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Self-experimentation, ethics, and regulation of vaccines

Christi J. Guerrini[1], **Jacob S. Sherkow**[2,3,4], **Michelle N. Meyer**[5,6], **Patricia J. Zettler**[7]

[1]Center for Medical Ethics and Health Policy, Baylor College of Medicine, Houston, TX, USA

[2]College of Law, University of Illinois at Urbana-Champaign, Champaign, IL, USA

[3]Carl R. Woese Institute for Genomic Biology, University of Illinois at Urbana-Champaign, Urbana, IL, USA

[4]Center for Advanced Studies in Biomedical Innovation Law, University of Copenhagen Faculty of Law, Copenhagen, DNK

[5]Center for Translational Bioethics and Health Care Policy and Steele Institute for Health Innovation, Geisinger Health System, Danville, PA, USA

[6]Geisinger Commonwealth School of Medicine, Scranton, PA, USA

[7]Moritz College of Law, The James Comprehensive Cancer Center and Drug Enforcement and Policy Center, Ohio State University, Columbus, OH, USA

As the COVID-19 pandemic continues to sweep the globe, several groups have been working to develop and self-administer unapproved, unproven interventions that they describe as vaccines for COVID-19 (1–4). Some of the interest in these do-it-yourself (DIY) approaches apparently stems from a belief that self-experimentation is never subject to time-consuming ethics board review or regulation, such as by the U.S. Food and Drug Administration (FDA). This belief is legally and factually incorrect, and the misunderstanding has potentially important public health implications. Any failure by the FDA to regulate DIY vaccines would permit vaccines of dubious safety and effectiveness to endanger public health and would signal a lowering of standards that—in an age blighted by vaccine skepticism and during a highly politicized pandemic—could undermine public trust in all vaccines, however developed (5). Further, some self-experimentation can qualify as human subjects research that is required to undergo ethics review, by law or institutional policy. Even when ethics review is not required, citizen scientists must take seriously their heightened ethical responsibilities when promoting DIY interventions, especially those with potentially serious public health and societal effects, like COVID-19 vaccines. Given the proliferation of citizen science efforts to fight COVID-19 and the general confusion (even

guerrini@bcm.edu (CJG); jsherkow@illinois.edu (JSS); mmeyer@geisinger.edu (MNM); zettler.25@osu.edu (PJZ).

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Competing interests: Dr. Meyer reports having had conversations, for a brief period of time in early April 2020, with some members of what would become RaDVaC in which she provided comments consistent with this article. She also reports having served, from 2014 to 2019, on the Board of Directors of PersonalGenomes.org, a 501(c)(3) founded by George Church, a member of RaDVaC. Profs. Guerrini and Zettler report having participated in conversations with citizen scientists interested in establishing oversight mechanisms for citizen science. All other authors declare no competing interests.

among sophisticated scientists) that surrounds the regulation of DIY research, regulatory leadership is badly needed.

“The FDA can’t stop you”

In July 2020, six months after the first case of COVID-19 was confirmed in the U.S., scientists associated with the Rapid Deployment Vaccine Collaborative (RaDVaC) reported administering to themselves a product of their own making intended to be a vaccine against the disease. As described in the group’s white paper, the putative intranasal vaccine consists of synthetic peptides mimicking those of SARS-CoV-2, the virus that causes COVID-19, and is designed to elicit only a local immune response (6).

By its own account, RaDVaC is engaged in “citizen science,” which broadly describes activities having a scientific aim that invite public participation. RaDVaC’s chosen research path, which involves a homemade intervention, an evolving protocol, and unclear plans for collecting and analyzing outcomes data, is in contrast to traditional paths to vaccine development, which require randomized controlled trials (RCTs) with well-defined endpoints, such as demonstrated immune responses, and protocols concerning the retention and use of data.

Although some citizen scientists have anti-regulatory leanings, RaDVaC has explained that it is not anti-FDA. Rather, its stated mission is a humanitarian one, animated by a belief that open, crowdsourced vaccine efforts will hasten the widespread availability of a potentially life-saving vaccine through development efforts that it believes are not subject to FDA regulation (6). To that end, RaDVaC published on the internet instructions on how to self-manufacture and self-administer its DIY vaccine. RaDVaC also has provided materials for those activities, reporting, as of several weeks ago, delivering vaccine materials to 70 individuals (1). RaDVaC has made clear to potential users that its vaccine has not been reviewed or approved by the FDA. It also believes, as one of its leading scientists stated, “If you are just making it and taking it yourself, the FDA can’t stop you” (1).

RaDVaC is not alone . A small group of biohackers known as Project McAfee—after the antiviral software—reconstructed and injected themselves with a vaccine previously tested only in monkeys (2). Other known DIY COVID-19 vaccine efforts in the U.S. include a biohacker who self-administered a DIY vaccine that has reportedly been taken by at least 10 other people (3) and a microbiologist and founder of a small biotech company who sold and administered an unapproved vaccine to about 30 people (4). Given the global reach of the disease and widespread involvement of citizen scientists in biomedical activities, other efforts are likely underway, both in the U.S. and elsewhere.

The FDA and self-experimentation

In the U.S., it is true that the FDA’s authority does not extend to some instances of self-experimentation, for which there is a long tradition in medicine, including vaccine self-experimentation (7–8). But self-experimentation, for the FDA’s purposes, is a narrow category. The FDA’s jurisdiction would not extend to a citizen scientist insufflating an experimental vaccine that she created entirely from materials around her house. Nor would it

extend to the distribution of information about a DIY vaccine, such as suggestions where to acquire materials or instructions for making and self-administering it (9).

However, the FDA does have jurisdiction over other forms of self-experimentation. Under U.S. federal law, the FDA is authorized to regulate vaccines that cross state lines. This includes not only the final product itself, but also more mundane intermediate components, like reagents (9). The FDA's authority covers such vaccines regardless of whether they are developed by traditional industry players or citizen scientists; administered by a health professional or the patient; or, in many cases, sold for money or freely given away. The FDA's authority is meant to be broad and national in scope, rather than leaving things to a fractured pattern of state regulation or jurisdiction that turns on fine technicalities of how money may or may not have changed hands. This ensures that manufacturers and distributors do not easily escape expert public health oversight. Distributing materials intended for the self-manufacture of any vaccine therefore falls squarely within the FDA's jurisdiction and its public health mission.

Other self-experimentation projects have similarly crossed the line into FDA-regulated product development. For example, in late 2017, in response to concerns about DIY gene-editing kits, the FDA stated that any distribution of gene editing materials intended for use in humans qualifies as gene therapy subject to the Agency's requirements (10). This reach of the FDA's authority is justified. When self-experimenters provide interventions or their components to others who might follow in their footsteps, this has a serious potential to injure other experimenters, among other negative externalities.

The Common Rule and ethics

An FDA-authorized Investigational New Drug (IND) application permits unapproved drugs (and their components) to legally cross states lines and be investigated in humans, subject to certain requirements, including approval by an Institutional Review Board (IRB). Additionally, even with respect to DIY vaccines outside the FDA's authority, research with human participants is independently regulated in the U.S. by the Common Rule when the research is federally conducted or funded. Most self-experimentation is neither, but research institutions' own policies generally subject all human participant research in which the institution is "engaged" to the Common Rule's requirement of advance review by an IRB. IRBs help ensure that a study's risks are reasonable in relation to its expected benefits and that participants provide voluntary, informed consent. So long as a self-experiment meets the Common Rule's definition of "research" and the self-experimenter's institution is engaged in that research—say, because it occurs on institutional property or uses institutional resources—self-experimentation likely requires IRB review (11). RaDVaC's early systematic efforts to develop their product clearly meet this definition of research, but there is no evidence that any research institution was engaged in it.

Whether or not required by federal law or institutional policy, the kind of independent, prospective review that IRBs provide is ethically important, especially for public health interventions. Although the harms of some DIY interventions tend to be confined to

the researchers themselves, DIY vaccines have the potential to harm others, directly and indirectly.

Those potential harms are evident. Both users and bystanders are harmed by ineffective vaccines when users' false reassurance that they are immune from infection causes them to take risks that they might not otherwise take, such as traveling in crowds. Users of a DIY vaccine might also be unwilling or ineligible to participate in future clinical trials for traditional vaccines. The COVID-19 pandemic has already seen widespread off-protocol use of unproven interventions frustrate attempts to rigorously evaluate those or other interventions (12). At the same time, polls show that many are reluctant to take any COVID-19 vaccine. If scientists—and especially those with elite training or affiliations—herald a readily available vaccine, those who are not hesitant might refuse to take the risk of enrolling in a trial and being randomized to placebo.

Making an untested DIY vaccine accessible to the general public also runs the risk, as RaDVaC's white paper acknowledges, that lay users might injure themselves as a result of improper preparation, incorrect administration, or heightened allergic or other reactions. These risks raise questions about whether such users are able to give meaningful consent to a DIY vaccine. As demonstrated by reports of desperate individuals drinking cleaning products and toxic methanol in an effort to prevent or treat COVID-19, not all individuals attracted to DIY vaccines will have the technical know-how to safely engage in self-experimentation or will invest the time to learn how to do so. Experts like RaDVaC's leaders can sometimes suffer from a curse of knowledge that leads them to underestimate the risk that less sophisticated users who find their website may flub the instructions, to the detriment of themselves and those around them.

Finally, it is concerning that RaDVaC apparently hopes for its DIY vaccine to be very widely adopted but has not disclosed any plans for systematically establishing its safety or efficacy, such as through RCTs. During a pandemic, it is tempting to believe that an intervention that shows early promise has been "proven enough" to justify widespread use (13). Those who are intellectually invested in an intervention may be especially so tempted, perhaps even deeming RCTs, which randomize some participants to placebo, as unethical (14). All scientists must resist the temptation to view the rigorous study of COVID-19 vaccine safety and effectiveness as a bureaucratic step that can be skipped. Research that enables us to confidently conclude that a vaccine is safe and effective will take time, whether or not it is overseen by the FDA. But that research, simply, is critical.

Roles for the FDA and scientists

Given the risks to public health from unsafe or ineffective vaccines, regulatory leadership is needed. First, the FDA should issue a statement clarifying both its authority over, and its intent to regulate, DIY COVID-19 vaccines, as it did with DIY gene-editing kits. This statement should include, at a minimum, clarification that vaccine research, manufacture, distribution, and administration—*by anyone*—can be subject to regulation. For those activities within its jurisdiction, the FDA has a range of enforcement tools available to it, including sending Warning Letters and imposing civil and criminal penalties. Indeed,

the FDA has already sent a Warning Letter to one company, North Coast Biologics, whose founder sold and administered an unapproved COVID-19 vaccine to friends (4). Explaining how the Agency intends to enforce its authority against citizen science groups can help give fair warning to those who might underestimate the scope of FDA jurisdiction as well as reassure those who are not likely to face enforcement actions.

Although appropriate enforcement of the FDA's authority is critical, the objective should not be to stop all citizen science research; that would be futile given the popularity and reach of citizen science. But more importantly, such a strategy would imprudently deny society the many benefits of citizen science, including its potential contributions to scientific discovery (9, 15). In recognition of these benefits, the Agency should consider ways to support citizen science research while promoting trust in FDA and research processes, including establishing new channels for engaging with citizen scientists working on COVID-19 solutions. One possibility is designating Agency staff knowledgeable about citizen science objectives and communities to field questions from citizen scientists, provide feedback on their projects (such as through pre-IND meetings, which are an established way for the FDA to discuss product development plans), and, as necessary, help citizen scientists connect with other staff within the Agency with relevant scientific expertise. More citizen scientists would be encouraged to reach out to the FDA if it were easy for them to identify an office to call with questions. This would require the person speaking with them to be genuinely invested in helping them—even if that ultimately means explaining how a project might violate FDA rules.

By adopting a transparent, collaborative approach to citizen science, the FDA can encourage trust in the Agency, which is particularly important right now, amid concerns about political interference with the Agency's work. At the same time, the FDA can stay apprised of promising solutions that might emerge from these communities, as well as their failures. During a pandemic, this is precisely the kind of information that regulatory authorities should want to know—and without delay.

Although many citizen scientists appear to take seriously the ethical responsibilities associated with their activities, it is important to recognize that those responsibilities expand when public health is at stake, as with COVID-19 vaccine development. Characterizing or positioning research as self-experimentation does not eliminate risks to bystanders or the collective good. Given those potential risks, citizen scientists who are involved in open vaccine development and testing efforts outside of traditional scientific institutions should seek review by an independent IRB. The cost is not necessarily prohibitive for all projects and should be prioritized the same as critical safety equipment. Ethical and efficient development of a vaccine shown to be safe and effective against COVID-19, and broad dissemination of such a vaccine, are goals we all share and should be able to work together to achieve.

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