UNIVERSAL PLATFORM TO PREVENT ILLICIT GENE SYNTHESIS

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Current Situation: DNA synthesis has become common-place, and the risk that nefarious actors could use this technology to create and modify biological agents has grown. To guard against this risk, some governments and companies have placed an emphasis on screening DNA synthesis orders and customers for potential illicit use. In 2010, screening guidelines for both customers and DNA synthesis orders were implemented in the United States[1]. Members of the International Gene Synthesis Consortium (IGSC), established in 2009[2], voluntarily adopted these guidelines to guard against the creation of dangerous pathogens by nefarious actors.

Unfortunately, the incentives, standards, and technological approaches in place for screening have not kept up with the pace and reach of DNA synthesis technology, resulting in calls for revisiting the guidance and considering alternatives to enable sustainable global oversight[3]. The recent synthesis of horsepox virus[4] by Canadian scientists, with only a reported $100,000 in funding from a private U.S. biotechnology company[5], has also raised fresh questions from policymakers, the general public, and the research community about the future of DNA synthesis and the strength of existing global mechanisms to screen orders and customers. To preserve safe and secure access to the DNA synthesis tools that power the biotechnology revolution, it has become essential to revisit and improve screening of gene synthesis orders against misuse.

Challenge: Existing global norms for screening DNA orders have not kept pace with rapidly advancing technological capabilities, including the large-scale production of single-stranded DNA (oligonucleotides) and a growing trend towards the distributed synthesis of double-stranded DNA (dsDNA), both of which allow for the creation of viral genomes from scratch. While members of the IGSC voluntarily apply screening standards to assess gene sequence orders and customers, these companies only

[1] U.S. Department of Health and Human Services (2010). Screening framework guidance for providers of synthetic double-stranded DNA. Retrieved from https://www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf on 12 October 2018.
[2] Harmonized screening protocol v2.0 (2017). International Gene Synthesis Corporation.
[3] DiEuliis, D., Carter, S.R., Gronvall, G.K. (2017). Options for synthetic DNA order screening, revisited. mSphere 2:e00319-17. https://doi.org/10.1128/mSphere.00319-17.
[4] Noyce R.S., Lederman S., Evans D.H. (2018). Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments. PLoS ONE 13(1): e0188453. https://doi.org/10.1371/journal.pone.0188453.
[5] Kupferschmidt, K. (2017). How Canadian researchers reconstituted an extinct poxvirus for $100,000 using mail-order DNA. Science News, retrieved from https://doi.org/10.1126/science.aan7069 on 12 October 2018.

currently represent approximately 80% of global commercial gene synthesis capacity[6]. Companies that comply to the IGSC standards rely on implementing their own screening against an assembled common Regulated Pathogen Database (RPD), composed of organisms on the Select Agent List[7], the Australia Group List[8], and other national lists of regulated pathogens[9]. The mechanism is not flexible to allow companies to assess orders based on the latest scientific knowledge that connects genetic sequence to pathogenicity. In addition, DNA synthesis has quickly become a global industry, and most countries do not require companies operating within their territory to screen orders or customers.

At a more technical level, the administrative burden associated with screening DNA synthesis orders has markedly increased, creating strong potential disincentives for continuing and updating this practice in full. As the market for DNA synthesis has grown and the cost of synthesis has decreased, the costs of the bioinformatics reviews and customer follow-up associated with screening have become a larger percentage of the overall corporate cost of DNA synthesis. In addition, in instances where screening does identify a potential nefarious use, in many countries there is no appropriate authority to whom suppliers can report this activity[10].

A new, common screening mechanism could incentivize screening, allow for process updates to be more universally applied, and - ultimately - improve security while facilitating access to peaceful application of synthesis technology.

Proposal: We propose to pursue the creation and implementation of a common screening platform to help prevent the accidental or intentional misuse of DNA synthesis technologies to make dangerous biological agents. The advantages of such a platform would include: 1) allowing a common way to access and update screening algorithms as new approaches to pathogenicity are identified from natural or engineered threats; 2) economies of scale allow existing DNA synthesis companies to more affordably and sustainably co-develop and maintain a state-of-the-art screening system; and 3) barriers to entry for new synthesis companies would be lower, while still maintaining security, as these new companies could take advantage of a universal screening capacity as opposed to developing their own capacity or proceeding without adequate screening.

Governance will be an important component of this new platform. Such a platform could be “virtually” housed in an existing or new organization, or could be sustained via a networked approach. Likewise, financing the platform, and ensuring appropriate connections with law enforcement will be essential. Finally, such a platform should prioritize protecting the upside of new biotechnologies while mitigating risk.

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[6] Harmonized screening protocol v2.0 (2017). International Gene Synthesis Corporation.
[7] U.S. Department of Health and Human Services and U.S. Department of Agriculture Select Agents and Toxins List (2018). 7CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73, retrieved from https://www.selectagents.gov/SelectAgentsandToxinsList.html on 12 October 2018.
[8] The Australia Group (2017). List of human and animal pathogens and toxins for export control, retrieved from https://australiagroup.net/en/human_animal_pathogens.html on 12 October 2018.
[9] Harmonized screening protocol v2.0 (2017). International Gene Synthesis Corporation.
[10] DiEuliis, D., Carter, S.R., Gronvall, G.K. (2017). Options for synthetic DNA order screening, revisited. mSphere 2:e00319-17. https://doi.org/10.1128/mSphere.00319-17.

Importantly, this platform should be consistent with the need to protect the proprietary information and technology of both DNA synthesis companies and their customers.

Technical Challenges for Instituting a Common Platform for DNA Synthesis Screening: The technical challenges of implementing an effective DNA screening regime are considerable. DNA is a commodity with little to no difference in quality between vendors, leaving price as the key differentiator for most DNA synthesis companies. This has driven dramatic decreases in the cost of DNA synthesis over the past 20 years, in fact, this cost has improved faster than Moore's law for transistors[11]. As a consequence, the cost of screening can directly impact the competitiveness of a DNA synthesis company. This both encourages researchers to buy DNA from lower-cost companies that do not screen their orders and threatens to slow the growth of the bioeconomy if DNA prices stagnate.

In the event that full international coordination on synthesis screening efforts is possible, the emergence of "dark" sources of DNA is likely. For example, the equipment to construct a laboratory-scale DNA synthesis operation is widely available, and indistinguishable from other biological laboratory equipment. Similarly, a state-of-the-art synthesis facility can be built in a space comparable to a shipping container. The technology to further miniaturize DNA synthesis is rapidly advancing. Enzymatic DNA synthesis, which could be accomplished in a desktop device, is being pursued across academia and industry, with synthesis of 150 base pair oligos reported in October 2018[12]. A universal screening strategy must anticipate these advances and recognize that they are unlikely to be prevented via regulation.

Critically, this strategy must also recognize that the current centralization of DNA synthesis to a handful of companies could be disrupted by new entrants to the market, and that similar technologies in the biology space (including DNA sequencing) have quickly advanced from centralized core facilities to distributed desktop devices. And finally, the continually falling cost of DNA synthesis—coupled with democratized access to the technology—is a key contributor to the dramatic growth of the bioeconomy over the past decade. Effective international cooperation should encourage this work to continue in the open; ineffective policy could hasten the development of black markets for DNA synthesis and impede innovation by legitimate researchers.

Proposed Way Ahead: The World Economic Forum and NTI plan to convene a multi-stakeholder working group, dedicated to designing and realizing a first-of-its-kind universal screening platform to prevent illicit gene synthesis. The group would consist of a small group of public sector, private sector, and civil society leaders towards delivering a common screening platform, including interested members of the NTI Biosecurity Innovation and Risk Reduction Initiative. We propose to work toward launching the platform at the 49th World Economic Forum Annual Meeting in Davos in January 2020.

[11] Carlson, R. (2016). Retrieved from http://www.synthesis.cc/synthesis/2016/03/on_dna_and_transistors on 12 October 2018.
[12] Synbiobeta (2018). Retrieved from https://synbiobeta.com/news/dna-script-announces-worlds-first-enzymatic-synthesis-of-a-high-purity-150-nucleotide-strand-of-dna/ on 12 October 2018.

Tasks

1. Define the current landscape of screening and related challenges, opportunities, and priorities.
2. Articulate the necessity for and benefits of universal screening capability, as well as any risks.
3. Outline options for implementing a universal global screening mechanism.
4. Prioritize an approach to universal screening, based on agreed criteria.
5. Develop a roadmap to operationalize universal screening capacity.
6. Advocate and engage in resource mobilization towards launching universal platform.
7. Consider incentives for researchers to work with DNA synthesis companies that adhere to the universal global mechanism and incentivize pledges from governments to adopt norms and enforce DNA synthesis screening as a condition for DNA synthesis companies to operate in country.

Deliverables

1. Produce and publish a report recommending specific options for creating a universal screening platform.
2. Outline next steps for implementation, including determining implementation mechanisms, awareness raising, resource mobilization activities, leveraging events on international calendar.
3. Develop plans for curating and sustaining the platform.
4. If supported by the above, aim to announce the launch of a universal platform to prevent illicit gene synthesis.

Tentative Timeline

October 2018	Present initial plans and gain feedback during NTI Biosecurity Innovation and Risk Reduction Initiative meeting in Boston.
January 2019	Socialize concepts and next steps/gain feedback during the World Economic Forum Annual Meeting in Davos.
February 2019	Socialize concepts and next steps/gain feedback during the Munich Security Conference.
October 2019	Publish and launch report from Working Group.
October 2019-December 2019	Conduct outreach, determine next steps to make platform a reality, conduct, awareness-raising, and resource mobilization.
January 2020	Agree, at the World Economic Forum Annual Meeting in Davos, to launch the screening platform.