



Options for Synthetic DNA Order Screening, Revisited

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ABSTRACT Gene synthesis providers affiliated with the International Gene Synthesis Consortium (IGSC) voluntarily screen double-stranded DNA (dsDNA) synthesis orders over 200 bp to check for matches to regulated pathogens and to screen customers. Questions have been raised, however, about the continuing feasibility and effectiveness of screening. There are technical challenges (e.g., oligonucleotides and tracts of DNA less than 200 bp are not screened) and corporate challenges (e.g., the costs of screening are high, but other costs are dropping, so screening is an increasing portion of operating costs). In this article, we describe tangible actions that should be taken to (i) preserve the effectiveness of DNA order screening as a security tool and (ii) develop additional mechanisms to increase the safety and security of DNA synthesis technologies. Screening is not a perfect solution to DNA synthesis security challenges, but we believe it is still a valuable addition to security, and it can remain effective for some time.

KEYWORDS biosecurity, science policy, synthetic biology

DNA synthesis is a valuable research tool in the design of new biological products for medicine and manufacturing, and the ability to chemically synthesize long tracts of DNA has allowed for the development of influenza vaccines and diagnostic tests. As with many powerful technologies, however, it is vulnerable to misuse: using DNA synthesis technologies, a nefarious actor would not need direct access to certain pathogens but could chemically synthesize them using sequence information freely available on the Internet. Once synthesized, they could be “booted up” to become infectious. That many viruses can be made from scratch has been demonstrated repeatedly, including in the construction of poliovirus, 1918 influenza virus, and most recently, the virus that causes horsepox (1).

Over the past decade, measures have been taken to reduce the likelihood of misuse. Several commercial suppliers of double-stranded DNA (dsDNA), in the face of uncertain legal liability concerns if their products were linked to biological weapons, joined together in 2009 to create the International Gene Synthesis Consortium (IGSC) (<http://www.genesynthesisconsortium.org>). IGSC companies work together to develop protocols for individual companies to screen ordered sequences as well as to verify customers. The U.S. Department of Health and Human Services (HHS) also released guidance in 2010 for DNA suppliers, “Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA” (2). HHS recommended that DNA synthesis companies screen ordered sequences of dsDNA in excess of 200 bp and additionally screen the customer to ensure legitimacy. IGSC procedures exceed the HHS guidance; IGSC consists of 11 DNA providers from all over the world, representing 80% of the market, and these companies screen orders against a database that includes U.S. regulated pathogens (select agents) (3), Australia Group list agents (4), U.S. Commerce Control List (CCL) controlled sequences (5), and European Union (EU) sequences. The international orga-


Received 17 July 2017 Accepted 4 August 2017 Published 23 August 2017

Citation DiEuliis D, Carter SR, Gronvall GK. 2017. Options for synthetic DNA order screening, revisited. *mSphere* 2:e00319-17. <https://doi.org/10.1128/mSphere.00319-17>.

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 Screening synthetic DNA orders for dangerous pathogens is worth the effort for security, but the gene synthesis companies need help