

## research ethics: recipe for success

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**THE SOMEWHAT IRONIC** title of Spike Lee's 1989 movie, "Do the Right Thing," is emblematic of how difficult it can often be to *actually do* the right thing. This is particularly true in the face of urgent, often conflicting needs, and unknown outcomes, even with the best of intentions.

With that in mind, the purpose of this short article is not to serve as a primer on biomedical ethics—a complicated field with a history of cases like the law, and a fair amount of dispute among it practitioners. My primary purpose is to share some basics of research ethics debates and to issue two warnings, learned the hard way:

1. Beware of self-righteousness—your own and that of others—in the realm of clinical research. Others have probably wrestled with the same problems.
2. Beware of ever letting the end overshadow the means. This is particularly difficult because an AIDS vaccine is so desperately needed that there's a risk of moving forward too slowly as well as too fast, or not moving at all until everyone has confidence what the answer should be, even prior to conducting a definitive *clinical trial*.

Warning #1 will help you stay in the debate and be willing to listen to alternative points of view. Warning #2 will help you think about research from the perspective of participants and communities, which is always a good thing when faced with the demands of science, researchers and the epidemic. Perhaps the most important principle, which sounds obvious but has deep meaning, is this: Only good scientific research is ethical (because some risk may be justified); and only ethical research (based on important and objective questions) is good science.

If you're going to engage in any ethical discussion or debate about AIDS vaccines, it is important to know something about the accepted international ethical standards that apply, listed here in historical order:

#### *The Nuremberg Code*

Developed by an international tribunal after World War II to prevent abusive research.<sup>①</sup> It specifies that only qualified researchers may conduct human research using appropriate research designs, with a potential benefit greater than the risks taken. It codifies that *informed consent* is absolutely essential and that participants must be free to withdraw from the research at any time. It is less than a page long.

#### *The Declaration of Helsinki*

Written and revised by the World Medical Association (WMA), an organization still in existence.<sup>②</sup> A declaration for the medical profession, it focuses on protecting research subjects. Its broad and general principles are the underpinning of all subsequent, more specific standards. It was adopted in 1964 and contains 32 content-rich paragraphs.

In the last few years, efforts have been made to update the Declaration to remove some of its original paternalistic language (on "protecting" research subjects) and to emphasize instead the empowerment of volunteers and their communities in determining the course and limits of clinical research. WMA has amended the Declaration five times, with a recent and much-disputed note of clarification (on the use of *placebos* and *controls*) in 2002.

*The Belmont Report*

An internationally cited US government document, published in 1979, that codified the overarching principles of autonomy, beneficence (doing good) and justice as the primary and equally important ethical principles of medical research.<sup>③</sup> In fact, it is the difficulty of living up to these three principles simultaneously that often creates the complications and conflicts about ethical decision-making. Its fourth principle, nonmaleficence, derives from the ancient medical oath to “first, do no harm.” This can be distinguished from beneficence because there are unlimited degrees of doing good, and because there is always the option of not doing the research at all. Furthermore, it is widely believed to be unethical to do harm to individuals in the interests of some higher or greater good. *The Belmont Report* is 11 pages long. (For more on these principles, see chapter 16 on informed consent.)

*The Council of International Organizations for Medical Sciences (CIOMS) International Ethical Guidelines for Research Involving Human Subjects*

It consists of 21 guidelines, each with an introduction and sometimes detailed commentaries.<sup>④</sup> The CIOMS guidelines were written in 1982 and revised in 2002 for similar reasons as the Helsinki Declaration.

*Ethical Considerations in HIV Preventive Vaccine Research*

UNAIDS published its very focused ethical considerations in May 2000 after a series of international consultations that extended over almost two years.<sup>⑤</sup> It consists of 18 guidance points and is 48 pages long.

AS THIS SHOWS, the more specific and contemporary these documents become, the longer, more precise, complex and confusing they also become. It's a little like the US Declaration of Independence, which led to the need for the Constitution, and ultimately the many volumes of the Federal Register,

with ongoing case law and commentary from several levels of federal courts to interpret all of this.

For these reasons, the scientists who design and run research are subject to at least one but usually several boards of review at the scientific, ethical, governmental and local levels. These boards are supposed to be independent of the researchers and generally include an ethicist and a non-scientific member. They are the official forum for discussing the value and protections of the research, and they are usually held in private but with the list of members and decisions made public, so the public has some reassurance that they are legitimate and representative bodies. This review process itself can take many months (or longer) and require multiple rounds of revisions to *protocols* and procedures.

The key thing to remember, however, is that these review boards ultimately have to make *a decision* about whether, and how, to conduct a proposed trial. This need for a yes-or-no answer means that some people outside the process are likely to disagree about some of the outcomes, especially when they involved grappling with difficult problems.

Because AIDS research is so urgent and AIDS vaccine trials test unproven products in healthy volunteers (as opposed to testing products for treating sick people), the review process often raises a lot of internal and public debate about the study design, including the ethics of working with people at high risk for HIV infection and people who become infected during a trial through risky behavior. Reaching consensus is also complicated by the fact that knowledge of how to prevent and treat HIV is continually improving and changing, and that solutions vary in different places where this research is done.

If you read some of these guidelines and find that your head is spinning, wait until you meet a couple of professional ethicists. One at a time, they usually make perfect sense; it's just that they often don't agree with one another. And if this looks like a recipe for criticism, delay and inaction, you've got it right. As a discipline, ethics is a very mixed bag. Venture in at your own risk. It can be quite stimulating, but remember that generally no one has The Perfect Answer in this messy and very important activity.

references

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