**What is subject to ethics review?**

All research with human subjects should obtain ethics approval from a research ethics committee prior to its initiation. To meet the definition of research with human subjects, the proposal must constitute research and it must obtain information from human subjects. Research is defined as any social science, biomedical, behavioral, or epidemiological activity that entails systematic collection or analysis of data, with the intent to develop generalizable knowledge. Human subjects are defined as human beings (i) who become individually identifiable through investigator’s collection, preparation, or use of biological material or medical or other records, or (ii) who are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment. Research with human subjects includes studies that use tissues, samples, data or records from humans, as well as studies that involve the conduction of interviews, focus groups or surveys, or the observation of private behavior.

Activities that do not constitute research with human subjects are exempted from ethics review. These are activities that do not aim at the production of generalizable knowledge or do not involve human subjects in the ways described above. For example, the following activities do not constitute research with human subjects and are thus exempted from ethics review:

* Studies using data that are publicly available or generated by observation of public behavior.
* Studies using data, samples, or tissue that already exist (i.e. the data, samples or tissue have been obtained by others) and are received by the research team in such a manner that the identity of the individuals cannot be established.
* Public health activities conducted under recognized public health authority with the intent to prevent or control of disease or injury, including surveillance activities aimed only at the identification or control of a health problem. These are activities that seek the benefit of the participants or the participants’ communities, and do not intend to generate knowledge that is applicable to other populations.
* Quality assurance activities or program evaluations aimed at improving the program at stake, and with no intent to produce generalizable knowledge.

Projects might involve multiple components, some of which might constitute research with human subjects while other components might not. The components that constitute research with human subjects should undergo ethics review. Determinations about whether a proposal is exempted from ethics review should be made by an independent party such as an ethics review committee.

**What are the international ethical guidelines for research with human subjects?**

Declaration of Helsinki of the World Medical Association (2013 revision): <http://www.wma.net/en/30publications/10policies/b3/>

International Ethical Guidelines for Biomedical Research Involving Human Subjects of the Council for International Organizations of Medical Sciences (CIOMS): <http://www.cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm>

International Guidelines for Ethical Review of Epidemiological Studies of the Council for International Organizations of Medical Sciences (CIOMS): <http://www.cioms.ch/publications/guidelines/1991_texts_of_guidelines.htm>

**What are the standards of each country for research with human subjects?**

International Compilation of Human Research Standards (2015 edition): <http://www.hhs.gov/ohrp/international/index.html>

**How should ethics review committees function?**

Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants published by WHO: <http://whqlibdoc.who.int/publications/2011/9789241502948_eng.pdf?ua=1>

**Which questions should guide the ethics review of research with human subjects?**

Social value: Can the study lead to improvements in health or well-being? What is the potential value of the research for each of the prospective beneficiaries?

Scientific validity: Is the investigation methodologically valid and scientifically (and statistically) sound? Will the study generate valid and reliable data that can be generalizable? Is the study feasible? Does the study design ensure participants the health-care interventions they are entitled to? If not, are there methodologically compelling reasons and are participants protected from serious harm?

Fair participant selection: What are the criteria to include and exclude participants? Is selection of participants based on scientific criteria? Are research participants selected to minimize risks and maximize potential benefits? If participants are vulnerable, are there any safeguards to protect them? Are the risks and potential benefits of the study fairly distributed?

Favorable risk-benefit ratio: Can the risks for participants be minimized? Can potential benefits for individuals and society be improved? Do the potential benefits for society and individuals outweigh the risks?

Informed consent: Is the information provided to potential participants accurate, clear, relevant and complete? Are the recruitment procedures, consent process and incentives appropriate for their culture and context? Is there an appropriate plan for obtaining permission for those that can’t consent for themselves? Are the participants being made aware of their right to refuse to participate and are they actually free to refuse?

Respect for participants: How will the health and well-being of participants be monitored to minimize harms? How will their privacy be protected? Can participants withdraw from the study without penalty? What are the plans of care after the study is completed? Will participants be given any new information (including the results of the study)?

(Adapted from (1) Emanuel E, Wendler D, Grady C. An ethical framework for biomedical research. In: Emanuel E et al. eds. *The Oxford textbook of clinical research ethics*. New York, NY: Oxford University Press; 2008: 123-135. (2) Emanuel E, Wendler D, Grady C. What makes clinical research ethical? *JAMA* 2000;283:2701-27711. (3) Emanuel E, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? The benchmarks of ethical research. *JID* 2004;189:930-937.)