidance that is valuable to investigators and other individuals involved in biomedical research. This has been articulated in the published literature by RECS leadership at many of the pioneering institutions, including the NIH, Cornell University, Johns Hopkins University, and Stanford University, and has also been emphasized on the institutional websites of several of the CTSA-initiated RECS (Cho et al. 2008, de Melo-Martín et al. 2007, Taylor and Kass, 2009, Danis et al. 2012) (see appendix C for RECS websites).

Several secondary goals of RECS have also been proposed, including advancing ethics scholarship (de Melo-Martín et al. 2007, Danis et al. 2012), maximizing societal benefits from research (Cho et al. 2008), and improving institutional research culture (de Melo-Martín et al. 2007, Danis et al. 2012) and research environments. The extent to which individual RECS accept and work to achieve these secondary goals likely depends on local factors such as the experience and size of the RECS, relationships with other institutional agents, and institutional needs and priorities. Several of the potential secondary goals of RECS are natural extensions of, or are complementary to, the primary service-oriented goal. As one example, RECS are well positioned to identify emerging ethical issues related to frontier research,

and to initiate discussion of these topics at the institutional level and within the broader research ethics community.

Conflicts may exist within and among the varying objectives. Danis et al. use the example of a consultation that identifies one or more ethical issues in addition to the original reason for the consult, and the resulting need to balance the “interests of promoting broad ethical decision making and conduct with the possibility that being comprehensive may make the RECS seem like opening Pandora’s box” (Danis et al. 2012). Cho and colleagues, while acknowledging the ease with which REC generate material amenable to productive ethics scholarship, also note the possible consequence that scholarship-related intentions or incentives will influence case selection or the matching of cases and consultants (Cho et al. 2008). Thus, the enthusiasm of consultants to explore the complexities and layers raised in a consultation request may need to be tempered with the service-oriented goal of REC to serve the consultation requestor and address their specific question.

CONSULTANTS

The overarching function of a research ethics consultant is to provide ethical analysis and guidance for researchers and other RECS clients. While there are currently no established training requirements or core competencies for research ethics consultants, there are knowledge areas and skills that all such consultants should have, and additional attributes that may benefit those in the role. This list of broad areas is based on reviewing the ASBH core competency document (ASBH 2011) and the experiences of the CWG Steering Committee members.

Familiarity with ethical topics and ethical analysis: It is inherent to the role that consultants must be familiar with research ethics, including core topics, the history of the discipline, and emerging issues and current debates related to new techniques and research activities. (See appendices A and B for lists of research ethics topics and events based on several recent anthologies) It is also important that consultants are able to distinguish between ethical issues and issues that are not ethical in nature and more appropriately relate to a different discipline (Danis et al. 2012).

Knowledge of applicable regulations, laws, and policies: Closely related to research ethics expertise, it is also critical for consultants to be familiar with all applicable regulations, laws, and policies. This includes the history of ethical abuses and violations that prompted many of the current laws and regulations, as well as current interpretation and implementation of the regulations.

Institutional knowledge: Institutional awareness—including awareness of different groups, priorities, practices, and politics—is important for consultants in several ways. It can aid consultants in recognizing when an issue is under the purview of a different institutional entity, or when other groups should be involved in or made aware of a consultation. For example, in many institutions, the office of the ombudsman provides advice about research integrity concerns. Such awareness can also aid consultants in providing concrete, realistic suggestions to clients. Finally, institutional awareness is key to the identification and resolution of system-level issues that affect the research culture and environment.

Professionalism: REC is a young and evolving discipline, and it is incumbent upon consultants to adhere to professional standards. Specific to research ethics consultants, this entails maintaining an awareness of the limits of his or her knowledge, recognizing the potential for conflicts of commitment to the

institution and the requestor, and acknowledging the need to balance personal benefits with benefits to others.

Interpersonal skills: Communication and listening, attitude, and deportment collectively encompass interpersonal skills, which are as valuable in REC as they are in most other arenas. Strong interpersonal skills can promote trust and open communication between consultants and clients (Danis et al. 2012), which may increase the likelihood that the client would use the RECS again in the future or encourage his or her colleagues to do so.

Process skills: Process skills include the ability to gather information, recruit additional expertise, facilitate discussion, and build support and consensus. These skills are particularly useful and important for complex issues or cases that otherwise involve multiple parties.

Scientific expertise and biomedical research experience: From the earliest years of RECS, investigators have voiced the concern that ethics consultants have insufficient investigational experience and scientific expertise to understand their research (McCormick et al. 2006). A decent understanding of science and medicine enables consultants to grasp the special issues raised by particular research activities, however it may not be necessary—or realistic—for consultants to be so knowledgeable that they can immediately comprehend all possible scientific intricacies of a study (Cho et al. 2008). Instead it is more important that consultants have adequate resources to involve additional consultants and scientific experts as necessary.

SCOPE OF CONSULTATIONS & CONSULTATION SERVICES

Clients

Most RECS have a policy defining who is permitted to request a consultation, and many publish their eligibility criteria on their RECS website and other promotional materials (see appendix C, H, I, and J). Eligibility consistently includes investigators, and the 2010 CTSA survey of RECS found that principal investigators are the most frequent RECS clients (McCormick et al. 2012 draft). Many RECS also accept consult requests from other members of research teams (e.g. study coordinators, nursing staff, research assistants, trainees, and laboratory technicians), IRB members and chairpersons, and other institutional officials involved in research oversight. Some RECS accept consult requests from individual research participants or their legal surrogates, and a minority accept requests from individuals and groups that are not affiliated with the institution, such as non-profit agencies, governmental agencies, and companies or other for-profit study sponsors (McCormick et al. 2012 draft). See Table 1 for some examples of consultation questions that could be proposed by several different types of clients.

Table 1: Examples of Research Ethics Consultation “Clients”

- **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.

(Beskow et al. 2009)

Research Phases

REC is typically available to requestors throughout the lifecycle of a study and even outside of the context of a specific study (Beskow et al. 2009, Cho et al. 2008). While ethics consultation during earlier stages of research can be advantageous for anticipating issues (Cho et al, 2008), there is broad agreement that ethical issues can emerge or be identified at any stage of the research lifecycle (Van Laethem and Henry 2008). Many consultation requests relate to questions about determining appropriate research design and methodologies, recruiting and enrolling research participants, analyzing data, and reporting results (Danis et al. 2012). Table 2 includes examples of REC-appropriate questions from several different research phases.

Table 2: Examples of Consultation during Different Research Phases

- **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.

(Beskow et al. 2009)

Availability of Consultants

Some types of REC requests are more urgent in nature and require an immediate response. It may be appropriate to have 24-hour RECS coverage or another formal process for handling urgent requests at institutions where such situations are likely to occur. For example, the Consultation Service for the Department of Bioethics at the NIH Clinical Center frequently receives requests for consultations when there is uncertainty regarding an individual research participant's capacity to consent to a study and the prospective participant is on the premises. Accordingly, the Consultation Service is staffed at all hours and may be at the prospective participant's bedside within one hour of the consult request (Danis et al. 2012). At present, only a minority of RECS informational websites includes information about the expected response time for new consult requests, or processes for urgent cases.

Substantive Boundaries

The overall vision put forth by leaders in the field is that REC be available for “ethical question[s] related to *any aspect* of planning, conducting, interpreting, or disseminating results of research related to human health and well being” (emphasis in original) (Beskow et al. 2009). However, given the very broad range and scope of issues and questions for which investigators and other requestors might seek a consultation, some RECS have attempted to provide further clarity regarding which topics and types of issues and questions are, and are not, eligible for REC. This can be useful both in informing staffing decisions and appropriate consultant expertise and training, and also in proactively setting expectations for requestors

An issue may not be appropriate for REC because it is not an ethical question, or because it is more appropriately addressed by different institutional groups or resources; including IRBs, offices of research integrity, research oversight committees, institutional animal care and use committees, legal counsel, ombudspersons, and bioinformaticians; or relates to compliance with rules from governmental entities such as the FDA or the National Science Advisory Board for Biosecurity. Requestors may not be familiar with these groups, or might incorrectly believe their issue to be ethical in nature. In such situations, it is useful for RECS to have processes in place to refer requestors to the resource or group best equipped to address their issue or concern.

Only a small number of RECS publicize issues that are not appropriate for consultation, and among these there is considerable variation, likely reflecting variability in institutional resources and RECS experience. The most common types of issues for RECS to explicitly disclaim in written materials are matters of law (Danis et al. 2012, Harvard, University of Iowa, University of Miami, University of New Mexico), institutional policy (Harvard, University of Iowa, University of Miami, University of New Mexico), and

animal use and care (Harvard, University of Iowa). These limitations are typically justified because of other institutional resources that are available and can more appropriately address these issues. There are also some issues where RECS coverage varies among institutions, including questions of authorship, alleged misconduct and conflict mediation, assistance with regulatory review, and matters relating to individual research subjects.

While some RECS address issues related to individual participants, this is not common and these questions are more commonly handled by either clinical ethics consultation services or research subject advocates programs. As mentioned, at the NIH Clinical Center, the ethics consultation service includes both clinical and research issues about individual patients.

Services Provided

The nature and form of consultation services can vary based on the needs of the client and on the RECS. Client-based factors that influence consultation products include the novelty, scope, and complexity of the issue; the level of urgency; and the type of assistance requested by the client. RECS-based factors include the resources available to, and expertise of, the consultants, as well as institution-specific policy decisions regarding what types of services RECS will offer.

In addition to educating clients regarding ethical issues and providing advice related to the specific issues or questions that promoted the consultation, RECS may also provide other services to clients. Some consult service may provide advice on consent forms and processes, although such advice does not eliminate the need for IRB oversight. Some consult services, such as the one at the NIH Clinical Center, provide assessments the capacity of individual research participants to consent to be in research. Conflict mediation and resolution is likely less common in the research content than the

clinical ethics contexts, but some consultation services may address conflicts between members of a research team or between a research group and an IRB. Some conflicts may be addressed by providing advice to one party in the conflict. Occasionally, consult services may convene multidisciplinary groups of individuals all affected by or relevant to an issue, and identifying and seeking to address system-level issues that contribute to ethical challenges.

In contrast to IRBs and other institutional committees whose decisions are binding, RECS provide non-binding advice to clients (Beskow et al. 2009). A key divide among RECS is whether clients are provided with a specific recommended course of action, or are instead offered information and processes with which they can proceed and make their own decisions. The latter might include a summary of possible courses of action and the probable ethics-related consequences of each option.

CONSULTATION PROCESS & OPERATIONS

Consult Initiation

Individual institutions have devised a range of methods and media through which investigators and other eligible RECS clients can initiate a consultation. These include phone-, email-, and web-form-based systems. A majority of RECS maintain publicly available websites that include information on the consult initiation process (see appendix C).

As a part of the consult initiation process, it may be useful to have prospective RECS clients provide basic information such as their name, role, and contact information; a description of the issue or question; any relevant project or study materials; and an indication of the urgency of the request. This information

can aid in the initial evaluation and prioritization of requests. At present, however, only a minority of RECS websites asks prospective clients to prepare or provide this information.

REC are voluntary and client-initiated, so RECS utilization requires that investigators and other eligible individuals know that the RECS exists and how to initiate a consultation. As IRBs and other institutional agents involved in research practice and oversight may also refer investigators to RECS, it is also useful for these groups to be aware of the consult initiation process. The importance of both RECS publicity and institutional relationships are discussed in more detail later in the text.

Consultant-Client Interactions

REC initiation is followed by communication between the requestor and a consultant or administrator from the RECS to confirm the appropriateness of REC, clarify the ethical issue or question, and set expectations for the client related to the consultation process and products. Important information to share with clients at this early stage includes the non-binding and advisory nature of consultations, the expected time-frame for conducting and completing the consultation, and which aspects of the consultation are or can be kept confidential.

Some straightforward ethical issues and questions can be adequately addressed in a single exchange between the client and a consultant. However, the diversity of perspectives that results from involving at least two consultants can be valuable even for less complex questions. For consultations involving novel or nuanced issues, it is common to involve at least two consultants. In the event that more than one consultant is involved in a REC, it is useful to designate one lead consultant who is responsible for client communication, coordination of any external stakeholder involvement, convening meetings, and any written reports or other consultation products.

More complex questions and issues may require multiple exchanges between the requestor and the consultants, and the involvement of other individuals and groups. The latter can include individuals with subject matter expertise, other members of the research team who are involved in the issue or the study's decision-making process, and representatives from institutional groups that may be affected by or otherwise interested in the topic and outcome. While sometimes more logistically challenging, in-person meetings can facilitate relationship building between clients and consultants and allow for more open communication around complex or contentious issues. In general, consultants should be flexible regarding the method of communication and the involvement of others, and decisions should be based on nature of the consult and the resources available.

Consultation Products

More than half of RECS who responded to the 2010 CTSA survey indicated that they provide formal written reports to clients at least some of the time (McCormick et al. 2012 draft). The content of such reports likely varies among institutions, but can be expected to include background information; a description of the initial request; a summary of the discussion and the ethical, social, and other issues identified during the consultation; and any guidance or specific recommendations that were provided to the client (Cho et al. 2008, Danis et al. 2012). An example REC report from the University of Washington, is included as appendix D. This particular REC was subsequently developed into a publication (Tarini et al. 2008).

Written reports can have instrumental value to the RECS not only to document the consult for REC tracking, but also because of its symbolic impact on the requestor by providing a “tangible product”. In

some cases, the requestor may share the consult report with others such as IRBs, journal editors, or grant review bodies.

Tracking & Evaluation

In addition to documenting information to include in a formal written report for the client, RECS may wish to track additional types of information to facilitate RECS reporting and evaluation. While no national standards or best practices have been published regarding appropriate methods of evaluating RECS or the types of data necessary for such an evaluation, in early 2012 the CRE KFC Consultation Working Group Steering Committee defined a common set of data elements to be collected by RECS for purposes including internal tracking and institutional reporting. The proposed common data elements include information related to the client (e.g. name, department, role), the study (e.g. type and stage of research), and the consultation (e.g. the ethical question, services provided, and outcome), as well as process information (e.g. time to resolve, number of consultants involved, types of interactions between consultants and client) (see appendix E for the comprehensive data collection form). These data fields are currently available to CTSA consultants via the CTSA consultation web forum (www.ctsabiioethicsconsult.org) but are not yet in wide use. However, in January 2012, 11 institutions began actively collecting and sharing a subset of these data elements (see appendices F and G) to evaluate their utility as part of a yearlong demonstration project.

UTILIZATION OF CONSULTATION SERVICES

Frequency

There are at least 33 RECS across the US, with most located at institutions affiliated with the CTSA program (CTSAs) (McCormick et al 2012, draft). Few data exist describing the frequency of REC requests

at individual institutions, and the data that do exist show that there is significant variability in RECS utilization across institutions.

The 2010 survey of the 46 CTSA that existed at the time found that of the 33 CTSA with RECS, just 14 had performed any REC in the previous year. Of those who had performed any REC, a majority had done fewer than 5 consultations (see Table 3) (McCormick et al. 2012, draft). These numbers likely reflect the relative novelty of REC as a formal service at CTSA and inconsistent formal tracking of REC activities to date.

Table 3: REC in Previous Year	
# REC	% (N)
1 - 4	24 (8)
5 - 10	3 (1)
11 - 15	9 (3)
16 - 25	6 (2)
>25	3 (1)
(McCormick et al, 2012 draft)	

Institutions with RECS that preceded the CTSA program have reported slightly higher utilization rates. The Benchside Ethics Consultation Service at Stanford University performed 20 consultations between 2005 and 2008 (Cho et al. 2008). The RECS at Johns Hopkins University reported 76 REC between 2005 and 2007 (Taylor and Kass 2009). On the extreme end of the spectrum, the Clinical Center Bioethics Consultation Service at the NIH, has completed over 1000 consultations since they first instituted an electronic database to track consultations in 1999 (Danis et al. 2012).

Topical Distribution

Outside of a small number of institution-specific program summaries, little has been formally documented related to the range and distribution of questions and topics put forth for REC. The most detailed report on this topic to date was from Johns Hopkins University (JHU) in 2009. Taylor and Kass report that the RECS at JHU most commonly faces “issues related to the informed consent process,

study design, the population under study, and research risks and benefits” and encounters relatively few regulatory questions, even though the JHU RECS is open questions related to research regulations (Taylor and Kass 2009).

Several active projects will help to shed more light on the distribution of consultation topics. In April of 2012, the Clinical Center Bioethics Consultation Service at the NIH will publish a casebook based on the service’s decade of experience providing REC. The CWG Steering Committee of the CTSA CRE KFC recently commenced a demonstration project involving 11 institutions in which participating RECS will share both retrospective and prospective REC data via a centralized repository. (See appendices F and G) There are several goals of this project, one of which is improved characterization of the volume and types of REC at the national level.

Given the voluntary and client-initiated nature of REC, the topical distribution of REC can be viewed as an indication of the types of ethical issues that requestors *knowingly* encounter in their research, and not necessarily representative of the complete distribution of ethical issues that investigators and other clients face. Related to this point, in early 2012 Havard and colleagues, using six years of experience with RECS at Stanford University, proposed a list of triggers for REC (Havard et al. 2012). The triggers primarily broke down into two themes: frontier research topics that can raise novel issues that fall outside of the scope of current regulations and established ethical practice, and areas of known regulatory and ethical uncertainty. Examples of the former could include innovative therapies and procedures; studies involving rapidly evolving technologies with the possibility of incidental findings, such as whole genome sequencing; and studies involving novel approaches to subject recruitment or engagement, such as genotype-driven recruitment and planned return of research results. Examples of the latter could include questions of minimal risk in pediatric studies, research involving identifiable

groups or in developing countries, and studies with dual use implications. An additional trigger for RECS may be fine-grained ethical questions that come up in the course of a study for which there is no other appropriate resource within most institutions. The most common example of such a question would be uncertainty regarding an individual subject's capacity to provide informed consent. Table 4 provides some specific scenarios that illustrate several of the common topics encountered in REC.

Table 4: Examples of Research Ethics Consultation Topic Categories

▪ ***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

(Beskow et al. 2009)

INSTITUTIONAL RELATIONSHIPS

Goals of Relationships

Strong relationships and open communication between RECS and other institutional groups can contribute to both overall RECS efficacy and to improved outcomes for individual consults. In cases

where there may be perceived or actual overlap in function, such as between RECS and IRBs, relationships and communication can help to set common expectations, pre-empt unnecessary confusion, minimize redundancy, and negotiate boundaries. Similarities in the nature or function of groups also raise the possibility that individuals will initially approach one group when a different group would more appropriately handle the issue. Awareness of RECS among other institutional groups can improve the likelihood that an individual with an ethical issue or question will be appropriately referred to the RECS. Given the relatively recent advent of formal RECS as compared to many other institutional groups, it may be incumbent upon the RECS to initiate the relationship building process.

IRB

Perhaps no aspect of RECS has received more attention in the published literature than the relationship between RECS and IRBs (DeRenzo and Wichman 1990, DeRenzo and Bonkovsky 1993, MacKay 2001, Beskow et al. 2009, Havard and Magnus 2011, Cho et al. 2008). At its core this scrutiny relates to the question of what value RECS offer over and above existing institutional resources such as the IRB. Discussion of this topic has focused on the regulatory mandate of IRBs, including the absence of ethical expertise from the statutory requirements for IRB membership, and the explicit prohibition of IRB consideration of possible societal harms in the regulations that govern human subjects research (Beskow et al. 2009, Cho et al. 2008, US DHHS 2005). In July 2010, the Secretary's Advisory Committee on Human Research Protections discusses these issues at a open meeting (<http://www.hhs.gov/ohrp/sachrp/mtgins/mtg07-10/present.html>). The Committee's staff framed the issue in the following way, which illustrates the perceived tension:

"The responsibility for the ethical review of human subjects research has classically been the domain of the IRB; however, partly in response to criticism that IRBs focus largely on regulatory compliance with little time for rigorous ethical review, some academic institutions have developed a separate process for ethics consultation services (ECS). While some greet this development with approval and feel the IRB and ECS can act synergistically, others feel the

development of ECS erodes the appropriate authority of the IRB, creates conflicts in terms of allegiance and confidentiality, and helps ensure that the IRB plays only a regulatory role. This panel will discuss the nexus between ethics review and IRB review, and whether the ECS model is a positive step for human subjects protections overall.”

The discussion at this meeting noted the differences in scope and services between IRBs and RECS: RECs are available across the entire lifespan of a study and for a broader range of ethical questions than those fielded by IRBs; they are available to more types of individuals than those typically interacting with IRBs; and REC offer non-binding guidance in contrast to the binding authority of an IRB (Beskow et al. 2009).

Despite these meaningful points of differentiation, there are also similarities. Both IRB members and research ethics consultants work with investigators to promote the ethical conduct of research (independent of any regulatory mandate), they must be familiar with human subjects research regulations, they exercise judgment in interpreting the regulations in the context of specific research situations, and they help to support the institutional research enterprise (Beskow et al. 2009). What’s more, some IRBs include ethicists (and specifically research ethics consultants) as members or chairpersons (De Vries and Forsberg 2002, McCormick et al. 2012 draft), and IRBs may even perform REC (Beskow et al. 2009).

It is not yet clear whether there is a single best way to structure the relationship between an institutional IRB and a RECS. Local factors including resources, the types of research conducted, and available expertise may affect the structure of the RECS and whether it is most appropriately housed within the IRB, completely separate from the IRB, or separate with some degree of overlap (Beskow et al. 2009). What is clear is that IRBs frequently review ethically challenging protocols, and access to experts in research ethics is helpful to IRBs in such circumstances (Sirotin et al. 2010). (See Table 5)

Table 5: IRB Chairperson Resource Helpfulness Ratings	N				
	Respondents	Very helpful	Somewhat helpful	Somewhat unhelpful	Very unhelpful
When faced with a protocol that raises serious issues regarding human participants protections, which of the following would you find helpful?					
Talking to scientific colleagues who are familiar with this kind of research	85	65 (76.5%)	20 (23.5%)	0 (0%)	0 (0%)
Talking to experts in research ethics or bioethics	83	50 (60.2%)	28 (33.7%)	2 (2.4%)	3 (3.6%)
Using Internet resources, such as the IRB Forum listserv, for discussions of similar protocols	82	38 (46.3%)	34 (41.5%)	10 (12.2%)	0 (0%)
Looking up pertinent articles or books	83	32 (38.6%)	42 (50.6%)	6 (7.2%)	3 (3.6%)
Talking to other IRB members before the formal meeting	82	28 (34.1%)	34 (41.5%)	19 (23.2%)	1 (1.2%)
Talking to colleagues at other IRBs	80	27 (33.8%)	43 (53.8%)	10 (12.5%)	0 (0%)
Would the following be helpful to your IRB in reviewing a protocol that raises ethical concerns?					
More IRB access to individuals who can articulate the perspective of participants in such a study	81	53 (65.4%)	26 (32.1%)	2 (2.5%)	0 (0%)
More IRB access to experts in the relevant scientific disciplines	83	52 (62.7%)	24 (28.9%)	7 (8.4%)	0 (0%)
More IRB access to experts in research ethics	82	34 (41.5%)	38 (46.3%)	7 (8.5%)	3 (3.7%)
More specific guidelines from the federal Office for Human Research Protections on interpreting “minimal risk”	82	27 (32.9%)	29 (35.4%)	20 (24.4%)	6 (7.3%)
Obtaining guidance from the federal Office for Human Research Protections on this particular protocol, without triggering an investigation	80	24 (30.0%)	37 (46.3%)	12 (15.0%)	7 (8.8%)

(Siroten et al. 2010) (emphasis added)

Regardless of which type of relationship structure exists between the RECS and IRB, it is important for both parties to be aware of the relationship from the earliest stages of RECS implementation and mindful of the ways in which RECS can be valuable to IRBs and also potential areas of possible redundancy, conflict, or otherwise undesirable interaction. Currently unanswered questions that have emerged include whether it is appropriate for the same individual to perform a REC and to be part of an IRB deliberation on the same study or even be a voting member of the same IRB committee (Beskow et al. 2009), and whether and how IRBs should incorporate REC guidance into their evaluation process.

Other Institutional Groups

There are several other institutional groups with whom it may be appropriate or useful for RECS to establish and maintain relationships. These groups fall into two broad types. The first is groups that are traditionally and explicitly completely separate from RECS, but for whom familiarity and relationships can be important, such as human resources, legal counsel, the ombudsperson, and biostatistics and informatics consultation services. The second broad type is groups that are closely connected to RECS, including clinical ethics consultation services (CECS), offices of research integrity, research subject advocates, offices of institutional research and reporting, institutional animal care and use committees, data safety monitoring boards, and psychiatry consultation services. Research ethics consultants may also serve in these roles, and when there is no RECS, these programs may serve as source of ethical guidance for researchers (e.g. a psychiatric consult service may be able to assist in determining an individual subject's capacity to consent for a study).

In the 2010 survey, over half of responding CTSAs with a RECS indicated that they had a relationship with the institution's CECS, and a majority also indicated that individuals can and do serve on both consultation services at their institution (McCormick et al. 2012 draft). This likely reflects the both the limited ethical expertise and resources at many institutions, as well as the extent of overlap in the skills and core competencies required for ethics consultation, whether in a clinical or a research setting.

Apart from co-staffing, close relationships between RECS and CECS can be beneficial in several ways.

Clinical ethics consultation is an established practice that is familiar and uncontroversial to most individuals involved in clinical research or practice, and close alignment or interaction between RECS and CECS can help to reinforce the existence and utility of the former. RECS may be able to gain administrative efficiencies by harmonizing or merging their practices with those of the CECS, as is currently done at the NIH Clinical Center. Further, many RECS report referrals between RECS and CECS

(McCormick et al. 2012 draft), and a close relationship between the two groups can help to ensure this is an efficient process for consultants and clients alike.

Biostatistics and informatics groups commonly offer consulting services to researchers through the CTSA programs. To the extent that they do at a given institution, interaction between RECS and these services can facilitate referrals and help to reinforce the appropriateness and utility of ethical consultation for matters of study design and data analysis. For the convenience of requestors, it can also be useful to consolidate information about the range of consultation services available to researchers, as has been done at the University of California San Francisco: <http://accelerate.ucsf.edu/consult>. This can help to address the challenge of making eligible requestors aware of RECS in a way that does not put additional burdens on their time (de Melo-Martín et al. 2007).

INSIGHTS & FUTURE DIRECTIONS

Caveats & Anticipated Future Challenges

Institutions considering RECS should be aware of known areas of uncertainty and potential challenges for the practice.

Lack of Established Standards: While an increasing number of institutions have launched RECS, there is considerable variation in both vision and implementation from one institution to the next (McCormick et al. 2012 draft). Establishing common expectations about the policies of RECS regarding conflicts of commitment to requestors and institutions, confidentiality, and communication about these policies may aid in the ability of current and future programs to reach their full potential (Sharp et al. 2012

draft). It is also unclear to what extent RECS should localize their approach based on the specific institutional context, as opposed to aligning with efforts to standardize one approach to RECS.

Conflicts of Commitment: The multiple goals of RECS introduce the possibility that consultants will face competing obligations. Is the consultant's primary obligation to the client, the institution, or to the broader research ethics community? How should consultants manage tradeoffs (Spielman 2008)? While the nature and impact of these conflicts are just beginning to be characterized (Sharp et al. 2012 draft), it will be important to further evaluate when and how conflicts arise, and how they are best managed, reduced or eliminated (Spielman 2008). Interesting challenges can emerge when consultants also serve on an IRB that have oversight responsibilities for the same study related to role conflict, confusion, and influence. Such issues may be less of a problem between concurrent roles on clinical ethics committees.

Confidentiality: The option to keep some or all parts of a consultation confidential may be important to RECS utilization (Danis et al. 2012). However, there are circumstances where consultants may be required to breach confidentiality (e.g. a situation where the safety of an individual patient was in jeopardy or other legally required reporting), and there are benefits that can result from broad use of and access to consultation data (Sharp et al. 2012 draft). Bioscience companies are increasingly concerned about ethics (Mackie et al. 2006), and some RECS accept private, for-profit companies as clients. It is important for all RECS to be both clear and thoughtful about their approach to confidentiality in REC, and those that accept industry clients should proactively determine how they plan to handle requests for confidentiality from that client base.

Evaluation: While there are no established standards for consultations, there are several metrics that could be of use in evaluating the impact of REC. These include client satisfaction, client response to

consultants' assistance, level of consultation activity, and the frequency of identifying broader system or policy issues (Beskow et al. 2009). Some metric could be developed related to the impact of REC in reducing the time to IRB approval or reducing IRB requests for significant modifications to the protocol. However, IRB related metrics are indirect measures of REC quality and have the potential to inappropriately influence consultant or IRB behavior.

Success Factors

Despite the relative youth of REC and RECS and the current lack of established standards and best practices for the conduct and evaluation of REC, there are several clear ways that institutions considering RECS can position themselves for success.

Clarity of Services & Scope: It is helpful for RECS to proactively define which topics and types of issues and questions are, and are not, eligible for REC, both to inform staffing and consultant training decisions, and to proactively set expectations for requestors.

Publicity: Given the voluntary and client-initiated nature of REC, RECS utilization is dependent on investigator awareness of the service and understanding of the value of REC for their research. RECS should consider publicizing their services to investigators and other eligible clients directly as well as through the previously enumerated institutional groups who may be in a position to refer eligible individuals to RECS. Many RECS have developed informational materials (e.g. websites and brochures, see appendices H, I, and J) that can be useful in educating researchers regarding RECS. In addition to describing REC, it is useful for these resources to include several other types of information. These include:

- Eligibility

- Materials requestors should prepare or provide in advance of a consult
- Expected response time and process for urgent cases
- Description of services NOT covered (and information on who does)

Relationships: There are several groups at most institutions for whom communication and familiarity with RECS can be important. In cases where there are potential overlaps in function, these relationships can help to set common expectations, pre-empt unnecessary confusion, minimize redundancy, and negotiate boundaries. Institutional relationships are also important for RECS's ability to identify and address system-level issues.

Tracking use, satisfaction, and impact: It will be important for consultation services to be able to demonstrate their value to both to requestors and their institution. Collecting data about frequency of consultation requests, the types of questions raised, and the impact of the consultation to the progress of the research will be important. Further, obtaining feedback from requestors can be helpful in assessing if requestors perceived needs are being met.

Qualified personnel: As noted earlier, much of the success of a consult service requires that the consultants provide useful advice. Core competencies related to familiarity with ethical topics and ethical analysis; knowledge of applicable regulations, laws, and policies; scientific expertise and biomedical research experience; institutional knowledge; professionalism; interpersonal skills; and process skills are important. Perhaps most important is a sense professional humility about each consultant's personal limitations in each of these areas. Developing processes for communication between consultants within and among institutions are opportunities to both improve the quality of advice offered in an ongoing consult, and to learn how to improve subsequent consults.

Future Directions

Whether REC will prove to be a transformative resource for requestors and institutions remains an open question. Collaborative groups such as the CWG are well positioned to aid, evaluate, and enhance the potential of REC to elevate the level ethical research conduct at the institutional and the national level. A primary goal of the CWG is to provide mechanisms for research ethics consultants to share their experiences about complex consults and about strategies for addressing the complex operational issues and decisions they face. The CWG quarterly conference calls and the web-based discussion forum are two ongoing approaches. The currently ongoing data sharing demonstration project is a further step towards developing a system to facilitate the evaluation of the use of such services, and in the long run, the quality of the advice provided. While the CWG has been organized within the CTSA consortium, there is an appreciation that non-CTSA institutions, corporations, and government entities may also develop such consultation approaches. The current leadership of the CWG is interested in exploring how to leverage its activities beyond the CTSA environment. As the National Center Ethics in Health Care continues to develop and expand on the research ethics consultation activities it currently performs within the IntegratedEthics model, the CWG will be happy to explore how to actively involve the VA in ongoing CWG activities. VA's experiences and insights can contribute to improving the direction of this journey.

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6. The Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects
The World Medical Association
7. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research
The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
8. The Common Rule, Title 45 (Public Welfare), Code of Federal Regulations, Part 46 (Protection of Human Subjects), Subparts A–D
U.S. Department of Health and Human Services, National Institutes of Health, and Office for Human Research Protections
9. The International Ethical Guidelines for Biomedical Research Involving Human Subjects
The Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO)
10. The ICH Harmonised Tripartite Guideline—Guideline for Good Clinical Practice (ICH-GCP Guideline)
The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

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86. A Central Institutional Review Board for Multi-institutional Trials

Michael C. Christian, Jacquelyn L. Goldberg, Jack Killen, Jeffrey S. Abrams, Mary S. McCabe, Joan K. Mauer, and Robert E. Wittes

C. Institutional RECS Online Resources

Harvard University: <http://catalyst.harvard.edu/services/ethicsconsult/>
Indiana University: <http://bioethics.iu.edu/programs/bsap/t-rex/>
Johns Hopkins: <http://ictr.johnshopkins.edu/ethics/services/>
Mayo Clinic: <http://ctsa.mayo.edu/resources/research-ethics.html>
Medical University of South Carolina: <https://sctr.musc.edu/index.php/cre>
Mount Sinai School of Medicine: <http://www.mssm.edu/education/bioethics/medical-center-services>
National Institutes of Health: <http://www.bioethics.nih.gov/clinical/whatis.shtml>
Ohio State University: <http://ccts.osu.edu/content/biostatistics-design-ethics>
Stanford University: <http://cirge.stanford.edu/consultation/>
University of Arkansas for Medical Sciences: <http://www.uams.edu/humanities/RECS.asp>
University of California Irvine: <http://www.icts.uci.edu/biostatsConsult.cfm>
University of California San Diego: <http://ctri.ucsd.edu/clinical/Pages/ethics.aspx>
University of California San Francisco: <http://ctsi.ucsf.edu/about-us/programs/consultation-services>
University of Chicago: <http://medicine.uchicago.edu/centers/ethics/consults.html>
University of Colorado Denver: <http://cctsi.ucdenver.edu/Research-Resources/Pages/Research-Ethics.aspx>
University of Connecticut: <http://cicats.uchc.edu/services/ethics.html>
University of Florida: <http://www.ctsi.ufl.edu/research/research-support/research-ethics-consulting/>
University of Illinois, Chicago: http://go.uic.edu/CCTS_REC
University of Iowa: <http://www.icts.uiowa.edu/content/clinical-research-ethics-consultation-service-crecs>
University of Kentucky: http://www.research.uky.edu/faculty/benchside_ethics.html
University of Miami: <http://www.miami.edu/index.php/ethics/projects/recs>
University of Minnesota: <http://www.ctsi.umn.edu/research/services-resources/biomedical-ethics-consulting-service/index.htm>
University of New Mexico: <http://research.unm.edu/researchethics/ethicsconsultation.cfm>
University of North Carolina at Chapel Hill: <http://genomics.unc.edu/genomicsandsociety/html/recs.html> or <http://bioethics.unc.edu/consultation/>
University of Pennsylvania: <http://www.itmat.upenn.edu/ctsa/rec/consultation.shtml>
University of Pittsburgh: <http://www.bioethics.pitt.edu/clinical-consultation/>
University of Rochester Medical Center: <http://www.urmc.rochester.edu/ctsi/research-help/ethics.cfm>
University of Southern California: http://sc-ctsi.org/index.php/resources/get_expert_advice
University of Texas Medical Branch: <http://imh.utmb.edu/programs/institutional-ethics-program/research-ethics-consultation-service>
University of Texas San Antonio: <http://iims.uthscsa.edu/clinical.html>
University of Washington/ITHS: <https://www.iths.org/RSB>
Washington University: <http://icts.wustl.edu/cores/ccre.aspx>
Wayne State University: <http://macts.urcmich.org/divisions/participant/units/research-ethics/home>
Weill Cornell Medical College: http://weill.cornell.edu/publichealth/divisions/medical_ethics/research_ethics_consultation.html or http://www.med.cornell.edu/ctsc/services_and_resources/ethics_consultation_service.html

D. Example Consultation Report

Research Bioethics Consult Note

Risk category assessment for Newborn screening for lysosomal storage diseases



Patient Name:

DOB:

MR#:

Consult Date: 03/25/2007

Attending Consultant: [REDACTED]

Secondary Consultant: [REDACTED]

Requester: [REDACTED]

Requester's Service: Genetics

Reason for Consult:

To discuss ethical approaches for parental permission in a population based newborn screening study.

Other Issues Identified:

This is follow-up consult to discuss questions raised by the IRB about whether the study is minimal risk. This analysis focuses only on the screening phase of the study.

Background:

This is a proposed study of newborn screening for three lysosomal storage diseases (Fabry, Pompe, and MPSI). There are FDA approved enzyme replacement drugs for each of these three diseases, based on efficacy data in patients diagnosed after symptoms begin. There are limited data about the impact of early diagnosis and early treatment initiation on long term outcomes. This study includes a population based screening phase involving approximately all newborns, and a diagnostic phase will involve those with positive screening tests (less than 25 newborns per year). Treatment and long-term follow-up are not part of this study.

There are 80,000 annual births in Washington. The disease incidence for each disease is estimated at 1 in 40,000. It is estimated that there will be a positive initial test for each disease for 1 in every 10,000 births. This study will clarify these estimates.

The study includes a screening phase that would use blood collected from routine newborn screening from essentially all newborns in the State of Washington. If both the initial and routine 2 week samples show low enzyme activity, the investigators will contact the infant's primary care physician who will contact the family. The primary care physician will ask permission for the research team to contact the family to give them more information about the diagnostic phase.

The research team will contact the family and mail them the consent form, and arrange for the diagnostic phase study visit.

The diagnostic phase visit will include a clinical history and physical exam, a family history with a focus on related symptoms, blood draw for enzyme and DNA evaluations for the disease, and urine collection for metabolic byproducts.

Infants who have these disease or a disease variant will be referred to the Biochemical Genetics Clinic, where they will receive routine care, which typically includes clinical evaluations and decisions about interventions based on individual symptoms and enrollment in disease registries. The protocol draft says little about how the study results will be communicated to the families, whether the samples will be saved for further analysis, and whether there will be any further communications with these families. Infants who do not have the disease will be sent a letter summarizing the clinical evaluation.

The primary question that prompted the consult was the approach to parental permission for the screening phase. The investigators propose to request that the IRB waive the requirement for documentation of consent for the screening phase

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because this part of the study is minimal risk. They plan to disclose the study to families by using a supplemental page to be included in the newborn screening brochure and having additional information on the website. (The web site material has not yet been developed). Parents can choose not to participate in the study by including a signed form with the newborn screening card or by calling the investigators who will then send the refusal form in the mail to be signed.

After the diagnostic phase is completed, a moderate proportion of these participants will be determined to be false positives.

Process:

Study Investigators [REDACTED] and [REDACTED] met with [REDACTED], and [REDACTED], from the Children's Ethics Consults Service.

Analysis:

This study approach attempts to improve upon the approaches to permission used in similar studies such as newborn screening for cystic fibrosis in Colorado and Wisconsin in the 1980s and in Massachusetts in the 1990s. Those prior studies did not require documentation of permission for the screening phase. However, they did make explicit efforts to disclose the study to parents and to allow any who objected to decline participation. Wisconsin allowed parents to opt out by a phone call and Massachusetts allows parents to opt out by completing a check off box on the NBS card. The current study blends these methods by offering variants of both options. It will also use a separate and distinctly colored leaflet in the NBS parent brochure to describe the study and provide detailed study information on the web.

A waiver of documentation of consent can only be granted if a study is minimal risk. The primary risk of the research would be breach of confidentiality (present in most research).

The risks of screening include psychosocial distress related to being identified as a false positive or true positives with variable phenotypes that will not benefit from NBS. While these risk need to be seriously considered, it is not clear when these risks and the efforts to minimize them should be considered in the determination of risk for purposes of the consent approach. These are the risks of screening, independent from whether this is done as a research study.

One of the general policy challenges of NBS has been the introduction of new tests clinically, without any research. In this context, parental permission is not usually requested. It is laudable that screening for LSD is being considered here as a research activity rather than as a "pilot" program, and that the plan includes particular efforts to inform parents and offer the option to decline participation.

To explicitly address the issues of the risks of screening (as contrasted to the research), the number of false positives will be very low; approximately 1 in 3,000 (for all three diseases) and the risks to these families can be minimized by careful communications both in the diagnostic phase parental permission form and follow-up letters. Most importantly, each family will meet with a geneticist and genetic counselor to directly discuss these issues. As an empirical issue, there have not been significant psychosocial harms observed or reported from prior newborn screening studies.

Our analysis is that this phase of the study constitutes minimal risk to participants because of the low likelihood of risks and the efforts to minimize them. Further, the efforts at disclosure and the opportunities for refusal are clearly aimed at respecting parents' rights and welfare.

Recommendation:

An explicit waiver of documentation of parental permission is appropriate particularly if materials that are developed for an insert in the state NBS brochure and the website are well designed for clarity and simplicity.

E. RECS Comprehensive Data Collection Elements Form

		Intra-Institutional Reporting	Inter-Institutional Data sharing
Identifying Information			
Institution			X
Title of consult			
Primary consultant			
Consult ID <i>alpha-numeric code</i>			X
Date of consult <i>MM-DD-YYYY</i>		X	X
Requestor Information			
Name of lead requestor		X	
Other participating requestors			
Name of contact			
How requestor came to the consultation service <i>Select all that apply</i>	<input type="checkbox"/> Contacted individual consultant <input type="checkbox"/> Through CTSA service request <input type="checkbox"/> Other	X	
Referrals from other services <i>Select all that apply</i>	<input type="checkbox"/> Hospital ethics committee <input type="checkbox"/> IRB <input type="checkbox"/> Risk management <input type="checkbox"/> Biostatistics <input type="checkbox"/> Informatics <input type="checkbox"/> Ombudsperson <input type="checkbox"/> Conflict of interest committee <input type="checkbox"/> Legal counsel <input type="checkbox"/> FDA <input type="checkbox"/> NSABB <input type="checkbox"/> DSMB <input type="checkbox"/> Other	X	
Contact information			
Role of lead requestor on project <i>Select one</i>	<input type="checkbox"/> PI <input type="checkbox"/> Co-investigator <input type="checkbox"/> Research staff	X	

	<input type="checkbox"/> Post-doc/fellow <input type="checkbox"/> Student <input type="checkbox"/> Research participant <input type="checkbox"/> Administrative staff <input type="checkbox"/> IRB staff <input type="checkbox"/> Other		
Type of institution of requestor <i>Select one</i>	<input type="checkbox"/> CTSA institution <input type="checkbox"/> Other academic institution <input type="checkbox"/> Government <input type="checkbox"/> Industry <input type="checkbox"/> Funding agency <input type="checkbox"/> Other	x	
Department		x	
Project information			
Title of research project		x	
Source of research funding <i>Select all that apply</i>	<input type="checkbox"/> NIH (including CTSA pilot funding) <input type="checkbox"/> Other government <input type="checkbox"/> Not-for-profit <input type="checkbox"/> Industry <input type="checkbox"/> Internal <input type="checkbox"/> None <input type="checkbox"/> Other	x	
Research activities <i>Select one</i> The purpose of this question is to understand the types of activities that are associated with the research projects that generate consultation requests.	<input type="checkbox"/> Clinical intervention (drugs, devices, biopsies, imaging w/contrast) <input type="checkbox"/> Clinical observation (imaging, EKG, exams) <input type="checkbox"/> Behavioral/psychological/intervention <input type="checkbox"/> Behavioral/psychological/observations (surveys, Interviews,) <input type="checkbox"/> Analysis of existing samples/data	x	x

	<input type="checkbox"/> Other		
Research stage <i>Select one</i> These are discrete for an individual research project.	<input type="checkbox"/> Planning <input type="checkbox"/> Grant application <input type="checkbox"/> Regulatory review <input type="checkbox"/> Data collection <input type="checkbox"/> Analysis <input type="checkbox"/> Publication/dissemination <input type="checkbox"/> Post-publication translation	x	x
Translational Research Phase <i>Select one</i> These research trajectory phases arc from laboratory discovery to impact on community health. The same approach (e.g. randomized controlled trials, survey research, health system databases) can be used in different phases. These phases can be applied to drug development, genetic testing, or public health research.	<input type="checkbox"/> T1- Discovery <input type="checkbox"/> T2- Development <input type="checkbox"/> T3- Delivery <input type="checkbox"/> T4- Outcomes <input type="checkbox"/> Not Applicable	x	x
Research setting <i>Select all that apply</i>	<input type="checkbox"/> Research laboratory <input type="checkbox"/> Clinical <input type="checkbox"/> Multi-institutional <input type="checkbox"/> Community <input type="checkbox"/> Other	x	
Special Research Categories <i>Select all that apply</i> These categories may have special regulatory or ethical considerations and will be used a “key words” for searches for relevant consultations regarding categories.	<input type="checkbox"/> None <input type="checkbox"/> Indigenous population <input type="checkbox"/> Pediatric population <input type="checkbox"/> Innovative treatment <input type="checkbox"/> Randomized controlled trial <input type="checkbox"/> First-in-human trials <input type="checkbox"/> International research <input type="checkbox"/> Community-engaged research <input type="checkbox"/> Quality improvement research <input type="checkbox"/> Emergency research <input type="checkbox"/> Human biological samples <input type="checkbox"/> Human stem cells <input type="checkbox"/> Gene transfer <input type="checkbox"/> Vertebrate animals	x	x

	<input type="checkbox"/> Select agents <input type="checkbox"/> Other		
Consultation Information			
Primary ethical concern <i>Select one</i> This is the major ethical issue identified by the consultants (not by the requestor). Consider which category is the most important or controversial, and would be best “key word” to identify this consult.	<input type="checkbox"/> Benefit/risk assessment <input type="checkbox"/> Study design (use of placebo, randomization, active controls) <input type="checkbox"/> Subject selection and recruitment <input type="checkbox"/> Research/clinical practice Relationships <input type="checkbox"/> Ancillary care <input type="checkbox"/> Community considerations <input type="checkbox"/> Socially or economically vulnerable subjects <input type="checkbox"/> Undue influence/exploitation <input type="checkbox"/> Informed consent (assent, competence, proxy) <input type="checkbox"/> Privacy/confidentiality <input type="checkbox"/> Disclosure of Incidental findings/research results <input type="checkbox"/> Study withdrawal/termination <input type="checkbox"/> Communication of findings <input type="checkbox"/> Broader social impact <input type="checkbox"/> Research integrity (misconduct, authorship, data analysis) <input type="checkbox"/> Conflict of interest <input type="checkbox"/> Legal (liability, ownership, patent issues) <input type="checkbox"/> Other	x	x
Secondary ethical concerns <i>Select as many as applicable; be inclusive to facilitate key word searches</i>	<input type="checkbox"/> Benefit/risk assessment <input type="checkbox"/> Study design (use of	x	x

	<p>placebo, randomization, active controls)</p> <p><input type="checkbox"/> Subject selection and recruitment</p> <p><input type="checkbox"/> Research/clinical practice Relationships</p> <p><input type="checkbox"/> Ancillary care</p> <p><input type="checkbox"/> Community considerations</p> <p><input type="checkbox"/> Socially or economically vulnerable subjects</p> <p><input type="checkbox"/> Undue influence/exploitation</p> <p><input type="checkbox"/> Informed consent (assent, competence, proxy)</p> <p><input type="checkbox"/> Privacy/confidentiality</p> <p><input type="checkbox"/> Disclosure of Incidental findings/research results</p> <p><input type="checkbox"/> Study withdrawal/termination</p> <p><input type="checkbox"/> Communication of findings</p> <p><input type="checkbox"/> Broader social impact</p> <p><input type="checkbox"/> Research integrity (misconduct, authorship, data analysis)</p> <p><input type="checkbox"/> Conflict of interest</p> <p><input type="checkbox"/> Legal (liability, ownership, patent issues)</p> <p><input type="checkbox"/> Other</p>		
<p>Requested level of confidentiality <i>Select one</i></p>	<p>Information shared with:</p> <p><input type="checkbox"/> Local consultation service only</p> <p><input type="checkbox"/> Others if anonymized by individual and institution</p> <p><input type="checkbox"/> Others if anonymized by institution</p>		

	<input type="checkbox"/> Others not anonymized		
Process Information			
Consultants participating			
Collaboration with other services <i>Select all that apply</i>	<input type="checkbox"/> Hospital ethics committee <input type="checkbox"/> IRB <input type="checkbox"/> Risk management <input type="checkbox"/> Biostatistics <input type="checkbox"/> Informatics <input type="checkbox"/> Ombudsperson <input type="checkbox"/> Conflict of interest committee <input type="checkbox"/> Legal counsel <input type="checkbox"/> FDA <input type="checkbox"/> NSABB <input type="checkbox"/> DSMB <input type="checkbox"/> Other	x	
Meeting attendees <i>Select all that apply</i>	<input type="checkbox"/> No in-person meeting <input type="checkbox"/> Research team members <input type="checkbox"/> Research subjects <input type="checkbox"/> Representatives of other institutional entities <input type="checkbox"/> External consultants <input type="checkbox"/> Other		
Amount of interaction (hours) <i>Select one</i>	<input type="checkbox"/> < 1h <input type="checkbox"/> 1-4h <input type="checkbox"/> 5-10h <input type="checkbox"/> 11-15h <input type="checkbox"/> >15 hours	x	x
Additional service(s) provided <i>Select as many of the as appropriate for specific services provided.</i>	<input type="checkbox"/> None <input type="checkbox"/> Assessment/capacity of decision maker <input type="checkbox"/> Assistance with study design <input type="checkbox"/> Clarification of regulations, laws, or policies	x	x

	<input type="checkbox"/> Assistance with regulatory review <input type="checkbox"/> Assistance with consent process <input type="checkbox"/> Conflict mediation <input type="checkbox"/> Other		
Narrative report			
Reason for consult		x	x
Other issues identified			
Background			
Process			
Analysis			
Recommendations			
Follow-up			
Outcomes: requestors		x	
Outcomes: consultation service		x	
Evaluation		x	

F. RECS Minimal Data Collection Elements Form

Descriptive information:	
Consult ID: (alpha-numeric code)	
Title of consult:	
Date consult (MM-DD-YYYY):	
Research project information	
Research activities <i>select one</i> The purpose of this question is to understand the types of activities that are associated with the research projects that generate consultation requests.	<input type="checkbox"/> Clinical intervention (drugs, devices, biopsies, imaging w/contrast) <input type="checkbox"/> Clinical observation (imaging, EKG, exams) <input type="checkbox"/> Behavioral/psychological/ intervention <input type="checkbox"/> Behavioral/psychological/ observations (surveys, Interviews,) <input type="checkbox"/> Analysis of existing samples/data <input type="checkbox"/> Other
Research stage <i>Select one</i> These are discrete for an individual research project.	<input type="checkbox"/> Planning <input type="checkbox"/> Grant application <input type="checkbox"/> Regulatory review <input type="checkbox"/> Data collection <input type="checkbox"/> Analysis <input type="checkbox"/> Publication/dissemination <input type="checkbox"/> Post-publication translation
Translational Research Phase <i>select one</i> These research trajectory phases arc from laboratory discovery to impact on community health. The same approach (e.g. randomized controlled trials, survey research, health system databases) can be used in different phases. These phases can be applied to drug development, genetic testing, or public health research.	<input type="checkbox"/> T1- Discovery <input type="checkbox"/> T2- Development <input type="checkbox"/> T3- Delivery <input type="checkbox"/> T4- Outcomes <input type="checkbox"/> Not Applicable
Consult Information	

<p>Special Research Categories <i>select all that apply</i></p> <p>These categories may have special regulatory or ethical considerations and will be used a “key words” for searches for relevant consultations regarding categories.</p>	<ul style="list-style-type: none"> <input type="checkbox"/> None <input type="checkbox"/> Indigenous population <input type="checkbox"/> Pediatric population <input type="checkbox"/> Innovative treatment <input type="checkbox"/> Randomized controlled trial <input type="checkbox"/> First-in-human trials <input type="checkbox"/> International research <input type="checkbox"/> Community-engaged research <input type="checkbox"/> Quality improvement research <input type="checkbox"/> Emergency research <input type="checkbox"/> Human biological samples <input type="checkbox"/> Human stem cells <input type="checkbox"/> Gene transfer <input type="checkbox"/> Vertebrate animals <input type="checkbox"/> Select agents <input type="checkbox"/> Other
<p>Primary ethical concern <i>select one</i></p> <p>This is the major ethical issue identified by the consultants (not by the requestor).</p> <p>Consider which category is the most important or controversial, and would be best “key word” to identify this consult.</p>	<ul style="list-style-type: none"> <input type="checkbox"/> Benefit/risk assessment <input type="checkbox"/> Study design (use of placebo, randomization, active controls) <input type="checkbox"/> Subject selection and recruitment <input type="checkbox"/> Research/clinical practice Relationships <input type="checkbox"/> Ancillary care <input type="checkbox"/> Community considerations <input type="checkbox"/> Socially or economically vulnerable subjects <input type="checkbox"/> Undue influence/exploitation <input type="checkbox"/> Informed consent (assent, competence, proxy) <input type="checkbox"/> Privacy/confidentiality <input type="checkbox"/> Disclosure of Incidental findings/research results <input type="checkbox"/> Study withdrawal/termination <input type="checkbox"/> Communication of findings <input type="checkbox"/> Broader social impact <input type="checkbox"/> Research integrity (misconduct, authorship, data analysis) <input type="checkbox"/> Conflict of interest <input type="checkbox"/> Legal (liability, ownership, patent issues) <input type="checkbox"/> Other

Secondary ethical concerns <i>select as many as applicable; be inclusive to facilitate key word searches</i>	<input type="checkbox"/> Benefit/risk assessment <input type="checkbox"/> Study design (use of placebo, randomization, active controls) <input type="checkbox"/> Subject selection and recruitment <input type="checkbox"/> Research/clinical practice relationships <input type="checkbox"/> Ancillary care <input type="checkbox"/> Community considerations <input type="checkbox"/> Socially or economically vulnerable subjects <input type="checkbox"/> Undue influence/exploitation <input type="checkbox"/> Informed consent (assent, competence, proxy) <input type="checkbox"/> Privacy/confidentiality <input type="checkbox"/> Disclosure of incidental findings/research results <input type="checkbox"/> Study withdrawal/termination <input type="checkbox"/> Communication of findings <input type="checkbox"/> Broader social impact <input type="checkbox"/> Research integrity (misconduct, authorship, data analysis) <input type="checkbox"/> Conflict of interest <input type="checkbox"/> Legal (liability, ownership, patent issues) <input type="checkbox"/> Other
Consult Process Information	
Amount of interaction (hours) (select one)	<input type="checkbox"/> < 1h <input type="checkbox"/> 1-4h <input type="checkbox"/> 5-10h <input type="checkbox"/> 11-15h <input type="checkbox"/> >15
Additional service(s) provided <i>Select as many of the as appropriate for specific services provided.</i>	<input type="checkbox"/> None <input type="checkbox"/> Assessment/capacity of decision maker <input type="checkbox"/> Assistance with study design <input type="checkbox"/> Clarification of regulations, laws, or policies <input type="checkbox"/> Assistance with regulatory review <input type="checkbox"/> Assistance with consent process <input type="checkbox"/> Conflict mediation <input type="checkbox"/> Other
Narrative report	
Reason for consult <i>1-4 sentences</i>	

G. RECS Minimal Data Collection Elements User Guide

RECS Minimal Data Elements Collection Form

User Guide

Jan 3, 2012 version

Use "Other" when there is no reasonable fit and you believe the current categories are not sufficient and the standard fields should be amended. "OTHER" is captured in the REDCap repository as a separate text box immediately following the drop down/check boxes.

Consult ID: Enter the ID number either into REDCap directly, or into your excel import template.

Institution: The institution where consultants are based. Not the location of the requestors. Choose your institution from the drop-down menu.

Title: Use a title that provides enough specific information about the project and/or the consultation question to allow you recognize the consult. *Do not use specific identifiers related to the requestor, investigator, institution, etc*

Date of Consult (MM-DD-YYYY). This can be either the date the consult was initiated or the date completed, depending on your institutional convention.

RESEARCH PROJECT INFORMATION- this section relates to the research activity that is the reason for the consult

Research Activities-

Select one

The purpose of this question is to understand the types of research activities in projects that are associated with consultation requests. When a study involves more than one activity, select the first one on this list that is applicable.

Clinical interventions- includes the use of drugs, devices, invasive biopsies, invasive imaging(bronchoscopy, CT with contrast or sedation).

Clinical observations-includes medical history, physical exams, diagnostic tests (blood tests, EKG, pregnancy tests), non-invasive imaging, (Ultrasounds, MRIs, CT).

Behavioral/psychological/ interventions-includes engagements that are intended to change knowledge, attitudes or behaviors.

Behavioral/psychological/ observations-includes surveys, focus groups, interviews, and other observations to asses knowledge, attitudes or behaviors.

Analysis of existing samples/data -samples or data previously collected; already 'on the shelf' or 'in a database'.

Other: *Fill in the text box.* Use this category if none of the other categories apply and the issue is one for which you'd like a separate check-box/option in the future.

<p>Research stage- <i>Select one</i></p> <p>These are discrete for an individual research project.</p>	<p>Planning - includes all study planning and design except for grant-related activities.</p> <p>Grant application - includes writing or revising a grant application.</p> <p>Regulatory review - includes initial applications to IRBs, ESCROs, or federal agencies such as the NIH, FDA or RAC before the study is initiated.</p> <p>Data collection – includes questions that arise once a study has begun. Also includes questions that arise during recruitment are about.</p> <p>Analysis - includes questions that arise about the interpretation of data or other questions that arise after collection is completed</p> <p>Publication/dissemination - includes presenting research in public, publications, and media communications.</p> <p>Post-publication translation - includes issues specific to commercialization of research e.g., intellectual property or marketing.</p>
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Translational Research Phase
- *select one*

These are the phases of a research trajectory from the discovery to impact on the population health outcomes. These phases can be applied across a spectrum of research including drug development, genetic testing, or public health programs.

A particular research approach (observational research, randomized controlled trials, survey research, health system database) can be applied across phases and in different research contexts.

USE THE TABLE BELOW TO ASSIST WITH APPROPRIATE CHOICE

Not applicable- use this option if the translational phases do not apply to the research project

Translational Research Phase	Drug Development Research (inhaled steroids and asthma)	Genetic testing research (Carrier Testing and Cystic fibrosis)	Public health research (second hand smoke and lung cancer)
T1 Discovery	Do inhaled steroids reduce lung inflammation? (Laboratory research for molecular mechanisms, biomarkers, and safety; clinical research for safety and efficacy (Phase I and II))	What genes cause CF? (family genetic studies)	Does second hand smoke cause lung cancer? (questionnaires, health system database studies, population database studies)
T2 Development	Do inhaled steroids improve asthma symptoms and lung function? (clinical research for effectiveness) (Phase III)	Are women interested in carrier testing for CF? (questionnaires, randomized intervention studies, health system database studies)	Are household contacts at increased risk of lung cancer? (longitudinal studies, cross sectional studies)
T3 Delivery	Will doctors offer inhaled steroids to patients and will patients use them? (focus groups, questionnaires, randomized interventions comparative effectiveness studies, health system database studies)	How do physicians offer testing in practice? (questionnaires, randomized intervention studies, health system database studies)	What educational interventions reduce risk of second hand smoke? (questionnaires, intervention studies, observations)
T4 Outcomes	Does the incidence of hospitalizations for asthma decrease? (health systems database studies)	Does carrier testing decrease the incidence of CF in newborns (population database studies)	Does the incidence of lung cancer in non smokers decrease? (health system database and population database studies)

CONSULTATION INFORMATION	
<p>Special research categories <i>Select all that apply to the consult.</i></p> <p>These categories may have special regulatory or ethical considerations and will be used a “key words” for searches for relevant consultations regarding categories.</p>	<p>None- use this option if none of the following apply.</p> <p>Indigenous population - Involves participants who are considered ‘first peoples’ or natives of the location where the research is conducted (e.g., aboriginal persons, Native Americans).</p> <p>Pediatric population - involves children (0-18/21).</p> <p>Innovative treatment - includes activities that may be in the boundary between research and clinical treatment.</p> <p>Randomized clinical trial (RCT)-if randomization is used.</p> <p>First-in-human trials - Not previously been studied in</p>

	<p>humans.</p> <p>International research - location of the research activities will occur outside the United States.</p> <p>Community-engaged research - involves communities in the design, implementation and interpretation of the study.</p> <p>Quality improvement research - involves using established approaches to improve effectiveness.</p> <p>Emergency research - involves an emergency situation and where consent to participate may be waived under FDA regulations.</p> <p>Human biological samples - involves using human tissues, serum or DNA.</p> <p>Human stem cells - involves using any type of human stem cells (embryonic or adult). This does not include hemopoietic stem cells (HSC) or HSC transplants.</p> <p>Gene transfer- involves inserting new genes into humans, either directly or by modifying cells that are transferred.</p> <p>Vertebrate animals- involves animals ranging from rodents to non-human primates .</p> <p>Select Agents- involves microorganisms and toxins specifically identified in DHHS and USDA regulations as having the potential to pose a severe threat to human, animal, or plant health.</p> <p>Other: <i>Fill in the text box.</i> Use this category if none of the other categories apply AND the issue is one for which you'd like a separate check-box/option in the future.</p>
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<p>Primary Ethical Concern <i>Select one</i></p> <p>This is the major ethical issue identified by the consultants (not by the requestor).</p> <p>Consider which category is the most important or controversial, and consult would be best “key word” to identify this consult.</p>	<p>Benefit/risk assessment - Balancing or assessing benefits and harms of study activities. Include questions about data & safety monitoring (e.g., whether or not a plan is required, or what type of plan is required)</p> <p>Study Design - Options to design a study, including use of placebo, randomization, active controls. This category is a specific sub-set of ‘benefit-harm’.</p> <p>Subject selection and recruitment - Which populations to include, how to approach participants, whether to provide research incentives.</p> <p>Research/Clinical Practice relationships- When research and clinical roles overlap, such as when clinicians enroll patients in clinical trials, or concerns about participant understanding about research vs clinical care.</p> <p>Ancillary Care - Obligations to provide care in the context of research study, such as responding to elevated blood pressure.</p> <p>Community Considerations - Includes cultural concerns and religious concerns for participants and concerns about community attitudes or impact.</p>
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	<p>Socially/economically vulnerable subjects - Should be used when some or all of the research participants are socially or economically disadvantaged (homeless people, schizophrenia).</p> <p>Undue influence/exploitation - Concern that the participants may be pressured (undue influence) to join or remain in research. Concern that study participation may take unfair advantage (exploitation) of participants.</p> <p>Incidental findings/reporting results – Concerns about whether or how to disclose individual research findings about individual participants to themselves or family members.</p> <p>Communication of findings - Concerns about how best to communicate the overall, aggregate findings to the research population or the community.</p> <p>Broader social impact – Whether potential social impact of the research itself should influence decisions about study design and/or publication. In other words, should this research be done, at all, or should the results be published?</p> <p>Research Integrity - Concerns about misconduct, publication authorship, or integrity of data analysis.</p> <p>Conflict of Interest - Concerns researchers, institutions or sponsors may have competing financial commitments that are important to the design or conduct of research project.</p> <p>Legal - strictly legal issues such as liability, patent, or ownership, issues that require a analysis from legal counsel.</p> <p>Other: <i>Fill in the text box.</i> Use this category if none of the other categories apply AND the issue is one for which you'd like a separate check-box/option in the future.</p>
Secondary Ethical Concerns	<i>Select as many as applicable using the directions above. Be inclusive to facilitate key word searching</i>
Consult Process Information	
Amount of interaction	<i>Include time spent in conversation, research, and documentation by all consultants involved with the consult.</i>
Additional service(s) provided Select as many of the listed services as appropriate for the consult.	<p>None-use this option if the consult did not concern any of the options below; i.e., the consultant engaged in ethical consultation only.</p> <p>Assessment/capacity of decision maker - specific assessments of individual participants; either about the appropriateness as a surrogate decision maker or the capacity of a potential participant to decide to join a study.</p> <p>Assistance with study design - specific discussion about alternative design approaches to address ethical concerns.</p> <p>Clarification of regulations, laws, or policies - includes specific discussions about these as they apply to the requestor's research.</p> <p>Assistance with regulatory review- includes advice or assistance about regulatory decisions or processes.</p> <p>Assistance with consent process - includes assistance improving disclosure</p>

	<p>and understanding of information to join a study.</p> <p>Conflict mediation - Involves simultaneous discussion with multiple parties to a dispute to improve communication and resolution of conflict. Does not require an agreement to follow recommendations. Do not choose this option if all parties were not engaged with the consultation.</p> <p>Other: <i>Fill in the text box.</i> Use this category if none of the other categories apply AND the issue is one for which you'd like a separate check-box/option in the future.</p>
Narrative Report	
Reason for consult	<p>Two or three sentences to describe the reason for the consult. This should provide enough information so others have a general idea about research question, the project, and the ethical concern. <i>Do not use specific identifiers related to the requestor, investigator, institution, etc.</i></p>

Benchside Ethics Consultation Service [BECS]

THE BENCHSIDE ETHICS CONSULTATION SERVICE (BECS) is a service provided by Stanford consultants with science and ethics backgrounds to assist bioscience researchers in the resolution of ethical questions and social concerns that may develop in the course of their research. BECS is based on the model of clinical ethics consultation and is designed to provide real time, prompt, and practical advice for scientists. Since BECS is intended to be maximally helpful to researchers, the BECS team is committed to deliver recommendations to the client within an accelerated time frame.

HOW TO REQUEST A CONSULTATION:

Pager: 650-723-8222, 16835

Email:

becs-spectrum@lists.stanford.edu

Online form: Coming soon!

*Regardless of how you make your request, we will attempt to contact you within 24 hours to begin your consultation. Depending on the nature of your request, it might require a meeting with the BECS team of consultants.

* Our aim is to provide you with a preliminary report within 48 hours of your request, or within 48 hours of the team meeting if that is deemed necessary.

BECS FREQUENTLY ASKED QUESTIONS:

1. Who Can Use the Benchside Ethics Consultation Service?

BECS is available to any member of the Stanford University community. Requests may come from:

- Research investigators (the PI or anyone on the research team), study participants, coordinators
- Stanford faculty, staff, scholars, students and medical professionals
- Institutional Review Boards
- Regulatory committees and other institutional bodies

2. Who Staffs the Benchside Ethics Consultation Service?

BECS is staffed by Stanford University faculty and members of the Stanford Center for Biomedical Ethics. They are experts in research ethics and regulation, and they represent a wide range of disciplines including biomedical research, genetics, law and philosophy.

3. Is the Benchside Ethics Consultation Service confidential?

Yes; the identities of those requesting consultations and all research data, ideas and ethical issues are confidential.

For more FAQs and other information, visit:

<http://cirge.stanford.edu/consultation/>



I. Example RECS Brochure: University of Colorado, Denver

RESEARCH
ETHICS
CONSULTATION
SERVICE

CONTACT



To request assistance from the Research Ethics Consultation Service, please call 303-724-3994 or send an email to ResearchEthics@ucdenver.edu

A member of the service will usually be in touch with you within 24 hours of your initial request.

Confidentiality will be respected to the extent permitted by institutional policies.

For more information please visit
cctsi.ucdenver.edu

RESEARCH ETHICS
CONSULTATION SERVICE
MEMBERS

David Badesch, MD
Marilyn Coors, PhD
Jackie Glover, PhD
Barbara Hammack, PhD
Alan Prochazka, MD
and other consultants as needed



To Request Assistance

303-724-3994
researchethics@ucdenver.edu



12401 E. 17th Ave. | Aurora, CO 80045
Mail Stop B141 | cctsi.ucdenver.edu



RESEARCH
ETHICS
CONSULTATION
SERVICE

The Colorado Clinical &
Translational Sciences Institute
University of Colorado
Denver | Anschutz Medical Campus

*The academic home of
biomedical research that reaches
from labs and into lives*

CCTSI RESEARCH ETHICS CONSULTATION SERVICE

What is the Research Ethics Consultation Service?

The Research Ethics Consultation Service is a newly created, free service sponsored by the Colorado Clinical & Translational Sciences Institute (CCTSI). It is available to all biomedical and behavioral researchers at the University of Colorado Denver Anschutz Medical Campus, as well as its clinical affiliates, who seek advice about ethically complex aspects of their research.

When should I contact the Research Ethics Consultation Service?

Although you can contact the service during any phase of your research, we encourage you to utilize this service very early in the process of study design.

“The Research Ethics Consultation Service is staffed by the Research Ethics Core of the CCTSI.”

What are the kinds of issues that the Research Ethics Consultation Service can help me with?

Examples of the kind of questions that the support service might assist you with include, but are not limited to, the following:

- How do I know if the consent process that I am anticipating using for my research is the most appropriate one, given special characteristics of my research population?
- Should I do anything about the fact that my research is controversial in the eyes of many in the public?
- How should I determine how far to go in my efforts to minimize the risks of my research, especially if it might compromise my ability to test my hypotheses?
- How can I assure that my research team is honoring the privacy of our research participants, given the access we have to confidential information?



Is this service related to COMIRB or other campus Research Committees?

The Research Ethics Consultation Service is not a replacement for COMIRB review, nor is it an arm of COMIRB or any other university research oversight committee, such as the Committee on Research Ethics. However, like every other unit at the University, these other groups can utilize the services of the Research Ethics Consultation Service.

Who staffs the Research Ethics Consultation Service?

The Research Ethics Consultation Service is staffed by the Research Ethics Core of the CCTSI. Its membership is drawn from faculty of the Center for Bio-ethics and Humanities, campus Research Subject Advocates, as well as clinical investigators and others with significant research ethics and IRB expertise.



J. Example RECS Brochure: University of Washington



Research Bioethics Consultations

Providing a forum for discussion and analysis of ethical issues in clinical and translational research

The **Institute of Translational Health Sciences** provides a wide range of resources to promote translational research. ITHS Regulatory Support and Bioethics (RSB) core offers **Research Bioethics Consultations** to researchers, trainees, research staff, and human subjects protection program personnel.

EXAMPLES OF CONSULT QUESTIONS

Community Engagement

- How can I establish sustainable relationships with communities?
- How should I negotiate disagreements with community stakeholders?
- How should I share the research data with the community?

Study Development

- How should I provide incentives for participation?
- What if informed consent isn't practical for my study?
- When is a placebo-control ethically appropriate?

Study Implementation

- What should I do if a participant doesn't have the capacity for consent?
- Can I withdraw a participant against his/her wishes?
- What must I do if my participants need medical care or other help?

Study Analysis

- Should I tell participants about their research findings?
- What if a participant requests their data be withdrawn?
- Who should be an author on the publication of my study?

Bioethics consults are **advisory**, providing a forum for **in-depth conversation** and analysis of ethical issues in clinical and translational research. Recommendations are supplemental to the authority and oversight of review groups, like an IRB or DSMB.

Consultation discussions can take place by telephone or in-person. If requested, the consultant will provide a **written report** of relevant considerations and recommendations.

Consultation details may be discussed amongst the bioethics consultants, but otherwise will **not be discussed with others involved in the issue** without the requestor's permission.

To ensure a **balanced understanding** of the facts or to facilitate reconciliation of a conflict, the consultant is available to talk to others involved in the issue if desired by the requestor.

In some cases, the issue **may warrant referral** to offices such as the institutional ombudsperson, human resources, or legal counsel.

There is generally no charge for research bioethics consultations. ITHS membership is **not**

required to request a consultation. Hourly charges can be included in grant applications for projects that anticipate the need for future consultation or collaboration.

RSB Bioethics Research Consultants

Kelly Edwards, PhD, Dept. of Bioethics and Humanities
S. Malia Fullerton, PhD, Dept. of Bioethics and Humanities
Ann Melvin, MD, MPH, Seattle Children's
Benjamin Wilfond, MD, Seattle Children's

To request a consultation or to find out more:

rsbcore@u.washington.edu

www.iths.org

Or Call (206) 987-2000

Ask for the **Bioethicist (Research) on-call**



Research Bioethics Consultations

What happens after a consult?

- RSB maintains a database of bioethics consultations, including information regarding the participants, issues, and analyses. Access to this database is restricted to the bioethics consultants and RSB administrative staff.
- Requestors will receive an **evaluation email after the consult**. Feedback helps inform improvements to the RSB Research Bioethics Consultation Service
- Requestors will be **contacted by the ITHS annually**, as are all users of ITHS services, to collect information about grants and publications that have been assisted by ITHS services.
- The ITHS is supported by the NIH Clinical and Translational Science Award (CTSA) program which has two initiatives to improve consultation quality **by sharing consult information** with other CTSA bioethics consultants:
 - The CTSA consortium hosts a database of **minimally descriptive consult information**. This allows consultants to benchmark their activities and to seek advice from other CTSA consultants who have faced similar issues. Explicit identifying details are not shared; however, it may be possible to determine a requestor's identity based on the "reason for the consult". **RSB staff routinely enter limited consult information into this database.**
 - The CTSA consortium hosts a **web-forum** for discussion of ongoing bioethics consults. Web-forum participants agree to not discuss the details outside the forum. Posting questions to the forum in this way may allow the RSB consultants to provide more comprehensive analysis and recommendations. **We will only do this with your permission.**
- **Limits to Confidentiality:** In most circumstances, consult information is confidential, as described above. However in rare cases, the consultants have obligations to share consult information with others at their institutions. Examples include very significant concerns about safety, sexual harassment, research misconduct, or research non-compliance where participant safety is at stake.

Please let us know if you have any concerns about our confidentiality practices.