World Health Organization

Ethical standards for research during public health emergencies: Distilling existing guidance to support COVID-19 R&D

Introduction

There is an ethical imperative to conduct research during public health emergencies, as some research questions can be adequately investigated only in emergency contexts. Since the 2003 outbreak of the Severe Acute Respiratory Syndrome (SARS), the 2009-2010 H1N1 influenza pandemic, and the 2014-2016 Ebola outbreak in West Africa, authoritative guidance has been produced on how to conduct ethical research during emergencies. To ensure ethical research during the COVID-19 outbreak, we summarize the key universal ethical standards. They should be adhered to by researchers, review bodies, funders, publishers, and manufacturers during an emergency (Table 1).[1]

Table 1: Key ethical guidance documents
World Health Organization. (2016). Guidance for Managing Ethical Issues in Infectious Disease Outbreaks.
Nuffield Council on Bioethics. (2020). Research in Global Health Emergencies: Ethical Issues.
Council for International Organizations of Medical Sciences. (2016). International Ethical Guidelines for Health-Related Research Involving Humans (particularly Guideline 20).
Ezekiel J. Emanuel, David Wendler, Jack Killen, Christine Grady. (2004). What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research. *The Journal of Infectious Diseases*, 189(5): 930–937. https://doi.org/10.1086/381709

Table 2: Ethical standards that research must meet in this context	
Scientific validity	Social value
Collaborative partnership	Reasonable risk-benefit ratio
Fair and voluntary participation	Independent review
Equal moral respect for participants and affected communities	

In all cases, including emergencies, our obligation is to uphold internationally accepted ethical standards. However, these universal ethical standards may be adapted to particular circumstances and contexts.

[1] Note that this is not a full accounting of every ethical standard applicable in this context. This document is intended to provide a brief distillation of key ethical standards and considerations that are viewed as being most relevant to supporting the World Health Organization and Global Research Collaboration for Infectious Disease Preparedness Research Roadmap for COVID-19.

Ethical standards and their application to research during public health emergencies

1. Research should be conducted only if it does not impede emergency response efforts.

Research is a key aspect of response to public health emergencies, yet it should never impede response efforts. This means that research should not be conducted if it can be expected to take away personnel, equipment, facilities, and other resources from those required for outbreak response. In addition, resources allocated to research must not take away from routine health care and public health services.

Research projects should be coordinated nationally and internationally to avoid wasteful duplication and underpowered studies, and to ensure that priorities and activities are consistent with response efforts. Rapid sharing of information generated during research—subject to ethical requirements such as maintaining the confidentiality and privacy of personal information—with those participating in response efforts can also help strike an effective and mutually beneficial balance between research and response.

2. What should collaborative research partnerships look like in emergencies?

Research should be based in both international and local priorities, and so international collaborative partnerships are critical. Partners should jointly prioritize the challenges faced in the outbreak, determine the research projects that will best address those challenges, conduct the research (including recruiting participants), and ensure that the research ultimately benefits the participating community by, for instance, ensuring health systems themselves learn from research results so that they may be better prepared for future emergencies.

To better ensure that research is responsive and sensitive to local realities, needs, values, and cultures, it is imperative that communities and researchers from local contexts be engaged at all stages of research, if feasible. Partnering with local researchers can also help build relationships and trust, which can go a long way in promoting effective research and response. Collaborations should adhere to the requirements for fair research collaborations, such as those proposed by the Council on Health Research for Development (COHRED).

3. How should communities be engaged in research efforts?

Research during an emergency requires fair and meaningful community engagement and inclusive decision-making. The most inclusive level of engagement is one in which local stakeholders are not only consulted but also take part in decision-making processes with respect to research design, implementation, and evaluation. This involves inclusive and accountable decision-making. It requires that all reasonable steps are taken to ensure that all those concerned—including those who are the most vulnerable and marginalized—are included. Developing community engagement networks in advance to facilitate relationships is a key part of emergency preparedness.

4. What requires independent ethics review and how should that review occur in emergencies?

Emergencies may result in a lack of local expertise and resources, and as a result, the capacity of local communities or countries to provide independent ethics review may be diminished or absent. Efforts should therefore be made to support and coordinate local capacities for independent ethics review. This should be pursued via the usual Institutional Review Board/Research Ethics Board/Research Ethics Committee system, but other independent mechanisms for review can be established. In all cases, research involving human participants requires independent ethics review. Routine public health activities not constituting research do not require independent ethics review, but should still proceed with due attention to ethical considerations, as outlined in part in the WHO's Guidelines on Ethical Issues in Public Health Surveillance.

To minimize duplication of ethics review and oversight, in most cases independent ethics review should proceed collaboratively between one local and one international review body, with at least one being well-versed in research ethics. To facilitate expeditious ethical review in emergency situations without compromising human participants' protection, generic advance protocols (which can be rapidly adapted and reviewed), templates, and other tools for the ethical review of research can be employed.

5. Can research methodologies be adapted in emergencies?

All research conducted during a public health emergency must have scientific validity and social value. Proceeding otherwise exposes participants and researchers to unnecessary risk and is ethically unacceptable. The appropriateness of any research design should be informed by the context in which the research is to be conducted. As such, methodological orthodoxy (e.g., in favour of a particular trial design) should be eschewed in order to critically consider the research context, background information, risks of the research, and the most appropriate means of answering specific research questions with rigorous and reliable data to ensure the results are both valid and useful in shaping future response.

6. How should research participants be selected for recruitment in emergencies?

Participants should be treated with equal respect. They should be selected in such a way that minimizes risk, protects (but does not exclude) vulnerable populations, maximizes social value and collaborative partnerships, and does not jeopardize the scientific validity of the research.

Pregnant women, minorities, children, and other groups considered to be 'vulnerable' should not be routinely excluded from research participation without a reasonable scientific and ethical justification. Any exclusion from participation in research should be justified by robust and current scientific evidence, such as an unfavourable benefit-risk ratio.

7. What are the requirements for informed consent in emergencies?

Individual informed consent is a fundamental ethical requirement for research. Prospective research participants must be able to weigh the risks and benefits of participation. This can be particularly challenging in a public health emergency because of uncertain risks and the perception that any research-related intervention must be 'better than nothing'. Consequently, researchers and review bodies have an obligation to ensure that research activities do not proceed

unless there is a reasonable scientific basis to believe that the study intervention is likely to be safe and efficacious and that risks to participants have been minimized to the extent reasonably possible.

Cultural and linguistic differences, as well as confusions about the dual role of the clinician/researcher, may be heightened for research conducted in this context, and so processes for obtaining informed consent, including the wording of documents and methods of obtaining and recording consent, should be developed in consultation with local communities. Finally, researchers should inform potential participants about the circumstances under which their data or samples might be shared (see more on data sharing below).

8. To what extent should research data and samples be shared during emergencies?

Participants and stakeholders should be fully informed about the collection, storage, future use, bio-banking and export of human biological material. Researchers generating information that has the potential to aid response efforts have an ethical obligation to share that information as soon as it is quality-controlled for release (e.g., peer-reviewed). To ensure the greatest impact of the research, information should be shared with those involved in response efforts in addition to research participants, affected populations, and the global community. Researchers should share this information without waiting for publication in scientific journals. Journals can facilitate this by ensuring that data or preprints shared ahead of submission will not pre-empt publication in their journals.

9. How should research benefits be shared in emergencies?

Researchers, research funders, and countries should provide individuals and communities who participate in research with access to any benefits that result from their participation. Where interventions are found to be safe and effective, those interventions should be made available to local populations as soon as possible, including via monitored emergency use of unregistered and investigational interventions (MEURI) when appropriate. All efforts should be made to provide fair access for all to the benefits of research conducted during emergencies.

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