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Benchtop DNA Synthesis Devices:

Capabilities, Biosecurity Implications, and Governance

MAY 2023

EXECUTIVE SUMMARY

Synthetic DNA is used by bioscience laboratories around the world and plays a fundamental role in a wide range of science and biotechnology advances. DNA synthesis technology—which makes it possible to "print" DNA with any user-defined sequence—enables researchers to study and engineer biological systems to better understand how they work. It is also essential for a wide range of biotechnology advances, from agricultural products and pharmaceuticals to advanced fuels and other biomanufacturing applications. For example, this capacity has been critical for rapid characterization of new and emerging pathogens during the COVID-19 pandemic, as well as speedy development of diagnostics, vaccines, and other medical countermeasures. Access to synthetic DNA is crucial to these advances and to the broader bioeconomy.

However, increased access to synthetic DNA resulting from new, more widely available technologies to produce it—combined with scientific advances in our understanding of pathogens—may also empower malicious actors by providing the building blocks of potentially dangerous biological agents. As DNA synthesis technologies advance, governments, industry, and other stakeholders must act urgently to develop the safeguards necessary to prevent accidental or malicious misuse.

Currently, nearly all synthetic DNA is produced by centralized providers that screen their customers and orders to help ensure that DNA with a potentially harmful sequence is not sold to customers without a legitimate use for it. However, a new generation of benchtop DNA synthesis devices—machines designed to be used on any lab workbench and without special equipment—will soon enable users to more easily print DNA in their own laboratories. This emerging technology has the potential to disrupt the centralized synthesis market and its associated biosecurity practices by driving DNA acquisition toward a more decentralized model.

Without appropriate oversight, these devices could be used by bad actors to obtain pathogen or toxin DNA and to facilitate pathogen engineering.

Drawing on more than 30 interviews with experts from benchtop DNA synthesis companies, the broader biotechnology industry, the biosecurity and bioscience research communities, and other sectors, this report addresses key questions critical to the understanding of the current status of benchtop DNA synthesis device capabilities and the broader implications for biosafety and biosecurity.

Key Findings

These findings represent a snapshot in time for DNA synthesis capabilities and the associated risk landscape, which will evolve as the science and technology advance.

What is the current status of benchtop DNA synthesis device capabilities, and how will these capabilities evolve over the next 5–10 years?

- Current benchtop synthesis devices can reliably print DNA up to 200 bases in length, but it is very likely that newer devices will be able to reliably and automatically produce double-stranded DNA (dsDNA) up to approximately 5,000–7,000 base pairs in length within the next 2–5 years. Over the next 5–10 years, benchtop device advances may enable reliable synthesis of dsDNA up to 10,000 base pairs long. As a reference point, there are a few viral genomes that are shorter than 7,000 base pairs, but the vast majority are between 10,000 and 200,000 base pairs in length. Bacterial genomes are longer than 1 million base pairs.
- Technology developments that enable benchtop synthesis capabilities include advances in laboratory automation as well as new enzymatic DNA synthesis approaches, which are easier to use and require less hazardous reagents.
- Key factors limiting the capabilities of benchtop devices include sequence fidelity of the DNA—i.e., how well the synthesized version matches the intended sequence—and fundamental limits on capabilities to assemble DNA sequences into long fragments by using automated systems.
- Although the extent of the market for benchtop devices remains unclear, likely customer benefits include speed of DNA synthesis and potential confidentiality of requested sequences.

What are the biosecurity implications of these developments?

- Easy access to dsDNA of 5,000–7,000 base pairs in length is likely to increase the potential for misuse of synthetic DNA because it will lower one of the technical hurdles to synthesizing or engineering pathogens.

Traditional DNA Synthesis Versus Benchtop Devices

For decades, researchers have been able to order high-quality, low-cost synthetic DNA from companies that produce custom DNA to match customer needs. Customers submit orders through an online portal specifying the required DNA strand sequence and length, and companies synthesize the DNA, which is then shipped to the customer. This centralized process provides an opportunity for oversight: although customers can order DNA with any sequence, most DNA providers screen the ordered sequence to determine whether it matches pathogen or toxin DNA.

New benchtop DNA synthesis devices will enable users to obtain synthetic DNA more rapidly by synthesizing it in their own laboratories. This on-demand, decentralized production of synthetic DNA also allows more privacy, which could enable a user to create pathogen or toxin DNA without detection. These new benchtop devices will require new thinking about governance and oversight to guard against exploitation by malicious actors and catastrophic accidents.

- Notwithstanding the risks associated with benchtop devices, a nefarious actor seeking to generate or otherwise engineer pathogens to cause harm would face significant technical hurdles beyond access to dsDNA, including the challenges associated with assembling a full pathogen genome—generating DNA that encodes a pathogen's full genetic blueprint; "booting up" a functional pathogen; or altering or enhancing the properties of a pathogen beyond those found in nature.

What tools and oversight mechanisms can most effectively mitigate biosecurity risks?

- Oversight of benchtop DNA synthesis devices can meaningfully reduce biosecurity risks without unduly limiting the benefits to legitimate bioscience and biotechnology research and development.
- Many potential oversight mechanisms depend on device manufacturers to screen customers to ensure user legitimacy and to screen the DNA sequences that are requested, which is consistent with current screening practices by traditional DNA providers. There will likely be tension between the preferences of some benchtop device users to keep locally printed DNA sequences confidential and the need for biosecurity safeguards to reduce the risk that these devices will be misused.
- A range of incentives, including government guidelines, regulations, and financial support, should be considered to encourage adoption of biosecurity best practices by device manufacturers and users.

Recommendations

Drawing on insights garnered from expert interviews conducted for this study, the report authors developed the following recommendations. These recommendations do not necessarily reflect the individual views of the experts consulted for this report.

There are currently no formal guidelines for oversight of benchtop DNA synthesis technology, and no codified approach internationally. The only safeguards in place for benchtop devices are voluntarily implemented by some manufacturers.

Benchtop synthesis device manufacturers should conduct rigorous customer screening for those who want to purchase or use their devices.

- Manufacturers should screen customers prior to selling the device to ensure that each customer is a legitimate user.
- Customer screening should extend beyond initial purchase and include ongoing verification of end users.

Benchtop synthesis device manufacturers should ensure that each DNA fragment produced by the device undergoes rigorous sequence screening.

- Where feasible, manufacturers should use a direct oversight approach in which the benchtop device automatically reports sequences for screening to the manufacturer prior to synthesis.
- Device manufacturers should follow DNA sequence screening standards that at least match a minimum standard used by traditional DNA providers.

Governments should provide clear guidelines, strong incentives, and, in some cases, regulations for benchtop device manufacturers to incorporate vigorous customer and sequence screening.

- In the near term, governments in countries around the world should develop voluntary guidance to set clear expectations regarding customer and sequence screening practices by benchtop DNA synthesis device manufacturers which are consistent with guidelines related to traditional DNA providers.
- Within 2 years, national governments should plan to implement regulatory requirements for selling or operating benchtop DNA synthesis devices within their borders. Requirements should cover devices that are capable of automatically

synthesizing and assembling DNA to generate dsDNA with high sequence fidelity at a length of 200 or more base pairs.

- To support both voluntary and mandatory DNA synthesis screening practices, governments should provide guidance, resources, and/or tools to reduce ambiguity about which DNA sequences constitute a risk subject to additional scrutiny and oversight.
- Governments should provide financial incentives to support adherence to DNA synthesis screening guidance and compliance with regulations.

Civil society, private funders, journals, and the scientific community should provide tools and incentives for robust biosecurity practices and responsible oversight by benchtop device manufacturers. An international organization should support governance efforts by civil society and governments to ensure a coherent oversight approach.

- Civil society and the scientific research community should develop resources and tools to ensure that customer and sequence screening are as easy as possible for device manufacturers and that best practices are constantly improving.
- Civil society, the scientific research community, and industry should convene discussions about the trade-offs between the desire for privacy by some benchtop synthesis device users and the risks posed by inadequate biosecurity safeguards for this technology.
- Private funders, such as philanthropic organizations and venture capital firms, should require that funded researchers purchase benchtop DNA synthesis devices only from manufacturers that conduct rigorous customer and sequence screening. Journals could put in place similar requirements for publication of research.
- Civil society, private funders, and insurers should work together to explore liability and insurance mechanisms to encourage adoption of biosecurity best practices by benchtop device manufacturers and device users.
- An international organization, such as the International Biosecurity and Biosafety Initiative for Science (IBBIS), should track and support civil society and government efforts to ensure a coherent oversight approach.

DNA synthesis technology is fundamental to bioscience and biotechnology advances. The field is rapidly changing, with active development, commercialization, and market expansion of benchtop DNA synthesis devices. The new generation of these devices promises faster and more convenient access to DNA for researchers and biotechnology developers, facilitating valuable discoveries and innovation. However, expanded access also will reduce barriers for bad actors, including those seeking to cause catastrophic harm.

Policymakers and others must act quickly, on an international basis, to ensure that benchtop synthesis devices and the companies that provide them operate with appropriate biosecurity rules, expectations, and practices. The actions recommended in this report can help safeguard DNA synthesis technology against accidental misuse and deliberate abuse. By establishing these norms early, benchtop DNA synthesis devices can be used in a way that realizes their full benefits while minimizing biosecurity risks.

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Dr. Sarah R. Carter is the Principal at Science Policy Consulting LLC, where she focuses on societal and policy implications of emerging biotechnologies, including issues of responsible innovation, biosafety, and biosecurity. She is currently focused on the future of the advanced biotechnologies industry, synthetic biology and DNA sequence screening, and international norms for biosecurity. In recent years, she has worked with non-profit organizations focused on these topics as well as industry, academia, and U.S. government agencies. Previously, she worked in the Policy Center of the J. Craig Venter Institute, where she led influential projects on the accelerating pace of synthetic biology and the challenges it creates for policymakers. In 2009–2010, Dr. Carter was a policy analyst at the White House Office of Science and Technology Policy (OSTP). She is also a former AAAS S&T Policy Fellow and a former Mirzayan S&T Fellow of the National Academies. She earned her Ph.D. from the University of California, San Francisco, and her bachelor's degree from Duke University.

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Dr. Jaime Yassif serves as NTI Vice President for Global Biological Policy and Programs, where she oversees the organization's work to reduce global catastrophic biological risks, strengthen biosecurity and pandemic preparedness, and drive progress in advancing global health security. Yassif previously served as a Program Officer at Open Philanthropy, where she led the Biosecurity and Pandemic Preparedness initiative, recommending and managing approximately $40 million in biosecurity grants, which rebuilt the field and supported work in several key areas. Prior to this, Dr. Yassif served as a Science and Technology Policy Advisor at the U.S. Department of Defense and worked on the Global Health Security Agenda at the U.S. Department of Health and Human Services. Dr. Yassif holds a Biophysics Ph.D. from University of California, Berkeley; a master's degree in Science and Security from the King's College London War Studies Department; and a bachelor's degree in Biology from Swarthmore College.

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