LETTERS

Genome scientist Preston Estep administers the eighth iteration of a peptide vaccine to himself.

PHOTO: KAYANA SZYMCZAK/THE NEW YORK TIMES

Edited by **Jennifer Sills**

Transparency is key to ethical vaccine research

The Rapid Deployment Vaccine Collaborative (RaDVaC) is a free and open-source project that designs, tests, and shares vaccine designs and protocols. In their Policy Forum "Self-experimentation, ethics, and regulation of vaccines" (25 September, p. 1570), C. J. Guerrini and colleagues suggest that RaDVaC activities will cause a loss of public trust in all vaccines. An earlier Editorial ("The danger of DIY vaccines," A. L. Caplan and A. Bateman-House, 28 August, p. 1035) asserted that the RaDVaC project will cause people to lose trust not only in vaccines but also in science and public health efforts. However, restricting vaccine information and access to a privileged elite might be more likely to cause loss of public trust.

An article cited by the Policy Forum and the Editorial says that scientists are privately protecting themselves with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines, but the authors don't criticize these scientists for their unpublished vaccine designs and private vaccinations (*1*). Instead, they express concern about RaDVaC's "do-it-yourself (DIY)" vaccines. Given that we have created unrestricted access for all—non-profits, companies, governments, and individuals—this model is more accurately described as free and open-source than as DIY. RaDVaC's rapid iteration of vaccine designs and self-experimentation, although incompatible with typical institutional review board oversight and standard clinical trial testing, are among the project's foundational strengths, providing critical advantages in agility and alacrity at a time when delays are extremely costly in human life and welfare.

Both Guerrini *et al.* and Caplan and Bateman-House assert that our approach skirts safety considerations and suggest that vaccine safety will be established through clinical trials. However, they don't differentiate between short-term and long-term safety—or even mention the long-term risks that most concern scientists. As a result, their overall statements about safety are misleading. Over one hundred testers have contributed to a growing short-term safety profile for RaDVaC vaccines, which is very similar to the high degree of safety seen in earlier clinical trials of comparable nasal vaccines (*2*). As for long-term safety, certain vaccines have exacerbated subsequent infection, a phenomenon called vaccine-enhanced disease (VED) (*3*, *4*). The probability of detecting or predicting VED in pre-approval phases of clinical trials is very low. VED science is complex and still uncertain, but specific vaccine attributes are known to increase risks. RaDVaC-affiliated scientists have published analyses of VED risks and possible mitigation strategies, which RaDVaC has incorporated into its vaccine designs (*4*, *5*). We have less confidence in first-to-market vaccines because their designs do not include important discoveries made beyond the earliest weeks of the pandemic—a result of those vaccines being locked in place as required by the regulatory processes RaDVaC critics reflexively extol. Despite shortcomings in certain vaccines, we believe future retrospective analyses will show that vaccines adhering to good design principles and VED mitigation strategies are vastly safer than exposure to the virus, especially for people at highest risk.

All recent progress in vaccine research and development, including our own, has depended completely on accepted practices of science—especially the rapid and open sharing of scientific information. The claim that RaDVaC undermines public trust in vaccines, science, and public health efforts is analogous to criticizing firefighters for freely sharing their knowledge to help others fight their own fires—at a time when most of the world is engulfed in raging conflagrations.

We believe our actions could not be more clearly pro-vaccine, pro-science, and pro-public health. As we work to establish rapid response methods for producing safe and effective vaccines, our first ethical duty is to not restrict access to a privileged inner circle. Instead, we share information openly for broad deployment and maximum positive impact.

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Response

We share Estep and Church's goal of finding appropriate pathways for harnessing the benefits of citizen science. However, we respectfully disagree with their view of what responsible citizen science entails. The responsibilities of citizen scientists should be elevated when they develop and disseminate unproven public health interventions or online instructions for unknown persons to self-manufacture and self-administer such interventions.

Responsible citizen science should comply with applicable laws. Because some of those engaged in do-it-yourself (DIY) vaccine efforts might not appreciate the scope of regulators' authority over vaccine candidates, our Policy Forum clarifies the law and provides recommendations to both citizen scientists and regulators to help achieve compliance. We reiterate that these regulations are not mere red tape; they help ensure that rigorous evidence of vaccine safety and effectiveness is obtained—and obtained ethically. Failure to comply with and enforce these requirements, and the subsequent proliferation of unproven vaccines—whether developed through DIY efforts or traditional approaches—may undermine public trust in vaccine safety and effectiveness.

Responsible citizen science should also prioritize the safety of both its members and bystanders (*1*–*4*). Some citizen scientists might be willing to risk personal harm from their activities. But they should refrain from encouraging broad uptake of unproven interventions among healthy individuals whose risk-taking behavior may be affected and, in turn, affect others. Thus, although we applaud the Rapid Deployment Vaccine Collaborative's (RaDVaC's) commitment to open science, openly sharing interventions without sufficient evidence of safety and effectiveness is beside the point. Estep and Church liken their efforts to firefighters promoting safety, but responsible firefighters do not promote unproven—and potentially inflammatory—fire safety protocols.

Furthermore, responsible citizen science should engage in ethical reflection (*4*). Risks to bystanders generally warrant independent ethics review by an institutional review board (IRB) or a similar body. Estep and Church argue that both IRB review and "standard clinical trial testing" are "incompatible" with iterative studies and self-experimentation. But IRBs and adaptive trial designs have been used for just such activities, including during the pandemic (*5*–*7*).

Finally, we acknowledge that there is a lack of consensus on terminology for biomedical citizen science and understand that terminology choices have consequences (*8*–*10*). Although we respect RaDVaC's characterization of its efforts as "free and open-source," we believe those efforts are also fairly described as DIY. Indeed, openness is a defining feature of DIY biology and other strands of citizen science (*1*–*3*, *11*, *12*). We stand by our position that providing instructions for home production and self-administration of vaccine candidates—whether open source or not—constitutes a DIY effort.

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COMPETING INTERESTS

C.J.G. receives funding from National Human Genome Research Institute grant K01-HG009355. M.N.M. 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 Letter. She also 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. P.J.Z. has received honoraria from the Gray Center for the Study of the Administrative State at George Mason University Antonin Scalia Law School and The Ewha Institute for Biomedical Law & Ethics at Ewha Women's University for academic presentations and workshops about FDA and COVID-19 products. C.J.G. and P.J.Z. participated in conversations with citizen scientists interested in establishing oversight mechanisms for citizen science.

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Response

Estep and Church depict as their end goal the development of a safe and effective vaccine. We have a different goal: the production of a safe and effective vaccine that the majority of possible recipients will choose to use and that has regulatory and industry backing that permits its widespread deployment. In our view, what the Rapid Deployment Vaccine Collaborative (RaDVaC) gains in speed, it loses many times over by not producing the reliable data vital to engendering trust in the vaccine and enabling regulatory review. No open-source vaccine, no matter how simple, will be widely used globally; industry and regulators must be a part of any successful vaccine program.

RaDVaC supporters point to a long history of scientific self-experimentation to justify their actions, but the development of a COVID-19 vaccine has been politicized, making this precisely the wrong moment to do anything that might cause an eventual vaccine to be viewed as suspect or not fully tested. Whether it is deemed "DIY" or citizen science, the RaDVaC effort—which has no animal or safety trials; no dosage studies; no independent review of the candidate vaccine, protocol, or recruitment of volunteers; no plan to record all users or to systematically follow them; and no plan to provide help or compensation to anyone harmed by their participation—cannot meet society's needs.

Estep and Church maintain that their "first ethical duty is to not restrict access [or information] to a privileged inner circle." This commitment to transparency is laudable, but it should be met through peer-reviewed publication, not by posting information on a website. Furthermore, we disagree that either transparency or making their candidate vaccine available to those beyond "a privileged elite" is their first ethical duty. The maxim "first do no harm" applies here. Trust is the key ingredient in

any effort to facilitate a vaccine solution to the current pandemic. Transparency is often a key component to trust, but we believe that this effort will only breed further confusion about the process and standards of vaccine development, further alarming those who are already mistrustful of potential COVID-19 vaccines.

We agree with C. J. Guerrini *et al.* ("Self-experimentation, ethics, and regulation of vaccines," Policy Forum, 25 September, p. 1570) that citizen scientists have heightened responsibilities when public health is at stake. Equity in access is essential when it comes to vetted medical products, but there is no ethical obligation to provide equitable access to an experimental product that is not being developed according to the rigorous standards created to protect the welfare and interests of users.

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TECHNICAL COMMENT ABSTRACTS

Comment on "Meta-analysis reveals declines in terrestrial but increases in freshwater insect abundances"

Marion Desquilbet, Laurence Gaume, Manuela Grippa, Régis Céréghino, Jean-François Humbert, Jean-Marc Bonmatin, Pierre-André Cornillon, Dirk Maes, Hans Van Dyck, David Goulson

Van Klink *et al.* (Reports, 24 April 2020, p. 417) argue for a more nuanced view of insect decline, and of human responsibility for this decline, than previously suggested. However, shortcomings in data selection and methodology raise questions about their conclusions on trends and drivers. We call for more rigorous methodology to be applied in meta-analyses of ecological data.

Full text: dx.doi.org/10.1126/science.abd8947

Response to Comment on "Meta-analysis reveals declines in terrestrial but increases in freshwater insect abundances"

Roel van Klink, Diana E. Bowler, Konstantin B. Gongalsky, Ann B. Swengel, Jonathan M. Chase

Desquilbet *et al.* take issue with our data inclusion criteria and make several other dubious claims regarding data processing, analysis, and interpretation. Most of their concerns stem from disagreement on data inclusion criteria and analysis, misunderstanding of our goals, and unrealistic expectations. We maintain that our synthesis provides a state-of-the-art analysis of patterns of trends in insect abundances.

Full text: dx.doi.org/10.1126/science.abe0760

Transparency is key to ethical vaccine research—Response

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