Increasing Gene Synthesis Security: Global and US Perspectives

Amanda K. Mui, MPH

Johns Hopkins Bloomberg School of Public Health | Center for Health Security

Author contact information:
amui@jhu.edu

Risk of Misuse: Would We Even Know?

Gene synthesis technologies allow researchers to design and manufacture strands of DNA for use in scientific research, diagnostics, drug discovery, vaccine development, and many more applications. The ability to write longer fragments of DNA continues to increase while the industrial costs to do so continue to decrease, creating an environment in which these very important technologies are more accessible and affordable than ever[1].

However, these technologies and capabilities raise concerns over their potential misuse, either through accidental or deliberate means. Various experiments in recent years have highlighted gaps in screening policies versus operating realities.[2] Although there is a general consensus among biosecurity researchers and a large portion of the gene synthesis industry, like members of the International Gene Synthesis Consortium, for better security, screening for dangerous pathogen sequences and for dangerous customers lacks oversight mechanisms to ensure these steps are being taken by as many providers as possible. Currently, only around 80% of gene synthesis providers have agreed to conduct sequence and customer screening, making it difficult to know where the overall security of the field stands if potential misusers are aware of who may screen their orders.[3]

By the same token, research institutions and individual researchers also bear responsibility in ensuring that biosecurity protocols are followed when conducting dual-use research of concern. While guidance and resources like the IGSC do exist for gene synthesis providers, there is very little oversight or resources for research institutions to responsibly utilize gene synthesis technologies. Our team has done numerous projects in this area, two of which are highlighted here: (1) Initiatives with the US government to create legislation around gene synthesis security and (2) engagement with international researchers and stakeholders to understand institutional and national policies on gene synthesis.

Closing our Gaps: State of Play

Policies in Government

The US has been a leader in implementing policy to prevent the misuse of gene synthesis technologies. The US HHS's Screening Framework Guidance for Providers and Users of Synthetic Nucleic Acids has been a cornerstone in operating guidelines for the past decade and recently underwent a revision to keep it more current with the field as it evolves.[4] Recently, President Biden's Executive Order on Artificial Intelligence called for the Office of Science and Technology Policy (OSTP) and the National Institute of Standards and Technology (NIST), in collaboration with other federal agencies, to establish a screening framework for the procurement of synthetic nucleic acid sequences.[5] The Gene Synthesis Screening Framework incorporates and builds upon the 2023 HHS Guidance and will go into effect for US-based research institutes that receive federal funding in a few months.[6]

However, there are still critical gaps in these policies. There is currently no oversight mechanism to ensure that providers are fulfilling these requirements. The US DHS is tasked with developing a stress-testing framework that could possibly fill this gap, but this will not be implementable for some time. Additionally, private laboratories are not covered under the OSTP framework and must voluntarily commit to screening. Finally, although there is a short 2.5-year runway for benchtop synthesizers to comply with the framework, it is unclear whether or how the framework could be applied to machines sold before it goes into effect.

Policies in Research Institutions

In a study funded by the US Department of State, researchers at the Center for Health Security and CRDF Global held a series of virtual engagements with stakeholders from Kenya, the Philippines, Indonesia, and India to discuss risks related to gene synthesis technologies and explore national and institutional policies in those countries that might address those risks. Each country's stakeholder groups created a tabletop exercise framework that could be run in the future with research institutions in their home countries (see example in Figure 2).

A few common themes emerged from these exercise designs:

1. There was no national policy or guidance to reduce the risk of misuse of gene synthesis technologies.
2. It was unclear how research institutions, whether private or public, might implement oversight mechanisms for research conducted using gene synthesis orders.
3. The typical researcher is not trained to identify risks associated with the use of gene synthesis technologies, such as ordering sequences of concern or using a provider that screens orders.

Solutions from All Angles

Top-Down Approaches

Governments should:

- Create harmonized mandatory screening protocols for federally funded research entities and consider extending these protocols to the private sector.
- Incorporate stress tests and oversight mechanisms to determine that gene synthesis providers are following implemented guidance or national protocols.
- Consider creating non-public sequence databases for industry use to support industry players in complying with national or international requirements.

Gene synthesis providers should:

- Screen all orders (sequences and customers) in ways consistent with either national or international policy/guidance, or with IGSC or similar protocols.
- Implement multiple layers of control in order to prevent accidental or deliberate misuse (Figure 1).

Bottom-Up Approaches

Research institutions should:

- Train researchers and students on the risks and benefits of gene synthesis technologies, with a particular focus on individual responsibility to appropriately assess dual-use risks.
- Create institutional policies and clear guidance on who or what entities possess responsibility to screen or keep records of gene synthesis orders.
- Work with key governmental organizations to close gaps in national policy to better secure gene synthesis use.

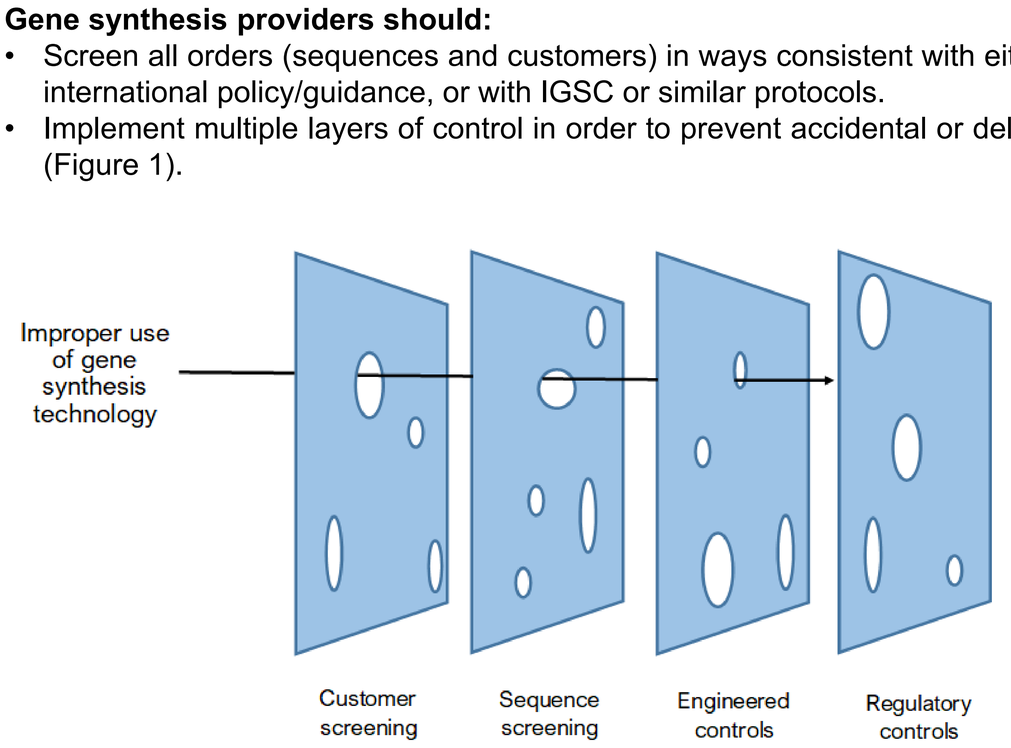

Figure 1. Visual representation of how multiple layers of security controls make commercial gene synthesis more secure against accidental or deliberate misuse. There are gaps and vulnerabilities in every mitigation measure but taken together they improve overall security.

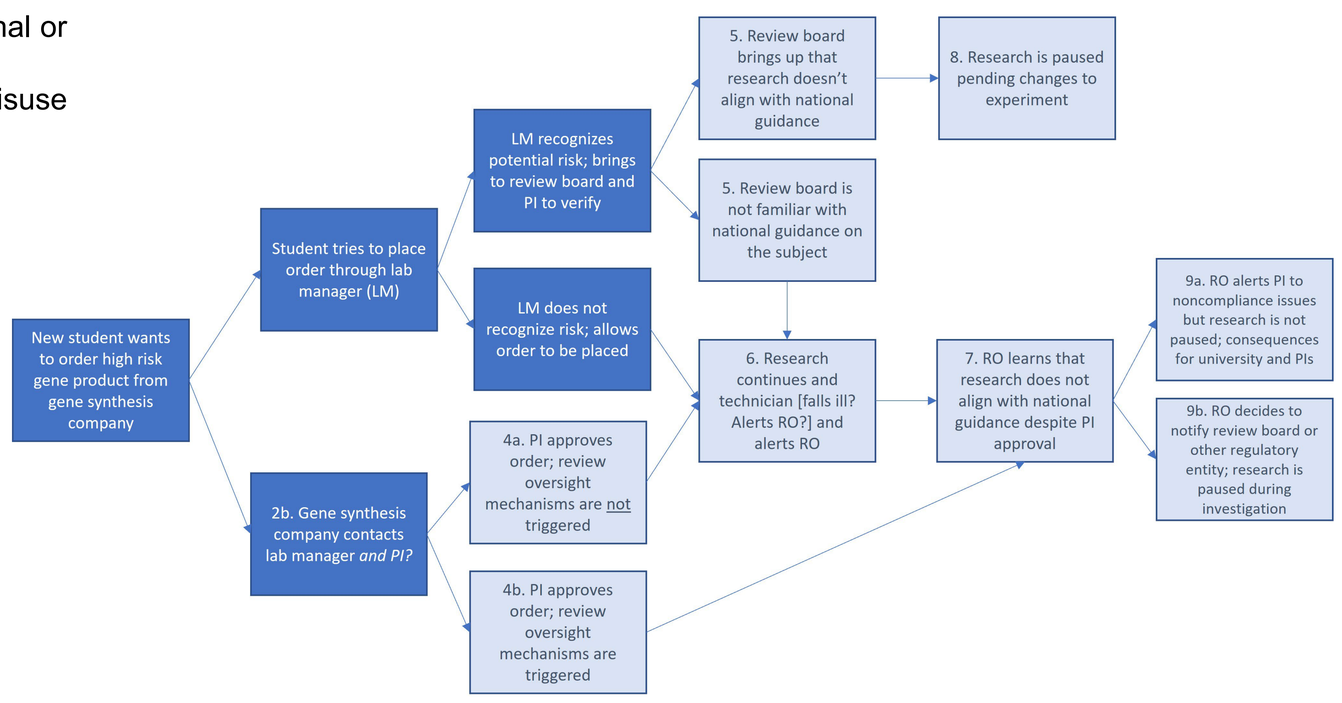

Figure 2. Example of a tabletop exercise framework developed by one of the country teams to explore institutional vulnerabilities in gene synthesis oversight. This exercise explored whether responsibility for cross-checking gene synthesis orders falls on the PI, laboratory manager, or research review board.

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