Realizing Present and Future Promise of DIY Biology and Medicine through a Trust Architecture

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Emergencies force societies to consider efficiencies and innovations for which they might otherwise not have the appetite or time. The speed and scale of the Covid-19 pandemic has highlighted the fragility and insufficiencies of health systems around the world. From ideas to materials to personnel, a faster response to the pandemic has at times been hampered by centralization, competition, lack of coordinated communication, or rigid, slow-moving bureaucracies. These problems suggest the inevitability of nonestablishment research, including do-it-yourself, or DIY, research, and the potential role such research can play in meeting public health needs during pandemics and in normal conditions.

Here, we examine one example of how DIY research is responding to the Covid-19 emergency: the open, collaborative approach taken by Just One Giant Lab (JOGL). While DIY research is not new, the Covid-19 pandemic has made more visible the difficulties faced by those conducting such research. These challenges may be mitigated through development of a *trust architecture*—a collection of systems, mechanisms, and approaches that can contribute to public confidence in and the scientific validity of the products of this research. We suggest multiple steps that could be taken to develop such an architecture.

Establishment versus Nonestablishment Research

In the most familiar research model, research is conducted in large institutions by researchers with robust formal training in accredited programs. This research is usually also covered by federal regulatory oversight and involves ethics acculturation with respect to research planning, implementation, and reporting expectations.[1] This model, which we call *establishment research,* also incorporates an institutional logic that locates ethics and oversight systems within research institutions. For example, in the United States, human subject research regulations arose to prevent mistreatment of research participants and help ensure scientific integrity, and institutions and researchers are charged with following these regulations. Important as these regulations are, they can also create centralized oversight and authorization processes that are slow and blunt. Regulators have various tools for exercising flexibility while continuing to serve the goals of protecting human subjects and ensuring data validity.[2] Nevertheless, during a pandemic in particular, when responses may need to be rapid, nuanced, and at times decentralized, this structure can lead to significant obstacles.

We use the term *nonestablishment research* to refer to work in which researchers may not necessarily have obtained accredited formal research training and that may not be conducted within institutions covered by federal regulatory oversight. This kind of research has also been referred to as "independent biology,"[3] "DIYbio," or "participant-led research."[4] "DIYers" are typically part of a community laboratory, paying monthly fees to use scientific equipment and participate in group research activities (although some may operate individually). Most DIYers use social media and online forums to ask questions and share information about their research and projects with research groups outside their physical labs.[5] Some also publish in traditional peer-reviewed journals. They can be engaged in basic biology research or in medical research for personal or community benefit, or they may straddle multiple areas.

Like entrepreneurs and "philanthropreneurs," DIYers are often particularly attuned to and driven by new challenges and opportunities. Some DIY organizations or projects, like The Odin, seem primarily commercial; some, such as

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Quantified Self, are motivated by a desire for self-sufficiency; and others, such as OpenHumans or OpenAPS, are committed to creating open-source solutions for free global dissemination. Still others are patients or health care advocates driven by a desire to find effective or affordable treatments for their own conditions.[6] For example, the Open Insulin Project aims to find an inexpensive way to produce and purify insulin so that more people can afford it.[7]

Unsurprisingly, nonestablishment research and production efforts have arisen to address the Covid-19 crisis. Loosely organized "maker" communities, for instance, began producing 3D-printed face shields for local distribution to hospitals and farm workers.[8] As another example, a group of MIT and Harvard scientists identifying as the Rapid Deployment Vaccine Collaborative (RaDVaC) created and self-administered what they describe as a Covid-19 vaccine in an unnamed independent Boston laboratory; they have also invited others to participate.[9] The list of nonestablishment research and production efforts related to the pandemic is long; we focus here on Just One Giant Lab as an illustration of potential benefits and challenges in the field.

Potential Benefits of Nonestablishment Research

JOGL is a nonprofit web platform headquartered in Paris, France, that provides a virtual "laboratory" in order "to catalyze the collective creation of knowledge and solutions to resolve humanity's most urgent challenges."[10] On March 1, 2020, while still technically in beta phase, JOGL launched the OpenCOVID19 Initiative with the goal of collectively developing "open-source and low-cost tools and methodologies that are safe and easy to use to fight the COVID-19 pandemic."[11] The initiative involves five separate "challenge" areas: Diagnostic, Validation, Treatment, Prevention, and Data. Over eighty-five formally organized projects have already been posted; their aims include developing lab tests to identify Covid-positive individuals, validating mask efficacy, and building ventilators. Many of these are being supported with microgrants provided by the AXA Research Fund. One project, the Open-Source Low-Cost Syringe Pump, is already in the testing phase and is undergoing validation for safety and effectiveness by nurses at the Assistance Publique Hôpitaux de Paris, the largest hospital system in Europe.[12] Another project listed on JOGL, the Reagent Collaboration Network, seeks to optimize reagent supply chains for independent biologists. Additionally, JOGL created an open vaccine channel on Slack, a messaging platform, for discussions (still underway) on the safety and ethical issues of RaDVaC to see if the JOGL community would be able to participate, based on JOGL's codes of conduct.[13] Though the JOGL initiative is still young, contrast the speed with which it was initiated and ramped up with the pace of U.S. federal grant programs that are, despite the fast and dedicated work of federal agency personnel, only beginning to get started months after the pandemic reached U.S. shores.

Benefits of the open-access, open-source approach in nonestablishment research include its potential to identify and solve problems quickly, tailor them to a local context, make the options affordable, and create and distribute resources when governments are unable to do so. Moreover, it does this with an open-access philosophy, which means that these groups are structurally and ideologically prepared to welcome new collaborators into existing networks with familiar vetting procedures and to share information even with noncollaborators. The decentralized nature of these networks and the potentially large number of contributors mean that they can iterate many new ideas and research projects simultaneously, increasing the likelihood of identifying and acting on successful ones. These decentralized groups will also likely be better positioned to incorporate local contexts into their solutions and establish effective local distribution mechanisms. By prioritizing open-source, low-tech, commonly available tools and solutions, the open-source approach might also avoid competition for rare ingredients or materials hampering emergency responses.

However, there is a significant limiting condition for this research, no matter how successful it might be: nonestablishment research faces what we call a *legitimacy challenge* that could prevent broad implementation of any of its fruits. Institutional systems of establishment research, such as federal regulations and formal training, were built to help ensure the reliability and validity of scientific outcomes and public trust in that research. Because nonestablishment research exists outside this framework, if it is to make significant contributions to pressing public health problems (without joining the establishment system), then it will need an equivalent legitimization in the eyes of regulators and the public.

Governance and Infrastructure Needs in Nonestablishment Research

Addressing the legitimacy challenge is one of the most pressing tasks for nonestablishment research and involves scientific, ethical, and legal dimensions.

Scientifically, ensuring data quality, reliability, and reproducibility is critical for earning public trust and enabling nonestablishment research to produce beneficial innovation.

Ethically, while the lack of institutional research oversight may provide enhanced flexibility for nonestablishment research to address pressing and immediate global challenges, it also raises concerns, such as whether such research should have consensus standards for protecting humans subjects involved in it. More broadly, nonestablishment research poses ethical questions about existing structures for research funding and dissemination. These structures make it difficult for those outside of large, well-funded institutions (such as universities and corporations) to contribute to the advancement of knowledge. For example, eligibility for grant funding is often dependent on institutional organizational structures (such as extensive accounting departments) that nonestab-

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lishment research cannot build. In turn, grant funding is often necessary for disseminating research results widely (for example, via paying to make publications open access). Finally, nonestablishment research raises ethical and practical questions of responsibility. For example, the RaDVaC website identifies those in charge of the DIY vaccine collaborative as "[a]nyone and everyone," explaining its intentional design as "decentralized" and "community-led." Because DIY initiatives like this might involve dozens or even hundreds of contributors, none of whom self-identify as a project leader, it might be challenging to identify who, if anyone, should be held responsible for harm or error.

Legally, these projects raise numerous questions. For example, there are concerns about regulatory pathways for disseminating successful products that may arise from DIY individuals and communities. If U.S. Food and Drug Administration authorization were sought based on data generated from DIY science, it is not clear how the agency would (or should) use that information. This is particularly true if the underlying research did not technically comply with all regulatory requirements that apply to federally funded or FDA-regulated research (such as the U.S. National Institutes of Health Biosafety and Recombinant DNA Policy.[14] Such questions remain even in times of public health emergency, when the FDA has the flexibility to grant temporary "emergency use authorizations" for medical products. These require less safety and effectiveness data than typical medical product approvals do, but they do not exempt the underlying research from existing regulatory requirements.

Possible Solutions: Building a Trust Architecture

To harness the potential of nonestablishment research while mitigating risks, a new *trust architecture* for nonestablishment research is needed for open, accessible, valid, trustworthy, ethical work.[15] A trust architecture is a set of structures—formal, informal, or a combination—that build legitimacy and trust for an enterprise while also protecting from a particular kind of harm.[16] For example, federal bank insurance helps us trust banks with our money; FDA regulation helps us trust that our medicines are likely to have more benefits than risks; and neighborhood community associations build trust among neighbors while enforcing neighborhood regulations. Though no trust architecture is perfect, these structures ideally provide us with more confidence in a venture than we would have if we had to assess trustworthiness on our own. In nonestablishment research, several steps could contribute to such a structure.

First, establishment scholars and regulators should not try to import establishment norms of research ethics into DIY research. Instead, they should seek to build on work these communities have already been doing. For example, beginning in 2009, U.S. communities established a working relationship with the Federal Bureau of Investigation,[17] and in 2011, the community developed codes of conduct for the United States and Europe,[18] incorporating issues such as safety, respect, and modesty. In 2013, DIYbio.org and the Woodrow Wilson Center's Synthetic Biology Project established and hosted the Ask a Biosafety Expert program, which provided access to professional biosafety officers. And in 2019, through a grant from the Open Philanthropy Project and in partnership with the Association for Biosafety and Biosecurity (ABSA International), North Carolina State University conducted the first biosafety bootcamp course at Baltimore Underground Science Space (BUGSS), a community laboratory in Baltimore.[19] These groups have already worked to address biosafety and security issues related to their work and to share the tools developed.[20] Building on the DIYbio codes of conduct work in 2011, a new community ethics document was cocreated by hundreds of attendees at the 2019 Global Community Bio Summit,[21] and other participant-led research initiatives are producing governance frameworks to assist in considering ethical implications.[22] Other related groups and organizations have also developed ethical norms; for example, the International Genetically Engineered Machines competition supports ethical practices through its human practices hub and its biosafety and security requirements.[23]

Second, government bodies should recognize that solutions may arise from nonestablishment researchers and identify ways to assist, incorporate, or endorse appropriate efforts even if they have not traveled a conventional road to success. Consider, for example, Dana Lewis, founder of OpenAPS, who hacked her insulin pump to improve its usefulness for her particular needs.[24] As a deep sleeper, she worried about sleeping through the alarm designed to warn her of an impending health emergency. She was able to create the open artificial pancreas system that helped her, and she later shared the code with others at no cost but with safety steps in place. Studies have suggested that at least certain patients using the system have had improved glycemic control without experiencing significant adverse events.[25] However, in 2019 the FDA issued a warning about a se-

rious adverse event associated with DIY artificial pancreas systems. Although the FDA has not publicly asserted jurisdiction over OpenAPS or similar efforts, that doesn't mean there isn't value in engaging with regulators. In fact, some of us have urged regulators to engage with nonestablishment research communities to find ways to co-construct processes that reduce unnecessary burdens while encouraging innovation, especially during a crisis,[26] and recent presentations at the NIH and a related article outlined ways federal agencies can change their practices to incorporate DIY approaches and foster ethical practices.[27] A crisis does not mean that scientific and ethical standards should be loosened, but it does mean that new pathways may need to be created for nontraditional research to prove that it has met these standards.[28] Importantly, these new paths must not create loopholes for those who might seek to bypass corporate responsibilities or market fraudulent products.

Finally, intellectual property rights could be relaxed during emergencies to promote innovation.[29] For example, patent holders have been asked to take the "Open COVID Pledge,"[30] granting temporary, free licenses for their copyrighted or patented property to be used during the pandemic, with an expiration date of one year after the World Health Organization declares an end to the pandemic. Patentees including Sandia National Laboratories have committed to free licensing of their IP for use in the diagnosis, prevention, containment, and treatment of Covid-19 via the pledge. Although this framework benefits all researchers, some establishment researchers could afford a license to the covered IP if required to obtain one or could avoid infringement altogether by partnering with rights holders. By contrast, the vast majority of nonestablishment researchers do not have the resources or connections to take advantage of these strategies and would particularly benefit from relaxed IP controls.

Future collaborations between DIYers, academics, and regulators could knit the above efforts together, bringing progress on ethical issues in DIY research into conversation with research ethics and regulations. Nonestablishment research like DIY science has tremendous potential and is here to stay, both during and independent of emergencies. Whether it can help depends at least in part on whether the trust infrastructures proposed are built and accepted by regulators, society, and the "gatekeepers" of science. These stakeholders should attend to these trust infrastructures now and build on them—quickly—in the future.

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