Evidence for the UK's Biological Security Strategy from the Department of Health and Social Care, and Department for Environment, Food & Rural Affairs.

Title: Empowering Do-it-yourself Biology by Doing-it-together: Collective Responsibility in Maximizing Benefit and Mitigating Risk

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Reason for submitting evidence: Our evidence addresses the following questions,

- What are the key biological security opportunities, challenges, threats and vulnerabilities facing the UK
- What are the key global, regional and domestic trends affecting UK biological security out to 2030?
- Are there successful examples of surveillance and/or wider approaches and capabilities for mitigating biological risks in other countries that we can learn from?
- What further steps should the UK take to maximise our resilience to and preparedness for natural hazards, accidental release, malicious biological threats, and emerging zoonotic pathogens?
- Should research and laboratory standards, safety and security play more of a role (domestic and international), and what else should we be doing?
- Which are the key successes we should look to develop and build on, and where are areas for development?

Evidence

Rapid technological advances in genome editing and synthetic biology have created an unprecedented ability for science to be conducted outside traditional research institutions. This open science movement, known as do-it-yourself biology (DIY Bio) has gained significant traction and has grown exponentially in the last decade with over 160 active groups and thousands of DIY Biologists from a range of backgrounds worldwide. As a result, the movement has become a platform for biotechnology entrepreneurship and an instrument for discovery-based science education and outreach (Kolodziejczyk 2017; Landrain et al. 2013). The COVID-19 pandemic has also further emphasised the potential positive impact that the DIY Bio community can bring towards enhancing the innovative capacity of the larger scientific enterprise. As DIY biologists and scientists from traditional institutions share experimental data and designs on various platforms including online forums in response to the current pandemic, it is becoming evident that the scientific ecosystem has much to gain by being more inclusive. However, the inherent fast-evolving, open and relatively unregulated nature of DIY Bio creates substantial safety and security concerns. Here, we discuss the benefits and risks of DIY Bio and how multiple stakeholders, especially the government and academia, might work together with the DIY Bio community to co-develop global and locally contextualized policies, regulatory frameworks and action plans for maximum benefit and minimum risk.

Enhancement of Scientific Knowledge & Translation Potential with DIY-Bio

Improving Science Education and Engagement: Rockefeller University runs DNA Barcoding programs for high school students such as Sushigate, in which students work in collaboration with professional scientists to identify the genetic origins of the fish in sushi (Landrain et al. 2013). The International Genetically Engineered Machine (iGEM) competition encourages students to use genetic tools and various biological platforms to create innovative solutions for a variety of societal issues such as climate change, globalization and sustainability. These solutions have included the development of new bacterial sensors that monitor the environment and genetically-engineered bacteria that produce renewable energy sources and new materials (Cruz and Van Sluys 2015). The on-going insecurities associated with the COVID-19 pandemic have driven the expansion of community biology spaces and initiatives that are targeted towards finding novel solutions for COVID-19 testing and therapies (Paul 2020). These DIY Bio programs provide novel science education and engagement opportunities. Allowing the youth to appreciate the scientific method and participate in the discovery process of science is key in securing a future generation of scientists who are keen to find solutions for various challenges.

Expanding the Collective Scientific Capacity: DIY Bio also has the ability to expand the intellectual resources needed to solve complex scientific problems by overcoming capacity and resource limitations of traditional academic institutions. Projects such as Foldit and EteRNA illustrate the added value of DIY Bio participation (Burnett et al. 2016). Similar to the 'distributed computing' approach, these projects leverage on the power of gamification to have people working creatively on solving a particular challenge. The generation of more information on the folding and structure of proteins or RNA facilitates the design of new diagnostic and therapeutic modalities for a myriad of diseases (Burnett et al. 2016). For example, data generated from the EteRNA project was used in OpenTB to develop cost-effective tuberculosis detection devices (Burnett et al. 2016). Through DIY Bio, our collective ability to solve complex grand challenges facing humanity is significantly enhanced.

Promoting Entrepreneurship and Wealth Creation: The DIY Bio movement has also led to several successful inventions that have reduced costs and created new markets within the biotechnology industry (e.g., polymerase chain reaction (PCR) machines by the OpenPCR project and Bento lab) (Landrain et al. 2013). This cultivation of an entrepreneurial culture has also led to the development and commercialization of new companies such as OpenTrons. Founded at the first DIY Bio community laboratory, Genspace, OpenTrons is now a multinational and multimillion-dollar company that

produces liquid handling robotic devices at a fraction of the cost of that offered by major biotechnology companies (Woods 2018). Lower costs are not only essential to drive research but are a crucial substrate for scientific progress, especially for developing countries. The DIY Bio community has also created the Open Insulin Project that aims to develop an off-patent insulin manufacturing protocol for personal use; potentially eliminating the significant costs needed to manage diabetes (Gallegos et al. 2018). The open and dynamic nature of the DIY Bio movement therefore not only increases the capacity of science by lowering research costs but it also catalyzes innovative business opportunities with significant economic potential.

Accelerating Scientific Response during Emergencies: In March 2020, the international online science coalition Just One Giant Lab (JOGL) reported a record number of engagements as they started the OpenCovid19 program. The programme aims to develop open-source and low-cost solutions that are safe and easy to use in response to the COVID-19 pandemic, and hosts various projects such as the development of contact tracing software and COVID-19 tests, as well as the manufacturing of face masks and ventilators. Scientists from the University of California Santa Barbara developed a potential point-of-care COVID-19 test, CREST (Cas13-based, Rugged, Equitable, Scalable Testing) using equipment created by the DIY Bio movement such as Bluetooth-enabled and battery-operable PCR thermocyclers (Tsang and LaManna 2020; Rauch et al. 2020). The Australian citizen science lab, Biofoundry also announced that they had created a COVID-19 rapid test which is cheaper, simpler, and faster than the traditional PCR that was being used for COVID-19 testing (Slezak 2020). The test, which uses loop mediated isothermal amplification (LAMP) is based on a design reported by scientists from the University of Pennsylvania in the United States, and is even amenable for home-use (Mohamed et al. 2020). Besides driving innovation, the DIY Bio movement also provides greater resource and talent pool that can be tapped into and mobilised during emergencies. For example, thanks to the availability of certified designs of medical/laboratory equipment and personal protective equipment that were openly shared by some manufacturers online, fablabs and makerspaces around the world were able to adapt these designs and produce them for local communities and hospitals, thus relieving the acute demand (Arancio 2020). The disruption caused by COVID-19 has certainly highlighted the critical role DIY Biologists can play during emergencies. Besides accelerating scientific advancement and producing potentially life-saving tools, the community also provides the access and ability to mobilise a greater magnitude of resources.

Challenges, Biosafety & Security Concerns

Regulatory gaps and limitations: Unlike food products and drugs, which have legislation and regulatory bodies responsible for oversight, DIY Bio is largely unregulated. Most governments that regulate DIY Bio projects do so by extrapolating rules that govern closely related technologies or follow protocols from ratified international agreements such as the Nagoya and Cartagena protocols (National Academies of Sciences, Engineering, and Medicine et al. 2018). Therefore, variations are bound to occur in the interpretation and implementation of regulations within the DIY community. Germany and Australia are the only countries that have taken specific actions to regulate DIY Bio activities. In Germany, any individual conducting genetic engineering outside certified spaces will be fined up to €50,000 or imprisonment up to 3 years (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL) 2020). In Australia, a license is required from the Office of the Gene Technology Regulator (OGTR) for DIY Biologists who intend to use certain types of genetically modified organisms (GMOs) (OGTR 2020). Nevertheless, the Australia's Therapeutic Goods Administration introduced temporary emergency exemptions that allowed the supply of COVID-19 diagnostic tests to accredited pathology laboratories.

Many DIY Bio communities have expert board members and/or consult experts from traditional scientific institutions for guidance regarding biosafety and security concerns, and are proactive in developing self-regulatory measures. For example, at Genspace, every new lab member and project is vetted for safety prior to commencement of projects and additional consultations with a safety

advisory committee is held if required (Grushkin et al. 2013). Regarding higher risk projects such as COVID-19-related activities, most DIY Bio communities are aware that tests on human samples should not be conducted at uncertified lab spaces, although tests on non-viable viral material may be permitted. For example, in the SoundBio community lab in the US, all projects are carefully reviewed to ensure safety and adherence to their BSL-1 facility requirement (Weinberger 2020). Both JOGL and Biofoundry have also explicitly expressed their desire to connect with professional labs with adequate biosafety facilities to robustly evaluate the performance of their COVID-19 tests before making these tests widely available (Weinberger 2020; Slezak 2020). Some DIY Bio groups have even designed their own policies to address bioethics and biosafety concerns. One example is the Citizen Science Policy Brief #2 by DITOs (Doing It Together Science); an initiative by the European Commission (DITOs Consortium 2017).

Nevertheless, there are several problems with self-regulation: (i) the current DIY Bio codes of ethics/conduct are neither comprehensive nor specific enough to cover all types of DIY Bio activities, (ii) self-regulation is subjective and can be heavily biased and (iii) compliance to codes may be low especially when not coupled with oversight and punitive action. Instances such as the contamination of DIY CRISPR kits with pathogenic multidrug-resistant bacteria and the rise of self-experimenting entrepreneurs indicate to the inadequacies of self-regulation (Gallegos et al. 2018; European Centre for Disease Prevention and Control (ECDC) 2017). There have also been recent reports of DIY Biologists who have designed and injected themselves with their own COVID-19 vaccines, and subsequently shared their work online for others to reproduce (Estep et al. 2020; Brown 2020; Yu et al. 2020; Zayner et al. 2020). Although both groups have extensive disclaimers for those who attempt to replicate their work and self-experiment, these developments have certainly raised major safety and security concerns. They also shed a spotlight on the increased availability of commercial tools for DIY Biologists to develop sophisticated biological products.

Risks of Open Science: The DIY Bio field relies on information that is either obtained from open access sources or within the DIY Bio community itself. Despite the obvious benefits, open access to knowledge increases risks particularly that of Dual Use Research of Concern (DURC), where well-intentioned research can be hijacked for malicious purposes. For example, the availability of DNA sequence information allowed researchers to resurrect the previously extinct horsepox virus (National Academies of Sciences, Engineering, and Medicine 2018). The publication of the landmark H5N1 studies raised the dilemma of choosing between censuring the diffusion of scientific knowledge and increasing the risk of nefarious intent; a conflict between scientific transparency and public safety/security (National Academies of Sciences, Engineering, and Medicine 2018). The *de novo* synthesis of dangerous pathogens is increasingly being made easier through technological advances, and the availability of this information considerably heightens the risk of malicious intent. Since the DIY Bio community is not usually subjected to the same level of surveillance that scientists in traditional academic institutions are subjected to and there are neither oversight nor universal regulations established specific to DIY Bio, DURC risk and fear are significantly raised (National Academies of Sciences, Engineering, and Medicine et al. 2018).

IP issues and entrepreneurship: The COVID-19 pandemic has certainly encouraged members of academia and industry to embrace the 'open science' movement which may be key to promote scientific innovation and advancement while avoiding patents and copyright infringement. However, in the current climate, there may be increased risk of intellectual property (IP) infringement for materials that are have not been designated as open-source or for open-sharing; especially for those related to the manufacturing process. Conventional material transfer agreements (MTAs) are generally effective in safeguarding the intellectual property (IP) rights of creators and in determining the legal responsibility on safety issues. However, it does not motivate others to build on existing materials or patents due to the fear of infringement. As a result, some DIY Bio groups (e.g., BioBricks Foundation) use open MTAs to allow for flexibility in the transfer of IPs and provide autonomy to commercialize end products (Landrain et al. 2013). Nevertheless, the increased exchange of material

and data within the DIY Bio community and with traditional academic institutions will give rise to other types of IP conflicts and management issues due to the unregulated nature of DIY Bio. In addition, new DIY Bio applications generated based on traditional and indigenous knowledge may also compromise the interest of these communities.

Policy recommendations

International Framework for DIY Bio Regulations: The regional DIY Bio codes of ethics and conduct and international agreements such as the Nagoya and Cartagena protocols are insufficient to adequately regulate the fast-evolving DIY Bio field; particularly due to its voluntary approach to compliance. This contrasts with traditional research institutions that are guided by more robust regulatory frameworks provided by several organizations. For instance, the Australia Group created a set of regulations for monitoring the transport of chemical and biological agents and the International Federation of Biosafety Associations addresses multifactorial biosafety issues with the help of its multidisciplinary stakeholders (National Academies of Sciences, Engineering, and Medicine et al. 2018). The International Gene Synthesis Consortium has taken steps to mitigate the risks of gene technology by screening for potentially dangerous or pathogen-related DNA sequences using a 'harmonized' screening protocol (National Academies of Sciences, Engineering, and Medicine et al. 2018). While these initiatives ensure the safety of biological research in traditional research institutions, there are none for DIY Bio. There is therefore a need to develop frameworks to establish proper global governance of DIY Bio at both national and international levels to ensure accountability amongst DIY Biologists.

Formal DIY Bio Licensing & Local Engagement: Given the potential impact of DIY Bio projects on public safety, we believe that governments should work towards establishing licensing programs and a registry of DIY Bio projects. This registry of existing DIY Bio projects and individuals working in it has to be consistently updated; similar to that of the already established GMO registry that is routinely updated by the OGTR in Australia (OGTR 2019). There have been unofficial efforts to create a licensing program for researchers in synthetic biology. However, these efforts mostly rely on a self-administered-licensing approach that is inherently biased. A formalized DIY Bio licensing approach would require individuals working in DIY Bio laboratories to undergo training in biosafety, bioethics, and risk assessment. Local governments and law enforcement agencies should engage more closely with DIY Bio communities to better understand the motivation and nature of DIY Bio activities. This engagement at a local level will also help to build mutual trust and enhance licensing compliance within the DIY Bio community. This will also promote transparency and provide the robust ethical dialogue needed to guide best practices in DIY Bio.

Reformed Self-regulation: Despite its limitations, self-regulation enculturation within the DIY Bio community is a necessity. However, the current self-regulatory system adopted by the DIY Bio community must be reformed. An international code of conduct that considers country-specific variations is much needed. Cases such as the contaminated DIY Bio kits distract the attention from the positive impact and innovative capacity of DIY Bio. The decision by Germany to prohibit the use of CRISPR kits for the production of GMOs is an example of how regulations can be formalized in the field. Nevertheless, universal formal regulations must be balanced between maximizing benefits and mitigating risks. A more structured self-regulatory framework with well-defined standards should be complemented with specific legislations that govern DIY Bio activities. This framework should also be tailored to the type of DIY Bio experiments. In addition, the ratification of this framework by the global DIY community is imperative to ensure that the biosafety and biosecurity risks of DIY Bio experiments are managed. Robust conversation between biosafety experts and the DIY Bio community (e.g., the 'Ask a Biosafety Expert' forum) must be actively encouraged and further developed to enhance reach and compliance (Grushkin et al. 2013). The potential role of responsible conduct of research education in the enculturation of a self-regulating responsible DIY Bio ecosystem should also be further explored (Chau et al. 2018).

It is evident that the DIY Bio movement has tremendous potential to benefit science and society at multiple levels. It creates diverse novel opportunities for all members of society to be involved in science; thus, promoting inclusivity and expanding the resource pool. As DIY Bio enhances science engagement and creates innovative solutions for unique problems, it will continue to foster entrepreneurship and new profitable niche economies. The pandemic has demonstrated the potential of the DIY Bio movement in accelerating scientific progress and innovation capacity. However, to ensure that the positive progress of DIY Bio is sustained and promoted globally, the introduction of a universally accepted formal regulatory framework that is complemented with efforts to foster a DIY Bio culture of responsibility is necessary in order to reduce the associated risks. The responsibility to maximize the positive impact of DIY Bio and mitigate the risks extends beyond the DIY Bio community. It is the collective duty of the larger scientific community, policymakers and law enforcement agencies.

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