A Protocol Review Companion for Activists

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January 2015

The Community Research Advisors Group (**CRAG**) created this *Protocol Review Companion for Activists* to facilitate community reviews of clinical trials protocols and to ensure community participation in protocol development. This document suggests key questions to ask while reviewing the different sections found in most clinical trials protocols. The content reflects the CRAG's experience reviewing protocols for the Tuberculosis Trials Consortium (TBTC), but the questions raised apply to community groups advising research institutions working on diseases other than TB. This is not an exhaustive outline of all the elements that need to be considered when reviewing a protocol; instead, this document is designed to flag key considerations and highlight areas where community input is especially important. We suggest keeping this list nearby when reviewing protocols. The questions can function as a checklist, or be used more informally to aid one's thinking when reading and commenting on a protocol.

Community advisory boards (CABs), like the CRAG, are made up of non-scientists, who represent the communities they serve or share common geographical locations, racial or ethnic makeup, values, cultures, beliefs and interests. These non-scientists review protocols, monitor clinical trials, and help educate and inform the rest of the community about ongoing or planned studies. CABs are established to:

- provide oversight and guidance for the protection of participants in clinical trials;
- help define research questions;
- communicate the interests and needs of the community to research teams; and
- represent a specific community group infected with or affected by a particular disease.

Clinical trials form the heart of clinical research and look at new ways to prevent, detect, or treat disease. Clinical trials might evaluate new drugs or new combinations of drugs, new surgical procedures or devices, or new ways to use existing treatments. The goal of clinical trials is to determine whether a new test or treatment works and is safe. Clinical trials can also look at other aspects of care, such as improving the quality of life for people with chronic illnesses. People with a particular illness or disease participate in clinical trials to help others, but also for the possibility of receiving the newest treatment options and to benefit from the additional care and attention given by clinical trial staff. Clinical trials offer hope for many people and an opportunity to help researchers find better treatments for others in the future.

The CRAG is an international, community-based advisory body that works to ensure the meaningful participation and engagement of affected communities in research conducted by the U.S. Centers for Disease Control and Prevention's (CDC's) Tuberculosis Trials Consortium (TBTC). This group of research-literate activists supports a robust and innovative TBTC research agenda that reflects both community needs and scientific priorities.

Protocol: a plan that states the specifics of a clinical trial, such as the hypothesis to be tested, drugs to be used, methods of administration, length of the trial, endpoints and eligibility criteria.

Protocol Description and Background

1. Does the **protocol** provide the purpose, relevance and scientific justification for the current study?

2. Is there enough information or details from past trials provided to support this study?
3. Based on the answers above, are the researchers in true **equipoise** about conducting the study?
4. What is the study design? (e.g., quantitative, qualitative, mixed methods, quasi-experimental, randomized controlled study)
5. Will the study have a control group? Have the principal investigators explained the procedures and purpose of using a control group?
6. Do plans for the control group at minimum match the existing standard of care for the patient group in question?

Equipoise: a guiding principle of ethical medical research that requires that genuine uncertainty exist in the expert medical community about whether an intervention under study will be beneficial or better than the control (no intervention or standard of care).

Locations where Research will be Performed

1. Are diverse countries or regions with high disease burdens represented? (Note: many regulatory authorities require drugs and drug regimens to be tested in their countries before approval.)
2. Will study drugs be made available in these countries after the trial ends? Through what means will access to study drugs continue after the trial? (e.g., compassionate use programs, open-label extension studies, phase IV implementation projects)

Requirements of Study Participants

1. How many participants will be enrolled in the study? (Note: this is important to ensure results are not misinterpreted, that studies are large enough to generate valid results, and that results will be generalizable to the larger patient population outside of the trial.)
2. What activities will the participants be expected to engage in by participating? (e.g., surveys, focus groups, interviews, diagnostic procedures, blood draws, medication adherence)
3. What is the duration of the activity, the number of times the activity will occur, and total time period of active participation per participant? (e.g., days, weeks, months, years)
4. How long will researchers follow participants? Is this information clearly described in the consent forms and supporting materials?
5. Where will data collection take place? (e.g., waiting room, research office, other location)
6. Will participants be paid for their participation through financial or other forms of compensation? (Note: common forms of payment include reimbursement for transportation to and from the research site, compensation for time off from work or a small incentive awarded for participation.)
7. If participants will receive payment after their participation in the trial ends, how will research staff link the names/contact information confidentially to their compensation?
8. Will the study collect any private or sensitive information from participants? How will this information be protected?
9. Does the study use interpreters, and if so, what are the procedures for recruiting interpreters and ensuring their cultural competency? Will study materials be translated into local languages?

Description of Research Risks and Benefits

1. What are the risks, if any (physical, psychological, social, legal, or other), to the participants?
2. What is the likelihood of these risks occurring, and/or their seriousness?
3. How have the investigators worked to minimize these risks?
4. Does the study protocol include any plans for ensuring necessary intervention in the event of a distressed participant and/or any referral sources if there is a need for psychological and/or physical treatment or assistance?
5. What are the potential benefits to the participants by participating in this study? (e.g., access to drugs, diagnostics, evaluations, screening, counseling, training, additional screening and monitoring at no cost to the participants)

Eligibility Criteria

1. Does the study include **vulnerable populations?**
2. Does the study exclude any classes of participants? (e.g., by gender, class, race, age)
3. If the study purposely excludes any class of participants, do the investigators present an adequate scientific justification for this exclusion?
4. Does the study leave out important groups of people affected by the disease? (e.g., adolescents and children, women, pregnant and lactating women, people with HIV, people with HIV on antiretroviral medication, incarcerated populations, people who use drugs, people who use alcohol)
5. Are any classes of subjects excluded from early stage (phase I and II) versus late stage (phase III) trials?
6. If certain populations are excluded from research, at what point in the product development pathway will these populations be included?
7. Are the populations that are either included or excluded from the trial represented in the community advisory structures like a CAB?
8. What are the specific data the researchers plan to collect, and have they explained how these data and the participants selected will help to answer the research question(s)?

Description of Recruitment and Procedures

1. Does the study describe the methods used to recruit participants?
2. How and from where will subjects be recruited? (e.g., flyers, announcements, word-of-mouth, snowballing, clinic-based recruitment)
3. Are there existing, site-specific community engagement structures in place? If not, are there plans to create them? How will these community engagement mechanisms be structured? (e.g., site CABs, a consortium-level CAB with site representation, a combination of the two)
4. Will budget be allocated to support community engagement structures and activities?
5. How will investigators protect the identity and personal information of participants? (e.g., codes, pseudonyms, masking of information)

Procedures for Obtaining Free and Informed Consent

1. What is the procedure for obtaining a participant's free and **informed consent** to enter the trial?
2. Is the consent process in a language that is understandable to likely participants? Are there supporting materials to ensure that people understand the consent process?
3. Does the consent process give people enough time to read, understand and ask questions about the trial and to make a choice free of coercion and undue influence?
4. Does the consent process include the names and contact information of the researchers and/or community members in a position to address potential questions about the trial?
5. Are the risks posed to participants by the trial clearly and comprehensively described in the informed consent materials?
6. If there are no direct benefits to participants from participating in the trial, has the study protocol stated this in the informed consent form?

Vulnerable Populations: groups of people that are not well integrated into health care systems because of ethnic, cultural, economic, geographic or other forms of discrimination and marginalization. Vulnerable populations face a greater risk of poor health status and health care access. In addition, some vulnerable populations might lack the capacity to provide consent freely (e.g., because they are in prison) or to fully understand what they are agreeing to (e.g., because of age, maturity, or limited mental ability). These persons should be given additional protections by investigators and review committees.

Informed Consent: a process designed to protect study participants in research. Before entering a study, participants must sign a form stating that they have been given and understand important information about the study and voluntarily agree to take part.

Results Dissemination

1. Does the protocol include draft materials for results dissemination, or outline other means to share study results with participants and their communities? (i.e., a findings letter addressed to individual participants or site-specific dissemination plans)
2. Before recruitment begins, will the trial be registered in a publicly accessible location, such as clinicaltrials.gov or the World Health Organization's International Clinical Trials Registry Platform (http://www.who.int/ictrp/en/)?
3. Are there plans to vet results dissemination materials through a community engagement structure?
4. Is there a post-trial communication plan in place that has been shared with community representatives?

Financial Conflicts of Interest

1. Do the investigators have any financial interests in any non-site sponsors or funding sources for this research?
2. Is research being conducted in partnership with a privately or publically funded entity? In either case, does the protocol detail who is accountable in terms of both human and financial resources for ensuring access to investigational products post-trial? (Note: where public funds have been used to help advance the development of new drugs, the price needs to be fair and accessible so that the public can benefit from the investment of its tax dollars.)

Ethics Reviews

1. Will the trial be reviewed by one or more **institutional review boards** (IRBs) or independent ethics committees?

Institutional review board (IRB): a committee made up of medical or scientific professionals and nonmedical or nonscientific members whose responsibility is to ensure the protection of the rights, safety and well-being of human participants involved in a clinical trial and to provide public assurance of that protection.

Additional Resources

Many of the concepts in this document are elaborated on in guides that have been developed to help activists and community representatives understand the fundamentals of clinical research. For more information, we recommend consulting:

[1] **Research Fundamentals for Activists**. Developed by: Consortium to Respond Effectively to the AIDS and TB Epidemic and Treatment Action Group. Available from: http://www.treatmentactiongroup.org/sites/g/files/g450272/f/201305/RFA%20FINAL.pdf

[2] **Clinical Trials: A Community Guide to HIV Research**. Developed by: HIV i-Base. Available from: http://i-base.info/wpcontentuploads/2009/07/8-clinical-trials-mar09.pdf

[3] **Basic Scientific Literacy Training Module**. Developed by: HANC HIV/AIDS Network Coordination. Available from: https://www.hanc.infocp/resources/Pages/BSL-Training-Module.aspx

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The CRAG would like to thank Debra Shelly for her contributions to earlier drafts of this document and Chad Heilig for his very thoughtful review and suggestions.