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### Journal of Medical Ethics blog

## A Tool to Help Address Key Ethical Issues in Research

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*Guest post by Rebecca H. Li and Holly Fernandez Lynch*



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One of the most important responsibilities of a clinical project lead at a biotech company or an academic research team is to generate clinical trial protocols. The protocol dictates how a trial will be conducted and details background information on prior research, scientific objectives, study rationale, research methodology and design, participant eligibility criteria, anticipated risks and benefits, how adverse events will be handled, plans for statistical analysis, and other topics. Many protocol authors use as a starting point a “standardised” protocol template from their funder or institution. These templates often provide standard language, and sections for customisation, sometimes with various “pick-and-choose” options based on the nature of the research. They inevitably cover each of the key topics listed above, but often fail to include ethical principles and considerations beyond the regulatory requirement of informed consent. Indeed, the process of protocol writing has traditionally focused on scientific detail, with ethical analysis often left to institutional review boards (IRBs) and research ethics committees (RECs); unfortunately, robust discussion of specific ethical issues is often absent from clinical trial protocols.

When IRBs and RECs convene to review protocols, they are expected to evaluate whether the study will adequately protect enrolled participants. When the protocol fails to address potential ethical concerns explicitly, reviewers are left to speculate: did the investigator consider the concern, but dismiss it as not relevant in this particular context; did the investigator fail to understand the concern; does the investigator have an appropriate plan in place to resolve the concern, but has left it unstated in the protocol? This uncertainty can contribute to delays as reviewers debate among themselves, and can require lengthy back-and-forth with researchers, including series of protocol revisions and re-reviews until clarity is established. In some cases, it may also be that reviewers with less experience or expertise fail to identify an ethical concern that has not been brought to their attention in a protocol.

To address these problems, a diverse group of stakeholders convened by the [Multi-Regional Clinical Trials Center of Brigham and Women’s Hospital and Harvard](#) came together to develop a [Protocol Ethics Toolkit](#), explored further [in the JME](#). This Toolkit is designed to supplement available clinical trial protocol templates, encouraging both protocol drafters and protocol reviewers to directly address ethical issues that might otherwise go unexplored.

The Toolkit is formatted to allow dynamic input by both protocol writers and reviewers, for which the tool may have differing but complementary end uses. We have identified 11 essential elements that should be considered for discussion in a dedicated ethics section within the protocol:

1. Relevance of the Research Question – covering issues related to scientific integrity, social value, and contribution to medical knowledge
2. Choice of Control and Standard of Care – covering issues related to study risks, scientific validity, and equipoise
3. Choice of Study Design – addressing study risks and burdens, and scientific validity
4. Choice of Subject Population – addressing equitable subject selection and fairness to vulnerable groups
5. Potential Benefits and Harms – addressing likelihood, necessity, and balance
6. Informed Consent – covering both content and process
7. Community Engagement – covering identification of the relevant community and operationalizing how it can be engaged
8. Return of Research Results and Incidental Findings – covering both individual and aggregate results
9. Post-Trial Access – addressing plans for sharing benefits when a trial is over

10. Payment for Participation – covering concepts of coercion, undue influence, and reasonable compensation
11. Study Related Injury – addressing how things will be handled if a research participant is injured.

For each essential element, the Toolkit provides points to consider in the form of questions to guide a protocol writer, examples, and references for further information.

Why is this Toolkit needed? Although each of its elements is likely familiar to ethicists and practitioners, we have documented that they are not consistently addressed in protocols. This can limit both the effectiveness and speed of IRB review, as issues may be overlooked, or more likely, failure to explicitly address ethical issues head-on can result in IRBs having to repeatedly query investigators, leading to frustration on both sides. The Toolkit helps to create an efficient way both for protocol drafters to articulate any anticipated ethical challenges (and to utilize the tool as a means to ensure that they understand and identify all relevant challenges) and for review committees to orient easily to those issues when reviewing a protocol. Ideally, this should improve the comprehensiveness and quality of review. Finally, even in instances where the writer is familiar with an issue, the Toolkit will help facilitate a comprehensive explanation of the plan to address it to the IRB.

The Toolkit is currently available for [use](#), and we look forward to further improvements as we obtain feedback on its function in practice, from protocol drafters, investigators and IRBs.

*Read the full paper [here](#).*

## We recommend

Hopes for Helsinki: reconsidering "vulnerability".  
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The job of 'ethics committees'  
Andrew Moore et al., J Med Ethics, 2015

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Lay REC members: patient or public?  
Kristina Staley, J Med Ethics, 2013

Ethical considerations in accident and emergency research.  
P A Nee et al., Emerg Med J, 2002

Research on persons with impaired decision making and the public trust.  
Robert Michels, American Journal of Psychiatry, 2004

Ethical principles and practices for research involving human participants with mental illness.  
Psychiatric Services, 2006

Medical students as human subjects in educational research.  
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Toward revising the ethical boundaries of research with noncompetent subjects.  
Spencer Eth et al., American Journal of Psychiatry, 2009

The randomized controlled trial as a demonstration project: an ethical perspective.  
Franklin G Miller, American Journal of Psychiatry, 2009

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