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Safe DNA Synthesis

Commercial DNA synthesis enables the UK's cutting-edge biological and biomedical research and innovation. However, it could also be used by malicious actors to develop bioweapons. We propose that the Government Office for Science, along with the Engineering Biology Leadership Council, establishes a working group of experts from academia, industry, funders and government to develop UK policy and regulation for DNA synthesis screening. In formulating their policy proposal for government, the committee should evaluate the following measures to secure DNA synthesis:

1 Technical aspects of screening	**3 Incentivising screening**
a) Co-developing, with relevant partners, a comprehensive and precisely specified screening protocol, and endorsing an implementation in standardised software freely available to DNA synthesis companies	a) Working with relevant funders (such as UKRI and Wellcome) to require that grantees only use synthetic DNA from accredited screening-compliant providers
b) Co-developing, with DNA providers, efficient record-keeping systems to track orders of potentially dangerous synthesised DNA	b) Instituting screening requirements for DNA synthesis companies based in the UK, or otherwise penalising non-compliance
c) Regular (2-yearly) benchmarking and quality assurance of these screening protocols	c) Working with publishers to require that UK academic journals develop guidance for authors to use synthetic DNA that has been screened
2 Benchtop DNA synthesisers	**4 International Collaboration**
a) Working with companies in the UK manufacturing or selling benchtop synthesisers to develop appropriate screening functionality	a) Working with partner countries through fora such as the BWC to advocate for robust international agreements on DNA screening
b) Developing record-keeping systems to track the transfer and re-sale of benchtop synthesisers	b) Strengthening the IGSC by ensuring the protocol in 1a meets their minimum standards, and encouraging all UK synthesis companies to become members

DNA Synthesis: Promise and Perils

- DNA can be custom-synthesised to exactly match an arbitrary genetic sequence.
- Synthetic DNA is essential for life sciences research, especially synthetic biology, with applications ranging from medical research, food and plant science, to biomanufacturing.[1]
- An increasing number of specialised companies synthesise DNA, with the international market already valued at $2.47B and forecasted to grow rapidly to $10.58B by 2030.[2]
- Malicious actors could use DNA synthesis services to acquire parts of the genome of dangerous pathogens, an important step in the creation of bioweapons.[3]
- A key preventative intervention to combat bioweapons creation is to screen all synthetic DNA orders for signs of malicious use based on both customer and sequence data, and only fulfil safe orders.

[1] https://ktn-uk.org/wp-content/uploads/2021/07/EBLC-Building-back-better-with-Engineering-Biology_upload.pdf
[2] https://www.biospace.com/article/gene-synthesis-market-size-to-hit-us-10-58-billion-by-2030
[3] The WHO defines bioweapons as biological agents "produced and released deliberately to cause disease and death in humans, animals or plants." https://www.who.int/health-topics/biological-weapons

Screening Methodologies

- Customers without a recognised institutional affiliation, or who give a residential shipping address, are often denied their order or are flagged for further investigation.
- People who work at legitimate institutions could still have malicious intent, or they might lack the biosafety skills to properly handle dangerous sequences so customer screening alone is insufficient: the sequence must be screened too.
- A prevalent sequence screening approach is to search databases of all known DNA sequences to find the closest match of the ordered sequence, and flag any orders that best match a sequence from a dangerous pathogen for further investigation.
    - A key difficulty with this method is that sequences from pathogenic and non-pathogenic organisms can be sufficiently similar that they are hard to differentiate.
    - Specifying which sequences are of concern is controversial and non-obvious.
- More recent screening tools[4] use functional prediction software for creating their databases that match proteins and their biological functions to DNA sequences.

Benchtop Synthesisers

- As DNA synthesis technology improves and miniaturises, benchtop synthesis devices are being developed that will allow more researchers to synthesise DNA in-house.
- Currently, benchtop synthesisers are more error-prone and can only produce shorter sequences than corporate synthesis services.
- More reliable, versatile, and affordable benchtop synthesisers becoming available will further democratise synthetic biology, accelerating innovation but also expanding the pool of people with the capability to cause catastrophic harm with bioweapons.
- The prospect of better benchtop synthesisers coming to market increases the urgency of developing effective screening systems before then.

Governance Approaches

- Almost all countries are parties to the Biological Weapons Convention, an international treaty that prohibits the development, stockpiling and use of bioweapons. However, it lacks a verification mechanism and it does not directly address DNA synthesis screening.
- The International Gene Synthesis Consortium is a voluntary industry body representing synthesis companies that meet minimum customer and sequence screening standards, but it has no governance power.[5] Of the seven UK DNA synthesis companies, two are in the IGSC and five give no indication of doing any customer or sequence screening.[6]
- The United States Department of Health and Human Services (HSS) is currently updating its initial 2010 guidance recommending but not requiring that synthesis companies screen customers and sequences for biosecurity dangers.[7]
- While many US companies do screen, the lack of a regulatory requirement means some do not. Meanwhile, states may take their own approach: California, where many synthesis companies are based, is currently considering legislation that requires state universities to develop screening guidelines for their researchers.[8]

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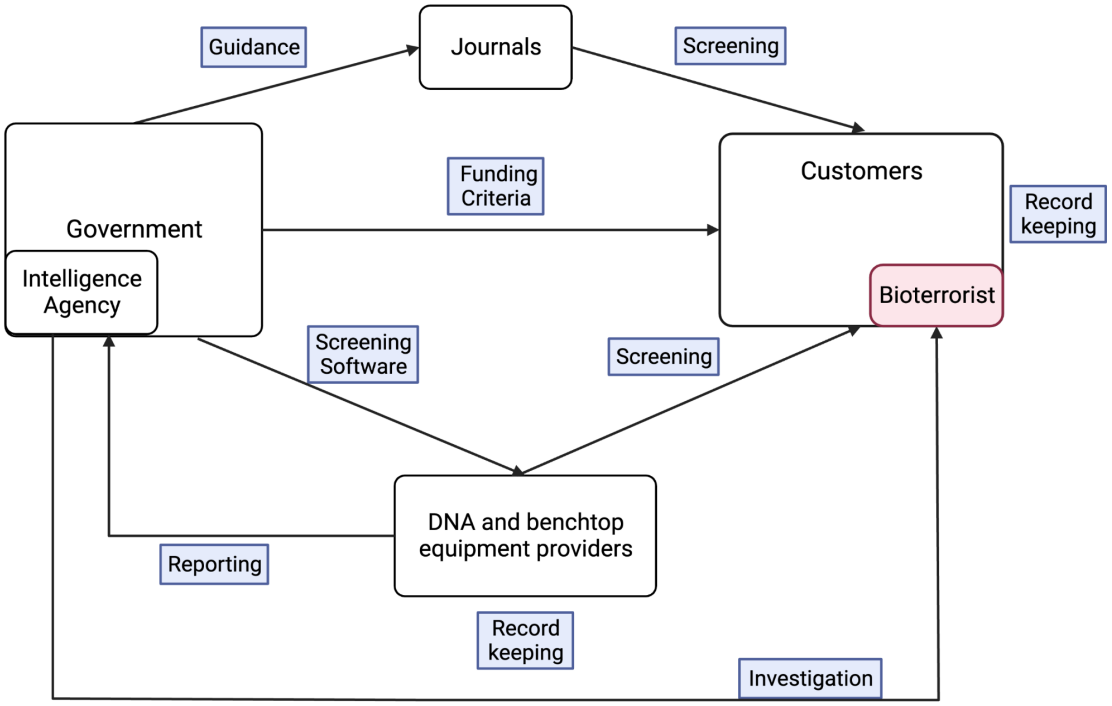
[4] SeqScreen, ThreatSEQ, Fast-NA, Aclid, NTI's Common Mechanism

[5] https://genesynthesisconsortium.org/

[6] Evonetix and Nuclera are listed on the IGSC website, 4basebio, NBSbio, Camena, Horizon Discovery and Touchlight are not, but Camena is in the process of joining.

[7] https://www.federalregister.gov/documents/2022/04/29/2022-09210/screening-framework-guidance-for-providers-and-users-of-synthetic-oligonucleotides

[8] https://leginfo.legislature.ca.gov/faces/billNavClient.xhtml?bill_id=202120220AB1963



Proposed interactions between agents involved in DNA synthesis.
DNA and benchtop equipment providers should screen the sequence and the customers of all orders and flag potentially dangerous orders to the relevant Intelligence Agency. The government should create legislation around screening and financially support providers in adopting screening software. Further, it should give guidance for journals and funding bodies to screen research groups they publish or fund. Customers should keep records of exchanged sequences and equipment.