The University of Minnesota's Clinical Research Support Center Feasibility Review: An Objective Protocol Assessment Carving a Pathway to Study Success

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Abstract: *To initiate clinical research studies successfully and efficiently, it is critical to develop a strong, feasible, and well-written study protocol early in the start-up phase. The University of Minnesota's Clinical Research Support Center designed and implemented a structured Feasibility Review process in 2018 that addresses common start-up challenges such as poor study design, inappropriate outcomes, and limited resources. This process has been shown to turn an unfeasible study into a well-designed protocol that is IRB-approved with few protocol-related stipulations and well prepared for execution. It has also educated study teams on how to write better-quality and more robust protocols for subsequent studies. Once a draft protocol is available, the entire process takes just six working days and is free of charge to investigators, study teams, and departments.*

From 2018-2021, one hundred sixteen Feasibility Reviews (n=116) have been completed across eight schools or colleges. Mean satisfaction scores for study team members who responded were high (N=126, M=4.71 ± 0.5) on a 5-point Likert-type scale. Most respondents (96%) indicated that they planned to modify their protocol based on reviewer feedback. Open ended/ qualitative feedback was highly positive with most responses centered around the helpfulness of feasibility review, the high level of expertise, and fast turnaround time.

The Feasibility Review is a valuable and multifunctional program providing timely expert guidance to study teams to efficiently and successfully launch and execute clinical research studies. It can be easily replicated, adapted, and implemented at other institutions to increase the quality and efficacy of academic research.

Keywords: *feasibility review, protocol development, study start-up, clinical and translational science*

Introduction

Anyone who has conducted a clinical research study at an academic institution knows how complex and challenging the process can be. Barriers to successful execution often begin during start-up and may include poor study design, inappropriate outcomes, the length of time protocol development can take, and limited resources to navigate the process (Al Dalbhi et al., 2019; Alak et al., 2014; Campbell et al., 2015; Cullati et al., 2016; Djurisic et al., 2017; Duley et al., 2008; Gallagher et al., 2013; Higgins et al., 2010). The impact of these barriers can be far-reaching and include potential lost opportunities for extramural funding and industry partnerships. It can also lead to investigator frustration and disengagement, reduced collaboration across institutional departments, wasted time and effort for participants, and ultimately, fewer meaningful studies, discoveries, and translations (Yordanov et al., 2015). In a competitive research environment, it is critical to have a well-written and feasible protocol to get through the IRB process smoothly and be successful in execution.

In 2006, the National Institutes of Health (NIH) launched the Clinical and Translational Science Awards (CTSA) program with the goal of supporting a network of research institutions

working together to improve the translational research process to provide "more treatments to more patients more quickly" (National Center for Advancing Translational Sciences, 2015). One challenge that the CTSA program is charged with tackling is developing innovative processes to increase the quality and efficacy of translational research. This often starts with protocol development and assessment of trial feasibility.

Currently, more than 50 medical research institutions across the nation receive CTSA program funding. When surveyed, 64% indicated their institutions offer some form of an assessment of trial feasibility or a similar service, however few have been documented in the literature. Rockefeller University's Center for Clinical and Translational Science developed the Navigation Program which uses a structured supportive guidance process to expedite protocol development to the standards of good clinical practice (GCP), focusing on research ethics and integrity (Brassil et al., 2014). However, one limitation of this program is the length of time the process could take with some studies reaching 400 days before completion.

Vanderbilt University's Institute for Clinical and Translational Research implemented a Research Design Studio system that assembles a panel of three to six research faculty to provide guidance in hypothesis generation, study design, grant review, implementation, analysis and interpretation, manuscript review, and translation (Byrne et al., 2012). However, new or different research personnel participate in each studio, potentially leading to disparate and/or conflicting feedback.

Indiana University's Clinical and Translational Sciences Institute employs Project Development Teams that also help to accelerate the research process from initial concept to external funding (Sajdyk et al., 2015). However, investigators are sometimes so early in the research development process, the overall study design and resources necessary change, requiring additional meetings and/or starting from scratch.

In 2018, the University of Minnesota's (UMN) Clinical Research Support Center designed and implemented a formalized and structured Feasibility Review process that addresses these limitations and quickly helps investigators develop strong, feasible, and well-written protocols ready for Institutional Review Board (IRB) submission and successful execution.

Methods

Development of the Feasibility Review

Earlier in 2017, the UMN convened a design studio as part of its initiative to establish the Clinical Research Support Center; a "one stop shop" for investigators and study teams providing a full scope of resources to help ease the start-up burden. Under the leadership of the steering committee, cross-functional stakeholders were identified and invited to participate in twice-monthly design studio sessions for four months.

Thirty-four participants, including diverse faculty from different departments, research support staff, and institutional leaders were charged with conducting more than 100 interviews with individuals from the greater research community to gather feedback on the UMN's clinical

research process in its current state, what was working well, and what were the frustrations. Opportunities were collated and common themes identified, which included the need to assess study readiness and provide support for navigating the research process. This led to the concept of the Feasibility Review and subsequent process development to put the idea into action.

Feasibility Review Process

The Feasibility Review is managed by a team of approximately five Clinical Research Specialists from the Clinical Research Support Center. The Specialists are responsible for meeting with investigators and study teams who are in the process of protocol development. The Specialists assess investigator needs and help study teams create complete protocols by offering guidance, feedback, and language specific to their study needs. Once a protocol is complete, it is eligible for a Feasibility Review.

The team of Specialists review up to two draft protocols per week, along with consent forms, recruitment materials and budget, if available, with a broad panel of experts. This panel includes representatives trained in the Feasibility Review process (further referred to as "experts") from biostatistics, federal regulations (FDA), informatics, recruitment, monitoring, facilities, clinical/hospital partners, community engagement, accounting, local IRB regulations, and biorepository/lab pathology. Experts take one week to review the materials and provide feedback, guidance and suggestions through a shared review form in Google Sheets. See Figure 1 for example review prompts.

Figure 1. Panel of experts with example review prompts.
Note: Each expert has several review prompts.

Click here for larger image

Within one week, the Specialist facilitates a Feasibility Review group meeting with all experts and the study team. The experts discuss the protocol section by section to present their feedback, talk through any challenges or barriers, and suggest creative solutions. This meeting takes approximately 1.5 hours and is held via Zoom.

Within 24 hours, the Specialist provides a written summary of the feedback to the study team outlining strengths, opportunities for improvement, resources, action items, and all experts' contact information for follow-up support. The entire process takes six working days from sharing materials with experts to providing the study team with the written summary and is free of charge to study teams and their departments. See Figure 2 for a timeline of the Feasibility Review process.

Figure 2. Timeline of the Feasibility Review Process.

Next Steps/Follow-up Support

Study teams are encouraged to make changes to their protocol based on the Feasibility Review comments and to send a final version back to the Specialist. The Specialist then shares the final protocol with a Regulatory/Recruitment Specialist to develop/revise consent forms, recruitment flyers/ads and other participant-facing materials, and submit for regulatory review (IRB, FDA and others as required).

After study approval, the Specialist offers the study team study activation support. This often entails guidance, resources, and planning to address financials (i.e., billing and expense tables), clinical operations planning (i.e., delegation of authority), lab/specimen management (i.e, lab orders), data capture and management plans, and opening to accrual. Study activation support can include weekly or bi-weekly meetings and often includes the Specialist, Principal Investigator (PI), Project Manager, and Study Coordinator.

Promoting the Feasibility Review

The Feasibility Review is advertised and promoted across the University through various channels,

including new faculty and staff orientations, departmental meetings, department websites, e-newsletters, blog posts, professional development seminars, email communications, and through referrals from experts and previous study teams. The UMN IRB may also recommend a Feasibility Review for studies that were previously disapproved or deferred.

Ongoing Quality Improvement

Ongoing quality improvement is an integral part of the Feasibility Review process. All study team members who participate in the review are invited to complete a 4-question survey assessing their overall experience with the process, whether they plan to modify the protocol based on reviewer feedback, what they liked most, and how the process can be improved.

The entire expert review panel (including the Specialists) meets each quarter to reflect on past reviews, highlight successes, discuss ways to improve the process, review responses from the survey, and engage in team building. One improvement opportunity that was identified involved reformatting the shared review form to better align with the IRB's protocol template. This improvement resulted in better understanding and adoption of reviewer feedback by study teams as it is now more explicit where in the protocol a suggested change should go. Another improvement involved increasing the number of experts from six to eight, with the addition of an expert from recruitment/research facilities and clinical trial monitoring. This improvement resulted in a more comprehensive and thorough review. Team building activities are among the experts and Specialists and include 'getting to know you' icebreakers, games such as trivia and special recognition or 'shout outs' to those who have gone above and beyond over the past quarter.

Even with a comprehensive Feasibility Review, the IRB may find an area of the protocol that requires further development or explanation. These requests for clarification are also supported by the Specialist and noted for quality improvement. By following the protocol all the way through the approval process, the Specialist is able to help resolve requests, note other issues that were not addressed during the review, and devise new prompts to help experts better address these issues in the future.

Results

Study Characteristics

As of December 31, 2021, the Clinical Research Support Center has completed 116 Feasibility Reviews across eight UMN schools or colleges. Most studies came from the Medical School (85%) in the Department of Psychiatry & Behavioral Sciences and Department of Medicine (both at 18%), followed by the Department of Pediatrics and Department of Rehabilitation Medicine (both at 13%).

The majority of the studies were investigator-initiated (97%; as opposed to business and industry) and written in the institutional biomedical protocol template (65%). Thirty-one percent used a randomized clinical trial study design with the primary purpose of treatment (40%). Most studies

were single-site (88%), and most did not require an Investigational New Drug Application (IND) or an Investigational Device Exemption (IDE; 55%).

Thirty-five percent of PIs were newer to research (having completed less than three clinical trials) while the remaining 65% were more experienced (having completed three or more clinical trials). Sixteen percent of PIs returned with a second, third or fourth protocol for review. See Table 1 for all Feasibility Review characteristics

Table 1. Feasibility Review Characteristics

	N (%) or Mean ± SD
Number of Reviews (January 2018 - December 2021)	116
Schools or Colleges*	
Medical School	99 (85%)
School of Nursing	5 (4%)
School of Public Health	4 (3%)
School of Social Work	2 (2%)
School of Dentistry	1 (1%)
School of Kinesiology	1 (1%)
College of Science & Engineering	1 (1%)
College of Education and Human Development	1 (1%)
Study Type	
Investigator-Initiated	112 (97%)
Business & Industry Sponsored	4 (3%)
Protocol Type	
Biomedical	75 (65%)
Social	25 (22%)
Other	16 (14%)
Study Design	
Randomized Clinical Trial	36 (31%)
Cohort Study	23 (20%)
Cross-sectional Study	22 (19%)

Before & After Study	20 (17%)
Case Series	6 (5%)
Case control Study	4 (3%)
Other	5 (4%)
Primary Purpose	
Treatment	46 (40%)
Basic Science	16 (14%)
Diagnostic	10 (9%)
Health Services Research	10 (9%)
Supportive Care	9 (8%)
Prevention	8 (7%)
Device Feasibility	7 (6%)
Screening	2 (2%)
Other	8 (7%)
Number of Sites	
Single-site	102 (88%)
Multisite	14 (12%)
Investigational Product	
Device	25 (22%)
Drug	24 (21%)
Device & Drug	3 (3%)
No Investigational Product	64 (55%)
Principal Investigator Experience	
Completed less than 3 clinical trials	41 (35%)
Completed three or more clinical trials	75 (65%)
Repeat Study Teams	
Returned with a second, third or fourth protocol for review (n=83 unique Investigators)	13 (16%)
Number of Experts Involved Over Time	
2018 (n=26)	6.27 ± 2.50
2019 (n=33)	8.06 ± 2.84

2020 (n=30)	8.83 ± 2.97
2021 (n=27)	8.15 ± 2.86

*Note the relative size differences of the schools. For example, the Medical School has 1,081 full-time faculty compared to the School of Public Health that has 118 full-time faculty.

Providing Valued Support

Mean satisfaction scores for study team members who responded were high (N=126, M=4.71 ± 0.5) on a 5-point Likert-type scale with 1.0 representing a "poor" overall experience and 5.0 representing an "excellent" overall experience. Most respondents (95%) indicated that they planned to modify their protocol based on reviewer feedback. Open ended/qualitative feedback was positive. Most responses centered around the helpfulness of feasibility review, the high level of expertise, and the fast turnaround time. See Figure 3 for study team feedback.

Figure 3. Study team feedback.

Case Studies

The benefits of the Feasibility Review process are demonstrated through case studies of three unique research projects.

Case Study 1

The first case is an investigator-initiated, longitudinal comparison of three groups of adolescents, using a device for measuring neurophysiological processes that was considered a non-significant risk investigational device exemption (NSR-IDE). This study was written in the biomedical protocol template and the PI was brand new to research at the UMN. The PI was referred on to a Feasibility Review by a colleague who had previously taken part in their own Feasibility Review.

The study included utilizing transcranial magnetic stimulation with electroencephalography and resting-state functional magnetic resonance imaging, and a follow-up at 3-6 months post intervention. Potential challenges with IRB approval and successful execution included an underdeveloped consent process, working with a vulnerable population (depressed adolescents with suicidal behavior), and minimal compensation allocated for participant time and effort.

After the Feasibility Review, the study team strengthened their protocol by incorporating reviewer comments on abbreviated Part 11 compliance due to the NSR-IDE, best practices for screening, consenting and assenting participants, additional safeguards for vulnerable populations, and feedback on adequate compensation for participants. They also worked with a Regulatory/Recruitment Specialist to develop consent/assent forms and participant-facing materials for submission to the IRB. The study required a full IRB review and was deemed greater than minimal risk.

The study was approved by the IRB with two minor protocol-related stipulations and received special acknowledgment noting how well-designed and clearly written the protocol and consent documents were. The PI also provided positive feedback through their experience survey, writing "[t]he process was very well organized and efficient. Reviewers' comments were well explained, and suggested changes/additions to the text of the protocol were very helpful. It was both educational and immensely useful as a PI who is new to the University." This case demonstrates how the Feasibility Review can limit the incidence of protocol-related IRB stipulations by anticipating and addressing potential challenges and concerns before a protocol is submitted to the IRB.

Case Study 2

The second case is also investigator-initiated, but was a cross-sectional study with no investigational drug or device. This study was written in the social protocol template and the PI was also relatively new to research at the UMN. This study came to the Clinical Research Support Center for a Feasibility Review after referral by the IRB, who had initially disapproved the study. Main concerns focused around the confidentiality and privacy of participants, recruitment methods that violated IRB policy, and possible coercion of participants due to an unmitigated power differential. This study was at high risk of abandonment based upon PI frustration and potential wasted time and effort.

After completing the Feasibility Review, the study team revised their study design (including new and compliant recruitment strategies suggested by the experts), addressed the privacy concerns, and mitigated the power differential to safeguard against coercion. The revised study was then IRB approved with only one minor protocol-related stipulation. This case demonstrates how the Feasibility Review can turn an unfeasible study into a well-designed, well-written protocol approved by the IRB and ready for successful execution. The PI was extremely pleased with the results of this study and returned to the Clinical Research Support Center for guidance and support on a subsequent project a few months later.

Case Study 3

The third case describes a portfolio of studies. These four studies were all investigator-initiated (by the same PI) and written in the biomedical protocol template. Unlike the two cases above, this PI was experienced in conducting research at the UMN. Three of the studies used a prospective cohort design while one was a randomized clinical trial, and one study included an NSR-IDE. This PI was referred for a Feasibility Review by their department administrator who had heard about the process through a seminar presentation.

After completing their first Feasibility Review, the study team incorporated much of the feedback received into their second study (strengthening the protocol before it even made its way to a review). Further feedback received from the second review was incorporated into their third protocol and so on for the fourth protocol. The first study was IRB approved with five minor protocol-related stipulations, the second study was approved with four minor protocol-related stipulations and the third and fourth studies were approved with no protocol-related stipulations. This case demonstrates that with each subsequent Feasibility Review, the instructional value of a review can lead to enhanced PI capabilities and to better quality, more robust protocols, as many expert comments can be adapted for subsequent studies. See Table 2 comparing case study characteristics.

Table 2. Case Study Characteristics

	Study Design	***Investigational Products***	***Principal Investigator Experience***	***Risk Level***	***Level of IRB review***	***Number of protocol -related stipulations***	***How this case demonstrates the value of a Feasibility Review***
Case study 1	Cohort Study	Device	Completed <3 clinical trials	Greater than minimal risk	Full review	2	The Feasibility Review limits the number of protocol-related stipulations by anticipating and addressing potential challenges and concerns, before they get to the IRB.

Case study 2	Cross-sectional	No investigational product	Completed <3 clinical trials	No greater than minimal risk	Expedited review	1	The Feasibility Review can turn an unfeasible study into a well-written protocol approved by the IRB and ready for successful execution.
Case tudy 3a*	Randomized clinical trial	No investigational product	Completed 3+ clinical trial	Greater than minimal risk	Full review	5	With each subsequent Feasibility Review, the instructional value of a review can lead to better quality, more robust protocols as many expert comments can be adapted for subsequent studies.
Case study 3b*	Cohort Study	Device	Completed 3+ clinical trials	Greater than minimal risk	Full review	4	
Case study 3c*	Cohort Study	No investigational product	Completed 3+ clinical trials	No greater than minimal risk	Expedited review	0	
Case study 3d*	Cohort Study	No investigational product	Completed 3+ clinical trials	No greater than minimal risk	Expedited review	0	

*Note the same principal investigator for case studies 3a-3d.

Discussion

The entire research process, from identifying the problem to formulating a hypothesis to collecting and analyzing data, is intrinsically challenging (Eapen et al., 2014; Ellis et al., 2001; Higgins et al., 2010; Kao, 2003). Many clinical research study teams struggle, and occasionally fail, during the start-up phase due to a lack of resources and support navigating the study design and protocol-writing processes. The University of Minnesota's Clinical Research Support Center has designed and implemented a Feasibility Review process that addresses limitations of similar programs by quickly helping investigators develop strong, feasible, and well-written protocols ready for IRB submission and successful study execution.

The Feasibility Review is implemented in just six working days at no cost to investigators, study teams, or departments. This ensures that time and resources are used most efficiently and encourages participation. The Feasibility Review also includes a designated panel of experts trained in the Feasibility Review process, as opposed to using ad-hoc faculty panels for each review. This helps to ensure consistency of reviews, camaraderie of reviewers, 'boots on the ground' experience, and limits the amount of training required for each new review session. Finally, the Feasibility Review requires a complete protocol for a study to be eligible for review. This reduces duplicative work when expert support and guidance is given to a study team too early in the research development

process, leading to additional examination and/or repeating the Feasibility Review.

Though a relatively new support process, the Feasibility Review has helped produce numerous high-quality protocols across several schools and departments with both new and experienced investigators. It has been shown to turn an infeasible study into a well-designed protocol, approvable with few or no protocol-related stipulations, and well prepared for execution. The Feasibility Review has also taught study teams how to write better quality, more robust protocols for subsequent studies. Feedback from study teams has been overwhelmingly positive with most indicating their overall experience with the Feasibility Review process as "excellent." Finally, the participation of experts continually engaged in the process demonstrates their continued commitment to providing valuable support to research teams across the University.

Although the Feasibility Review has shown great promise and continues to grow each year, there are some limitations worth noting. First, the review has been found to be most helpful for investigator-initiated studies, as opposed to business and industry sponsored studies, which are often rigidly structured by the sponsor. The Clinical Research Support Center continues to expand its capacity with a multisite working group and exploring adaptations to better accommodate business and industry sponsored studies. Second, the Feasibility Review does not give guidance on whether a study should move forward. Instead, the goal is to support study teams in developing the most robust, feasible, and well-written protocol possible. Despite these limitations, the Feasibility Review capability has been well received by the UMN research community and continues to grow and adapt each year.

Next steps include quantitatively assessing its impact on study approval and start-up timelines and how the program helps study teams meet enrollment goals. Considerations are also being made to expand the program to include grant reviews. It is clear, however, that the Feasibility Review is a valuable, cross-functional program providing timely expert guidance to study teams to efficiently and successfully launch and execute clinical research studies and to educate investigators as well. It can be easily replicated, adapted, and implemented at other CTSAs to continue the charge of developing innovative processes that increase the quality and efficacy of academic research

Authors' Note

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