

# What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research

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In recent years, there has been substantial debate about the ethics of research in developing countries [1–5]. In general, the controversies have centered on 3 issues: first, the standard of care that should be used in research in developing countries [6–13]; second, the “reasonable availability” of interventions that are proven to be useful during the course of research trials [14–19]; and third, the quality of informed consent. The persistence of controversies on such issues reflects, in part, the fact that existing ethical guidelines can be interpreted in multiple ways, are sometimes contradictory, or rely on unstated, yet controversial, ethical principles [6, 7, 9–11, 13, 20–24]. To provide unified and consistent ethical guidance, we apply a previously proposed ethical framework for clinical research within developed countries to developing countries, explicating a previously implicit requirement for collaboration [25]. More importantly, we propose specific and practical benchmarks to guide researchers and research-ethics committees in assessing how well the enumerated ethical principles have been fulfilled in particular cases.

## **MINIMIZING EXPLOITATION**

An ethical framework for multinational research should minimize the possibilities of exploitation [25]. A exploits B when B receives an unfair level of benefits or unfair burden of risks as a result of interacting with A [25, 26]. In developed countries, the risk of exploitation of subjects or host communities is minimized, because society funds research to improve health, researchers and research institutions are part of the larger community, and there is an infrastructure, even if imperfect, that translates research results into health-care practices for the benefit of the larger community. Research in developing countries creates a greater risk of exploitation: individuals or communities in developing countries assume the risks of research, but most of the benefits may accrue to people in developed countries [27]. Although poverty, limited health-care services, illiteracy, cultural and linguistic differences, and limited understanding of the nature of scientific research neither cause nor are necessary for exploitation, they increase the possibility of

such exploitation [16–20, 26–28]. Furthermore, the regulatory infrastructures and independent oversight processes that might minimize the risk of exploitation may be less well established, less supported financially, and less effective in developing countries. Guidelines for ethical research should minimize the risk of exploitation under these circumstances [28].

## **BEYOND PRINCIPLES TO BENCHMARKS**

Previously, we delineated a framework for ethical research that included 7 principles [25]. However, an ethical framework for research in developing countries must provide more than broad principles. As Macklin notes, underlying the apparent “harmony [on principles] we confront unanswered questions, as well as stark disagreements” [29, page 19]. Accordingly, we add an eighth principle—collaborative partnership—and elaborate these principles through 31 benchmarks that systematically specify practical measures to determine the extent to which the research satisfies the principles (table 1) [30, 31]. This framework of principles and Benchmarks is complex, because ethical evaluation of clinical research is complex. A single ethical principle is rarely absolute; most situations implicate multiple principles [32–34]. Consequently, the various principles and benchmarks will compete and must be balanced against each other—a process that inevitably requires judgment [30, 32–34]. Importantly, this framework functions