

Human Subjects Protection Issues in QUERI Implementation Research

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ABSTRACT

Background

Implementation research studies aim to foster the adoption of guideline-based care processes in routine care settings and increase understanding of how societies and their organizations can maximize guideline-based care. As such, these studies expose subjects to minimal risk and have high potential individual and social benefits. Yet Institutional Review Board (IRB) costs for these studies are formidable. We use the IRB-related experiences of the QUERI Translating Initiatives in Depression into Effective Solutions (TIDES)-related projects to discuss methods for optimizing the IRB process in implementation research (IR). This series of studies involving the Mental Health QUERI Center aimed to support and evaluate implementation of evidence-based care models for depression into routine Veterans Affairs (VA) practice.

Methods

As part of the studies' formative evaluation (FE), TIDES researchers sought to document the required IRB effort and the philosophy and methods used to support interactions with IRBs. We tracked common themes and application approval times. Concepts and tools presented that designed to maximize the efficiency and ethical correctness of the IRB process. These include a significant focus on ensuring the adherence of the research team to quality improvement ethical standards and clinical best practices.

Conclusions and Discussion

From 2001 to 2006, TIDES-related projects required 40 initial IRB submissions, 60 renewals and 60 modifications. The average time from submission to approval was 35.5 days in the initial TIDES project. Variation across sites in submission and approval methods was considerable. All sites successfully completed the IRB process.

Successful IRB work on implementation projects requires a substantial investment of time, effort, and IRB expertise on the part of researchers, clinical partners, and IRB members and staff. Improvements in the IRB process, as well as the development of clearer standards for guiding quality improvement aspects of implementation projects, may be a necessity for fostering future research/clinical partnerships. Process changes currently being contemplated, such as development of centralized IRBs, a specific IRB structure for Quality Improvement (QI), and clarification or revision of guidelines for implementation research may assist these partnerships in the future, but in the present, researchers carry the burden of structuring the process, and may be assisted in doing so by the tools and concepts we present.

DRAFT

BACKGROUND

There is a growing awareness that implementation research (IR) projects in general and VHA QUERI active implementation studies in particular (cite Stetler et al Enabling article this issue) must take into account the impacts of current controversies regarding Human Subjects protection issues.[1] IR focuses on clinical guideline or evidence-based quality improvement (EBQI).[2] IR often involves partnerships between researchers and clinical colleagues at multiple sites. Although there is relatively little research examining the issues, the number of multi-site studies has increased over the past three decades, imposing a greater burden on IRBs and potentially slowing review of IR and other studies. [3-6] Researchers report great variability in the way IRBs evaluate multi-site protocols for all types of studies. [3, 5, 7, 8]

For example, McWilliams reported that 31 IRBs generated study risk determinations from minimal to high for the same study. This resulted in 7 expedited reviews and 24 full reviews across the 31 sites. This variability can result in disparities in human subjects protection, be detrimental to the conduct of the study, increase the time needed to conduct the study, and increase costs.[3, 4, 9] Tod et al. and Cassell and Young raise similar concerns in their discussion of UK human subjects review. [10, 11] In addition, requiring documented consent for minimal risk research can reduce participation and increase participant burden, negatively affecting the scope and potentially the validity of research studies. [12, 13]

Complex ethical issues face IRBs trying to make risk benefit determinations for IR studies, beginning with a determination of whether the activity is “research” at all and therefore reviewable. Subsequent determinations focus on whether there are “human subjects” involved; whether minimal risk definitions are met; what type of consent mechanisms are appropriate; and how to weigh individual risk of breach of confidentiality (usually the primary risk) with potential

societal benefit. These determinations derive from IRB's interpretation of research; as well as from ethical, regulatory and liability-related principles and demands. Despite extensive discussion, there is no consensus on whether and how to review QI research. [9, 14-18]

The large costs of carrying out multi-site studies for which IRB approval is required at all investigator home institutions and all participating sites may have dampening effects on research. Health services researchers may avoid QI research entirely because of the burdensome and inconsistent aspects of obtaining IRB approval. [19] Given the societal health benefits likely to be associated with researcher involvement with clinical systems and practices, and the known risks of poor quality care, the ethical issues of adding burden to the process of improving care should also be considered. [20, 21]

The issues and tools presented here were developed to address concerns encountered in an integrated series of implementation projects that began in 2001 and are currently are ongoing. These projects were designed to improve, evaluate, sustain and spread collaborative care for depression in VHA primary care clinics. Together, they represent one of the first, and the largest, multi-region VA implementation research projects supported by VA HSR&D (Health Services Research and Development). Project investigators were tasked with exploring and documenting the challenges encountered including those related to IRB processes. As of 2006, TIDES-related projects span 20 practice sites in four VISNs (Veterans Integrated Service Networks), and involve investigators from four separate VA HSR&D Centers of Excellence in addition to the Mental Health QUERI Center. Table 1 contains descriptions of the TIDES related projects. The purpose of this paper is to make the approach and tools developed by these projects available to implementation researchers, and to support the development of future improvements in IRB and QI process that will enhance research/clinical partnerships.

THE IRB EXPERIENCE FOR TIDES-RELATED PROJECTS

In the following sections, we present a series of IRB-related challenges. Each section ends with the major tools and solutions we used to overcome each type of challenge. Challenges included presenting issues specific to IR, handling the IRB-related workload and timeline impacts, working with multiple site Principal Investigators (PIs), and managing differences among IRBs. Responses to IRB dilemmas include negotiated agreements, clear, consistent communication, standardized processes, and coordination of follow-up and tracking across sites. Table 2 presents the tools that we developed (and continue to develop).

Learning to Communicate Implementation Specific Issues: In TIDES projects, as in many IR efforts, patients, providers, and/or sites can be units of analysis. Each of these levels has its own set of IRB-related concerns and ethical issues. IRBs that are used to evaluating clinical trials may not understand the requirements of collecting information at each of these levels. IRBs also may not understand the extent to which QI principles and requirements guide clinical activities carried out in implementation projects.

In QUERI IR, the best practices to be implemented are not experimental. Earlier clinical, health services and QUERI research have documented the need for clinical improvement and have provided an evidence base. Unless carefully explained and supported, it may not be obvious to the IRB that the “research” issue is not the efficacy of the best practice but the ability of a particular QI strategy to introduce or improve the system’s ability to apply the evidence based practice. Thus, the research is usually minimal risk, with loss of subject confidentiality being the major source of risk. “Subjects” (more appropriately called “participants”) in IR have different relationships with researchers depending on their relationship to the health care system in which the implementation takes place. Patients may not encounter researchers or may have specific

aspects of their grouped electronic medical records examined for evidence that is relevant to the implementation. Providers are obviously key in the success of clinical improvement efforts. If they see themselves as subjects from whom consent is required, their buy-in and interest in sustaining the improvement after the investigative phase is over is likely to be vitiated.

Tools and Solutions: The TIDES team worked with IRBs to educate them about the necessity of data collection at a variety of levels for supporting the external validity of the implementation effort, as well as for monitoring its clinical and organizational outcomes. The TIDES projects promulgated the philosophy that IRBs have a helpful, rather than obstructive role, and that the translation of project needs into language and plans that addressed IRB concerns would strengthen the projects as a whole and assist the IRBs as facilitators of ethically appropriate implementation research. To actualize this philosophy, we aimed to do the following:

1. Guide decision-making about the content of the application based on general considerations about information needed and helpful to IRBs.
2. Discover individual IRB's information needs, processes, and key contacts.

This required research staff to gather information on IRB variations in interpretation of regulations, and to use that knowledge as the basis for thoughtful adaptation in the presentation of study protocols. We think this investment of effort and resources resulted in greater success than would have been the case with a more mechanical adaptation to local protocols and helped insure a high level of project integrity. As the IRB challenges of IR become more systematized, the accumulated knowledge may be codified, resulting in a more universal process that still would meet local concerns.

Incorporating Continuous Improvement into the IRB Process: In TIDES, as in many IR projects, the initial IRB applications usually could not specify all aspects of the project necessary for the IRB to judge risk-benefit issues. This was largely because, in order to change a care system in a sustainable fashion, interventions must be individualized to the resources and goals of the individual sites and must be dynamic, taking into account the inevitability of changing conditions. For example, evolution of both intervention and QI data collection through successive Plan Do Study Act cycles [22] (PDSAs) at participating sites is a standard part of many implementation projects. [23] Additionally, TIDES projects incorporated multiple levels of formative evaluation (FE)[24]. As the FE results were applied to the project through PDSA cycles, changes occurred that had not been foreseen at the projects' inception. For example, several sites were unable to identify a local champion. The COVES project requested IRB permission to modify the TIDES protocol to allow researchers to assist sites in this activity.

TIDES projects, like other IR efforts, incorporated many different components. For example, following the chronic illness care model, our intervention involved care management, provider and patient education informatics, and clinical policy aspects. [25] TIDES evaluation involved surveys, medical record reviews, and stakeholder interviews. This resulted in complex IRB decision-making, such that the entire project could be held up by one issue in one component. One of our sites (Table 1, IRB C) stated, "If the survey was the only thing that came to the IRB board, it could have been exempt or if the chart data had come to the IRB separately, it too, could have been expedited. But because it came all together, it would be hard to expedite it as a whole with all the different components presented."

Finally, if an IRB judged our initial proposal to be exempt, it became somewhat difficult to review a modification of the proposal that might have additional IRB implications. This

occurred, for example, when we learned that a study survey that we had envisioned as de-identified QI could not be carried out as planned. It required extra effort to then return to IRBs that had judged the survey as exempt to let them know of the new circumstances, a necessary step since not all activities in IR are without risk. Breach of confidentiality remains a risk even in minimal risk studies. Researchers should accurately assess the associated risks of the research including the evidence-based practice. Sometimes it is not the practice itself that is the risk but ill-defined relationships among researchers as facilitators and the system with which they are working that may add risk. An example in depression treatment IR would be if there were not clearly specified suicidality risk response protocols of which all parties were aware. These risks need to be clearly communicated with administrators and IRBs.

Tools and Solutions: We sought solutions to these issues that encouraged prompt submission and approval of an overall TIDES protocol, yet increased the accessibility of each component for IRB review. We attempted to avoid delay of the whole project due to the complexity of individual components or our inability to fully specify final components (e.g., when sites were involved in designing the component). Our approach was to submit an overall project IRB protocol, followed by separate submissions for each key component.

We used two major variations on this general principle, *depending upon the preferences of each IRB*. In the first approach, we submitted the first study component to be carried out along with an overview of the entire project. We then submitted additional project activities for individual review in the context of the project overview. This approach allowed IRB reviewers to judge project activities in context without having to judge all components at once. Reviewers had complete information for each component at the time of submission. It allowed the level of IRB review (e.g., exempt versus full) to be appropriate to a specific component. However, this

solution proved to be burdensome administratively to both the IRB and the research team due to the need to track each component as a separate application, complicating modifications and renewals.

The second approach we used was to submit an initial protocol that was as complete as possible, and then to submit modifications as needed. We submitted modifications whether or not the original proposal was considered exempt. We hope that future IRB developments will identify the best methods for introducing the unique features of individual components to the IRB. [17]

Learning to Define QI and Research Roles of Investigators and Staff: Implementation researchers have to deal with the all too frequent previous experience of clinicians that the researcher is there for research, only wants the involvement of the clinician to help meet the researcher's needs and when the study is done, they and the clinical intervention will go away (Stetler, personal communication). However, the roles of implementation researchers are quite different from researchers in clinical trials.

Researchers function both as facilitators and gatherers and analyzers of generalizable knowledge. As facilitators, researchers often function at the behest of the organizational entity. Actual implementation decisions may be made by organizational participants rather than by researchers. These organizational participants may hold considerably more power than the researchers by virtue of their decisional authority. Clinicians may encounter implementation researchers as facilitators, purveyors of CME and/or as gatherers of information regarding professional opinions and knowledge that may be relevant to the implementation project. IRBs are appropriately concerned when researcher/administrator/clinician roles are complex in that this can raise issues of possible coercion in recruitment of patients and staff. The IRBs also may

have concerns about possible confidentiality issues in keeping clinical, job performance, and research data separate. Additional issues regarding the role of the researcher are further discussed by Lavis, Landry, and Ross [26-28].

Tools and Solutions: To address these issues, we developed a memorandum of agreement or Charter with participating VISNs that specified our clinical QI responsibilities. Among other issues, for example, the memorandum indicated that we were designated by the VISN as responsible for training care managers (CMs), but that CMs were hired and supervised by appropriate clinical personnel. The memorandum also specified our adherence to clinical privacy rules for aspects of our project that were QI and the need for site participants who wished to utilize any QI data from the project for research purposes to seek IRB approval. The memorandum was successful in clarifying our roles and expectations with participating VISNs, and is currently being evaluated by VA IRB and legal experts in terms of its merits for promoting safe and effective IR.

Handling the IRB-Related Workload and Timeline Impacts: From project inception in 2001 to mid-2006, TIDES-related projects have required 40 initial IRB submissions, 60 renewals and 60 modifications. First, each project's IRB protocol was submitted to the IRB of each principal investigator's institution. Because these projects represent collaboration among four VA health services research Centers of Excellence, and Principal or Co-Principal Investigators come from each of these sites, protocols must be approved by multiple sites on the basis of investigator involvement. Then, each protocol was submitted to each participating VA medical center's associated IRB for review. Table 3 shows the time interval between submission and approval for the TIDES and ReTIDES studies. On average, TIDES protocols were approved in a little over a month (36 days), and ReTIDES approvals in a little less than half that time (14 days).

For both studies, the outlier times (82 days for TIDES and 30 days for ReTIDES) had substantial impacts on the timeline for the projects as a whole. The shorter times for ReTIDES are probably related both to improvement on our part in presenting implementation issues and to increased familiarity of participating sites with the approaches we took. This increased familiarity, as well as our high rate of final success in obtaining approvals, reflected collaborative work with IRB, and administrative staff. This work often required an additional three or four months as final materials were pilot-tested and adjusted to IRB stipulations and as final submissions were adapted to the variable formats and requirements of different IRBs. Variable lengths of time for IRB approvals and study delays have been reported by others. [3, 9] McWilliams and colleagues report a mean of 32 (range 9-72) days for those sites undergoing expedited review of their multi-site study and a mean of 82 days (range 13-252) for the same protocol experiencing full review at other sites. Stair et al in their study of IRB variation found the review and approval process took a median of 38 days to approve (range 26-62). [5]

Tools and Solutions: TIDES projects realized early on that IRB work would consume more than expected resources, and re-budgeted accordingly. In addition, each involved HSR&D and QUERI Center contributed IRB expertise. The primary experts we consulted included three individuals with IRB administrative leadership positions and special expertise in health services research and two HSR&D Center IRB experts. Project investigators devoted about .2 FTEE (Full time employment equivalent) to the IRB submission process. Other project staff devoted approximately 1.5 FTEE to IRB-related tasks over all study years; about half of this effort was at a PHD level and about half at a Research Assistant level. While this effort was substantial, we think that future projects should anticipate the challenges we faced, budget appropriately, and use tools such as those we present to organize IRB workload and cope with timeline challenges.

Requirement for Local Site PIs. In an IR project, local principal investigators (site PIs) initially may have limited understanding of the full study or limited understanding of IRB needs. This is because implementation projects are locally led primarily by clinician leaders and managers, who may not have prior research experience nor human subjects training, leaving the options of training the local TIDES leader in IRB principles or training an IRB-certified colleague about TIDES and implementation research.

TIDES Tools and Solutions: The TIDES coordinating team spent significant resources educating, supporting and working with site PIs. In addition, TIDES made every effort to reduce burden on site PIs by working with the site IRB, and doing the bulk of the preparation work for submissions. Nevertheless, the site PI's willingness to attempt to solve problems proved to be critical to the timeliness with which each site progressed through the IRB process. The primary tool in this area is an orientation checklist that structures initial discussion with a potential site PI.

Responding to Local Differences between IRBs: In systems such as in the USA, different IRBs have different forms, procedures, deadlines, and reporting requirements. Finding out about these requirements can be challenging. Some IRBs were initially reluctant to communicate directly with the project's central team. Many IRBs still do not have a general website or forms and instructions that are accessible to applicants outside their system. Yet study activities needed to take into account IRB schedules, and allow for probable approval delays. TIDES multiple study sites and multiple connected projects faced the challenge of carefully tracking the expiration dates, submission deadlines, and IRB meeting dates across all IRBs.

This timing issue was further complicated by interdependent project components. An example of this is that participating sites had to be determined before IRB approval could be

sought. In fact, as is the case with virtually any grant proposal, some sites had to be identified in the proposal. Therefore site preparation activities had to begin prior to funding. Yet, unlike clinical research studies, in our IR study the sites themselves were subjects of investigation. Once the research was funded, we obtained approval from investigator institution IRBs for recruitment activities. This created an odd implementation process, as we first enthusiastically marketed the project, and then asked sites to wait, sometimes for months, while we obtained local IRB approval. IRBs reviewed and approved our submissions at different rates; therefore project activities could not be conducted in unison.

In addition to variation across IRBs, other differences between sites in terms of training, type of experience, resources, and culture had an impact on the research implementation process. Often the PI, staff supporting the site PI, the IRB, and the local research administration were in different locations. Adding further complexity, some sites used affiliated university IRBs that fell under different regulations and requirements. Reflecting this diversity, types of review and approvals — such as exemptions, expedited review, & approvals with various waivers— varied considerably by site. This echoed prior research showing that variability among IRBs in their assessment of risks and benefits result in differing opinions about waivers in consent or in the documentation of consent [7].

Tools and Solutions: To track and log multiple site submissions, we used an IRB database. To learn about local requirements, we used interview templates to gather relevant information (Table 2).

DISCUSSION AND CONCLUSIONS

IRBs are essential participants in moving IR forward. Our experience shows that ethical solutions to most dilemmas posed by IR can be solved, if the level of commitment and communication among stakeholders is sufficient. Our experience also highlights the high costs of working with IRBs in multi-site IR projects, and the necessity of developing organized, efficient ways of dealing with these issues if researchers are to participate in improving clinical quality. Through lack of unambiguous guidelines and local liability concerns, IRBs are at risk of applying both variable and inappropriate or unnecessary standards to IR that are not consistent with the spirit of the Belmont report and impede evidence-based QI research.

The experiences of the TIDES-related projects echoed a set of common themes (Table 2), which often combine the issues faced by multi-site randomized clinical trials and QI projects. Use of frameworks that identify and delineate the relevant implementation features of these types of studies could help IRBs deliberate more effectively. Implementation projects share characteristics with these paradigms including use of multiple health care systems/sites, involvement of multiple IRBs and multiple local site investigators but also incorporate additional unique implementation issues that are often unfamiliar to IRBs. Two conceptual models [29-31] can be helpful in delineating specific aspects of IR that bear on human subjects' protection issues, the RE-AIM framework [30, 31] [32] and the Stetler model of Research Utilization [33, 34]. These frameworks may assist those interested in adopting or adapting the tools we present to decide what may be relevant for their situation. The models can also be used by researchers to inform their interactions with IRBs as they identify and address potential participant risks and benefits.

The RE-AIM framework identifies information sources that are needed to promote external validity and therefore the types of interaction among researchers and participants that will be required to obtain that information. The reach of an implementation study is determined by comparing participants of all categories (administrators, clinicians and patients) with eligible non-participants within participating sites. Measurement of reach requires information about non-participants (an IRB issue) and is affected by inclusion and exclusion criteria and by research consent. Reach is adversely affected by factors that reduce the participant pool in relation to individuals for whom the intervention to be implemented may be a best practice. Effectiveness applies to both individuals and organizations and requires documentation and measurement of outcomes, both positive and negative. For implementation studies, this can involve the following issues:

- Documenting variability in individual outcomes often requires the ability to merge data for individual participants across several databases, usually requiring at least the transitory ability to assemble crosswalks that may be indexed by identifying information such as social security number.
- Documenting any negative outcomes to individual participants is consonant with the need to report adverse consequences to IRBs.
- Documenting organizational outcome variability requires sites as units of analysis, and the study design should allow for measurement of potential negative effects at the organizational level.

Adoption also applies to both individuals, as “intervention agents,” and organizations. Research enrollment and consent processes that differ from routine organizational procedures may reduce the ability to examine adoption by individual participants. Similarly, using volunteer sites may

restrict participation in the project to settings with a culture of innovation. Adoption at the system level requires ownership and integration into usual care processes. The RE-AIM framework makes explicit the assessment of fidelity to the model being implemented and documenting the costs of implementation. Both of these measurement areas require collecting information on participants' activities. In addition, the Stetler model suggests that concurrent assessment of facilitators and enhancers of change at the local level is necessary to optimize achievement of the targeted goals. Finally, documenting maintenance involves both individual and site level data, the former of retention and maintenance or decay of individual participant outcomes attributable to the implementation and the latter, continued employment of the implemented practices by the sites and long term fidelity to the evidence base.

The Stetler model of Research Utilization [33, 34] consists of five phases that guide: 1. the selection of research evidence; 2. formal utilization critique of studies; 3. consideration of research findings in the context of other forms of evidence, fit to the setting that is considering implementation, alignment with current practice and feasibility of adoption; 4. the type of use decision and specifics of implementation; and 5. dynamic evaluation, the details of which depend on the use decision. The model formally mentions the role of IRBs in Phase 5 but we suggest that it is useful for the researcher to consider the IRB as an “influential, external factor” to be considered along with other factors beginning in Phase 1. Considering the IRB in this light motivates many of the tools we discuss that are designed to: 1. respond to the IRB's information needs and processes, as well as informing decision-makers and facilitators; and 2. guide decision-making as to the content of the application to encourage facilitative IRB processes in implementation of evidence-based quality improvement.

Although our interactions suggest that several of the IRBs we work with have become more knowledgeable with respect to implementation studies over the past 5 years, we have continued to experience wide variability in IRB responses to IR issues. IRB risk/benefit determination should include reformulation of risk/benefit to “society” in terms of risk/benefit to the applicable patient population of “NOT acting with the best available evidence in light of the current need”. [33] IRBs may lack sufficient expertise and guidelines to understand IR as part of routine, necessary and “quality” QI evaluation versus early phase research, leading to problems with obtaining evaluative information from clinicians and others. Some of this could be remedied by revised national guidelines (such as from the Office for Human Research Protections, OHRP, in the United States) and more flexible and facilitative regulations. There are also promising developments in the IRB community. IRB accreditation may eventually result in more accuracy and uniformity across IRBs. In November 2005, OHRP sponsored a workshop on alternative models for IRB review [35]. With regard to QUERI implementation research, the VHA has an opportunity to play a leading role in implementation research oversight through designing and planning to convene a central IRB for multi-site studies

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35. **Alternative Models of IRB Review - Workshop Summary Report**
[\[http://www.hhs.gov/ohrp/sac/hrp/documents/AltModIRB.pdf\]](http://www.hhs.gov/ohrp/sac/hrp/documents/AltModIRB.pdf)

Table 1. Description of TIDES related QUERI supported HSR&D Projects

Project	Type	Participants	Goals
TIDES ¹	Action research partnership with formative evaluation	Primary care, mental health, nursing & administrative leaders from 3 VHA* VISNs†; experienced depression care researchers; depressed veterans	Study feasibility and safety of evidenced-based quality improvement for depression care‡
WAVES ²	Site-randomized controlled trial	TIDES sites and matched control sites. Veterans enrolled in primary care clinics were screened for depression by researchers.	Implement & test depression collaborative care using TIDES evidence-based model
COVES ³	Mixed method; administrative data analysis and qualitative interviews	Stakeholders (patients, clinicians, administrators); VHA administrative databases	Understand cost and value tradeoffs of TIDES implementation using VHA system cost information and semi-structured interviews with TIDES stakeholders
ReTIDES ⁴	Regional demonstration project with program evaluation	All levels of VHA administrative structure including: Central Office; 4 implementing VISNs and administrative control VISNs; VAMCs¶; clinics; clinicians; administrators; patients	Support progress of TIDES collaborative care model toward national VHA implementation. Sustain and spread TIDES evidence-based depression care model to additional VHA sites

1 Translating Initiatives for Depression into Effective Solutions

2 Well-being Among Veterans Enhancement Study

3 Cost and Value of Evidence-based Solutions for Depression

4 Regional TIDES

* Veterans Health Administration

† Veterans Integrated Service Network

‡ Steps included: 1) Adapt depression collaborative care models to VA settings through Evidence-Based Quality Improvement for Depression (EBQID); 2) Support and evaluate depression collaborative care implementation; and 3) Prepare for dissemination of depression improvement methods and materials throughout the VHA

¶ Veterans Affairs Medical Center

Table 2. Implementation Research Issues, Challenges and Solutions

Issue	Challenge	Solution	Tools
<i>Implementation-specific</i>	External validity considerations	Explain issues to IRB*	Implementation evaluation theory exposition
	PDSA† intervention adaptation cycles	Use IRB's preference for component or modification approach	Component submission or Full submission with modification explanation
	Risk-benefit issues (minimal risk)	Request exemption or expedited review; Include explanatory text	Intervention evidence base description
	Multiple roles of researchers/facilitators	Explain issues to IRB	Implementation as action research text
	Multiple subject/participant classes	Explain different risks-benefit issues for varying classes	Participant role descriptions
	System-level unit of analysis	Explain goals of targeted implementation need & purpose of organizational data	Goals and intended products text
<i>Multiple Health Care Systems/Sites</i>	Transparency of system/researcher ethical responsibilities	Negotiated agreement	Implementation Charter
	Maintaining accountability across systems / sites	Centralize records retention at a single administrative site	Historical database of submissions to all sites; Record filing system for hardcopy and electronic submissions
	Relationships among IRB and participating organizational entities	Standardize process for inquiring about the nature of oversight relationships	Checklist for IRB Contact Interview
<i>Multiple Local Site PIs</i>	Recruitment	Involve System supervisors IRB Administrators. Negotiate Site PI‡ role	Interpersonal relationships and Memorandum of Understanding
	Varying levels of commitment	Invite to participate in work-group meetings; Solicit advice on implementation activities	Align site PI involvement with organizational or academic incentives.
	Varying levels of IRB experience; Limited time	Orient to role responsibilities; Provide high level of administrative support	Site PI Orientation Checklist
	Varying ethics certification requirements	Investigate and document approved training	Site PI Training Information
<i>Multiple IRBs</i>	Lack of standardized procedures and forms	Adapt explanatory text modules to each IRB	Compendium of adaptable descriptive modules
	Communication with IRB / R&D§ Administrators	Establish connections using both formal structure and individual preferences	Information Handbook sections on contact information and communication preferences.
	Multiple, competing renewal deadlines	Create, maintain and monitor deadlines and upcoming IRB / R&D meeting dates	Submission Deadline Report
	Inconsistent AE¶ definitions and reporting requirements	Maintain site AE definitions, forms, medical center policies & procedures, and reporting requirements	AE Reporting Comparison Table; AE Tracking Report
	Coordination & consistency in accomplishing IRB related tasks	Create IRB specialist position; Budget for sufficient resources; Form IRB Work Group; Schedule IRB specific project staff calls; Stagger applications	IRB Specialist Position Description; Structured IRB team telephonic and internet communication

* Institutional Review Board

† Plan – Do – Study – Act

‡ Principal Investigator

§ Research and Development

¶ Adverse Events

Table 3. TIDES/RETIDES IRB Applications Formative Evaluation Information

TIDES Study			
<i>Site*</i>	<i>Changes to submission required by IRB?</i>	<i>Approval Type†</i>	<i>Time Elapsed‡</i>
A	No	Exempt	32
B	No	Exempt	67
C§	Yes ¹	Expedited	75
D	No	Expedited	9
E	Yes ²	Expedited	5
F	Yes ³	Full	7
G¶	No	Full	82
H	Yes ⁴	Expedited	38
I	No	Expedited	5
			Average = 35.55
ReTIDES Study			
F	Yes ⁵	Full	22
I	N/A	Non-human subjects research	5
J	No	Exempt	3
K	No	Exempt	20
H	Yes ⁶	Expedited	30
L	Yes ⁷	Expedited	14
A	No	Exempt	6
M	No	Exempt	14
			Average = 14.25

* Site identification codes are uniform, showing both new sites for ReTIDES and some TIDES sites not (yet) participating in ReTIDES

† We experienced no variance between review type preferred and actual approval type granted.

‡ In days, starting with submission date, ending with approval date (weekends, holidays included)

§ IRB C stated: “If the survey was the only thing that came to the IRB board, it could have been exempt or if the chart data had come to the IRB separately, it too, could have been expedited. But because it came all together, it would be hard to expedite it as a whole with all the different components presented.”

¶ From IRB G Investigator Guide & Instructions booklet: “No research is exempt from review and there are no “expedited” reviews”.

|| This was the only site that required an electronic submission

1 Concerns included: consent form alterations, include contact info in mailing, storage of survey data, patient information protocol, number of interviews, adding written consent at local level

2 Concerns included: changes to allow better informed consent decision-making, protocol regarding number of times subjects are contacted, advance phone call consent, telephone interview protocol, recording interview protocol, time estimated for interviews, why are patients being interviewed, and obtaining consent

3 Concerns included: consent obtained to access patient data registry, justification for exemption of worksheet data forms, how does VA encrypt medical records, discrepancy in numbers, describe terminology in narrative, protocol regarding the movement of paper data, who administers oral consent procedure, clarification of anonymous/confidential, changes to worksheets, who has access to data, confirm study codes are not SSN, how is questionnaire used, oral consent concerns, typographic errors

4 Concerns included: typographic errors, further justification for no consent

5 Concerns included: coercion as possible risk, determining coordinating center, providing a consent form if requested by subject, how participation is / isn't related to job description, including text about participating not affecting job security

6 Concerns were administrative, related to the electronic submission process

7 Concerns were administrative