Developing a SARS-CoV-2 vaccine is crucial to saving lives during the COVID-19 pandemic. But given the risks of infection and other harms a trial vaccine could pose, physicians must make sure their research is scientifically solid and their patient volunteers are protected.

The AMA has created an ethics resource page, “Vaccine trials and healthy volunteers,” that offers expert advice on trial design and informed consent. Citing numerous opinions from the AMA Code of Medical Ethics, the page provides a concise yet comprehensive guide for physicians at all levels of experience.

More broadly, the AMA and the Centers for Disease Control and Prevention are closely monitoring the COVID-19 pandemic. Learn more at the AMA COVID-19 resource center. Also check out pandemic resources available from the AMA Code of Medical Ethics, JAMA Network™ and AMA Journal of Ethics®, and consult the AMA’s physician guide to COVID-19.

Design matters

“Scientific value and validity are the foundation of ethically sound research involving human participants,” the resource page notes.

Referring to opinion 7.1.3, “Study Design and Sampling,” it quotes the Code as stressing that physician-researchers have an ethical obligation to ensure that their trials ask “research question(s) that will contribute meaningfully to medical knowledge and practice.”

It also specifies physicians’ ethical obligation to ensure any study with which they are involved is “scientifically well designed to yield valid data” to provide answers to those questions, including by “using appropriate population and sampling controls, clear and appropriate inclusion/exclusion criteria, a statistically sound plan for data collection and analysis, appropriate controls and, when
applicable, criteria for discontinuing the study (stopping rules).”

And like any other clinical trial, vaccine trials also must minimize risks to participants as much as possible without compromising scientific integrity, the page notes.

“There are some highly controversial models for vaccine trials, such as the human challenge trials where patients are deliberately infected,” said Elliott Crigger, PhD, director of ethics policy at the AMA. “We want to remind the medical community of physician-investigators’ responsibilities, partly because many practicing clinicians are not well versed in research ethics.”

Learn more with the AMA about research ethics in a public health crisis.

Informed consent: More than a form

Because vaccine trials ask healthy individuals to take on a risk that they might otherwise avoid, they require a robust process of informed consent to be ethically acceptable.

“There are ongoing worries about the quality of that consent, even if all the forms have been filled out,” Crigger said. “Many people seem to think of informed consent the way they do of advance directives—that it’s the form that matters. But in point of fact, what matters is the process of discussing with the prospective participant what being in a trial entails and what randomization will mean, as well as that it’s not primarily intended for the individual's benefit—that it’s intended to be for the broader community and for future patients.”

Citing opinion 7.1.2, “Informed Consent in Research,” the resource page notes that, among prospective participants who meet inclusion criteria, physician-investigators should only seek consent from individuals who have decision-making capacity. It goes on to quote the Code as saying that physician-investigators have an ethical obligation to disclose “any known risks or foreseeable hazards” and the “nature of the research plan and implications for the participant,” which include both the risks posed by the candidate vaccine and the heightened risk of exposure to the disease.

“In all situations, physician-investigators should refrain from persuading the individual to enroll,” the page says.

The AMA ethics resource pages—which now address more than a dozen issues at the heart of the COVID-19 pandemic, including conducting clinical trials of plausible therapies, providing access to experimental treatments and DNR orders in a public health crisis—have been developed based on inquiries from physicians and policymakers.