

Preventing Bioterrorism: Regulating use of Artificial Gene Synthesis Technology

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In 1984, 10 restaurant salad bars in the town of The Dalles, Oregon were contaminated with *Salmonella enterica*. While there were no fatalities, 751 people developed salmonellosis, 45 of whom needed hospitalization. After one year of investigation, it was revealed that followers of radical spiritual leader Rajneeshee were responsible for tainting the restaurants' supplies. Their aim was to poison the voting population of The Dalles on election day in order to secure a victory for a cult-supported candidate. The 1984 Rajneeshee plot was the first and largest bioterrorist attack on the United States, and it awakened concerns about the ease with which biological weapons could be wielded and the threat of their use in the future [1].

What makes bioterrorism such a serious threat today is the rapidly increasing knowledge and availability of biological products. With a basic technical understanding of biology, one could obtain and culture bacteria such as *E. coli* or *Salmonella* for malicious purposes—just like the Rajneeshee followers. Moreover, a terrorist could release a bioweapon through a means as simple as an envelope in the mail, as the Anthrax attacks of 2001 were carried out [2]. If the illness is allowed to spread naturally, widespread infection could occur with minimal orchestration due to the ease of travel in modern society, such as via airplanes, trains, and other mass transit systems.

Predicting human casualties and suffering that may be incurred as a result of a biological attack presents a grim picture. According to the Duke Clinical Institute, 50 kg of

anthrax released in a city of 500,000 people would cause the deaths of nearly 250,000 people, 100,000 of whom would never have the opportunity to receive medical treatment. In addition, models predict that for every 100,000 people infected, response costs would total nearly 26 billion dollars

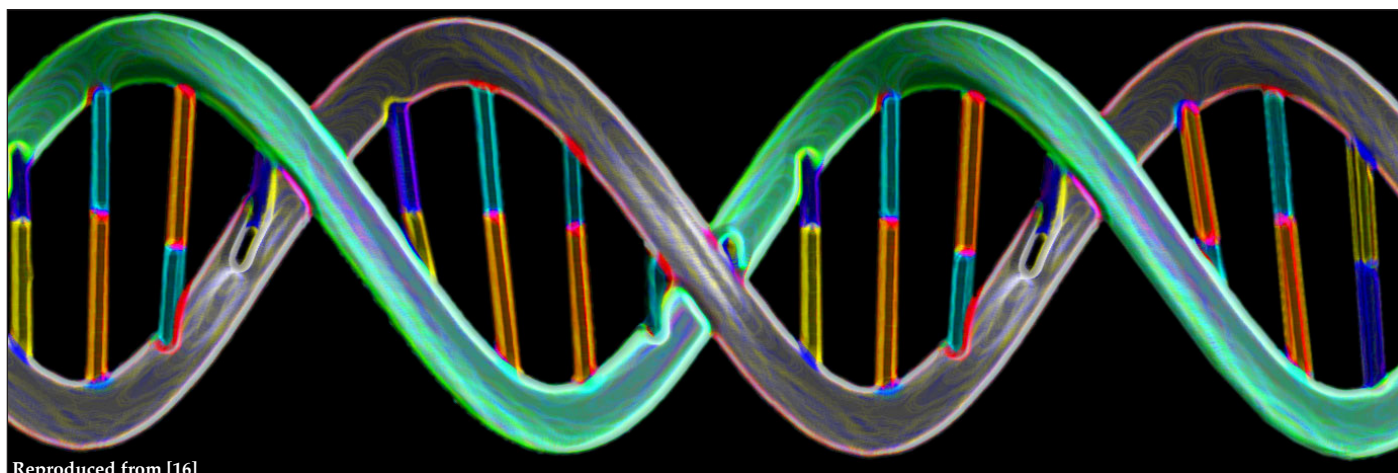
[3]. Additionally, considering that biological systems could evolve and accumulate mutations, the virus or bacteria used as a weapon could develop resistance to human attempts to contain it. These consequences present a compelling motive to consider the regulation of biotechnology companies to prevent the expansion of resources for such an attack.

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Artificial Gene Synthesis: Prospects and Problems

One burgeoning technology, artificial gene synthesis, presents a point of potential regulation in order to reduce the risk of bioterrorism. Gene synthesis is a flourishing field of biotechnology that involves the molecular construction of genes, usually through the polymerization of single-stranded, short DNA fragments called “oligos” [4]. Synthesizing genes was once a difficult and tedious task; it took a dozen scientists years to synthesize the first gene de novo in 1972 [5]. Today, DNA synthesis is a rapid, inexpensive process that can accurately produce long (over 50,000 base pairs) sequences of DNA. Over 25 companies in the United States can synthesize a gene for as little as 39 cents per base pair, and this price is still dropping [6].

DNA sequences for viruses and other pathogens, including polio, variola, and Ebola, are easily available online



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[7-9]. Cello et al. synthesized the polio virus genome in 2002 and published their groundbreaking results in *Science* for the world to see and potentially replicate [10]. The 1918 Spanish influenza virus was synthesized by another team in 2000, and their genomic data were published and made available as well [11]. Both of these examples illustrate the capabilities of this new technology and the challenging dichotomy it presents: this technology could be utilized to resurrect deadly pathogens but also holds immense promise for battling diseases.

Regulations for Companies

The logical place to implement safety regulations is at the company level. A company that wishes to enter the artificial gene synthesis market should be licensed or accredited. As a part of this accreditation process, company leaders should be educated in safe, ethical practices and methods to enhance biosecurity. Such regulation would create an enforceable industry standard for companies to adhere to, reducing the likelihood of exploitable security loopholes.

A body dedicated to corporate accountability already exists: the International Gene Synthesis Consortium, comprised of five charter companies holding 80 percent of the gene synthesis market. In order to join, companies must adhere to practices including gene sequence screening and customer background screening [12]. While this self-regulation is a crucial first step, it is essential to also have a third party for safety inspection (such as through the Centers for Disease Control). This reduces the risk that a safety mishap would provide a window of opportunity for a terrorist to manipulate the technology to create a harmful product.

Identifying Consumers

It is also important to monitor people attempting to access

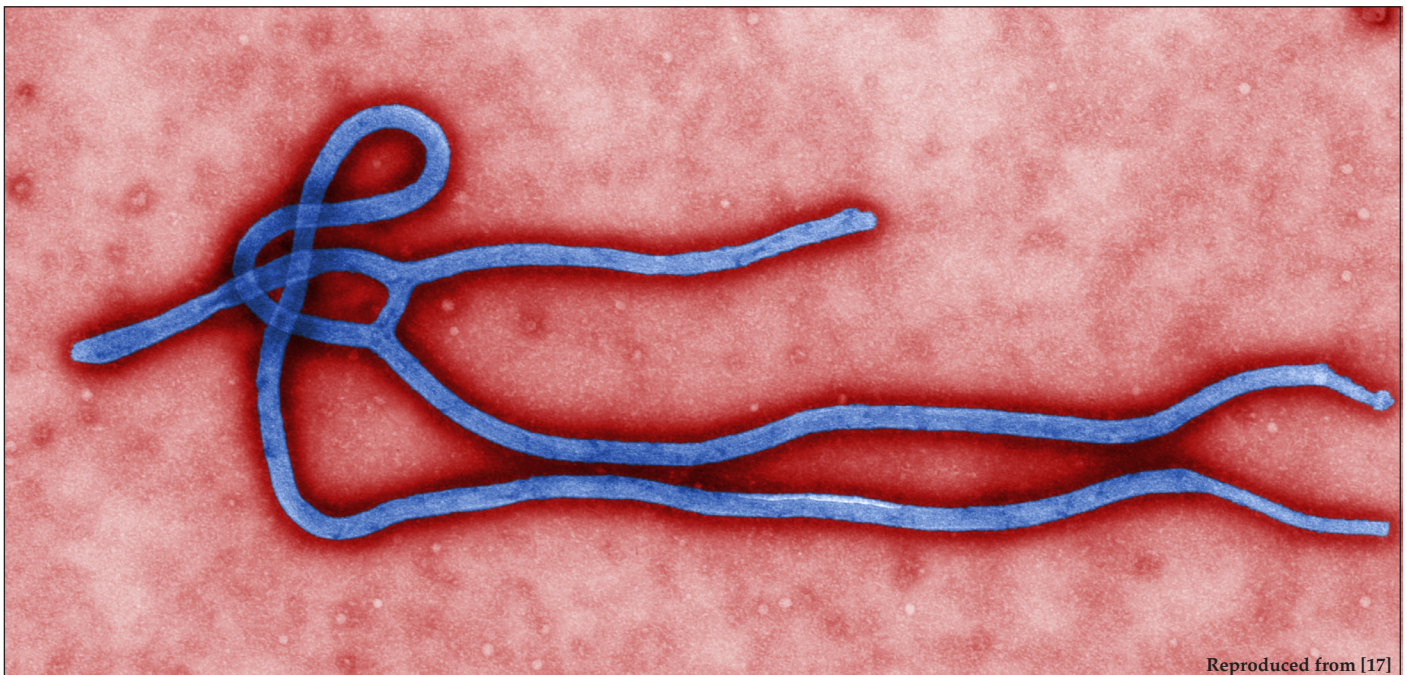
gene synthesis technology at the consumer level to ensure it is not used malevolently. First, it would be beneficial to screen new customers against a database of suspected terrorists. This could be achieved by partnering with national and federal bureaus, such as the Department of State or the Department of Homeland Security, as IGSB members already do [12]. This preliminary screening would act as a deterrent against using artificial gene synthesis technology as a bioterror weapon.

Secondly, a licensing process should be required for

research universities and biotechnology companies to reduce the hassles that might be associated with repeated review of academics and professionals with known motives. Individuals outside of this realm would have to file a letter of intent and references to determine their motives. Since non-academic, first-time buyers make up only a small percentage of all clients, the screening process would be

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efficient and streamlined save for these exceptional cases [13]. Currently, individuals seeking to obtain gene sequences for pathogens labeled “select agents” by the department of Health and Human Services are subject to FBI background checks. However, this system does not address the ability to build the whole select agent gene by ordering individual portions of the gene from different vendors, or by procuring the complementary DNA strands (cDNA) [14]. Considering the advances in gene synthesis and amplification and the potential risks such DNA fragments pose, the select agent regulations should be amended to include these strategy concerns. Reevaluating Artificial DNA Products at the biological level, a final screening is necessary to ensure DNA fragments being produced are not associated with virulent or pathogenic organisms. Current United States law requires companies to screen for DNA sequences that “are inherently



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capable of producing a select agent virus” [15]. However, such laws should be extended to cover specific gene sequences that enhance virulence in or confer drug resistance to bacteria or viruses. As the field of gene synthesis progresses, the law must adapt with new biotechnology. In addition, suspicious habits of customers, such as the rapid purchase of several discrete gene sequences over a short period of time, should be monitored and screened to determine if any gene sequences could be combined to form something more virulent. Currently, companies screen gene orders against various private gene sequence databases; the process differs by organization [13]. To ensure thorough and rigorous screening that is standard across all companies, a national database should be formed that would serve all gene synthesis companies and include fragments, cDNA, and near-match sequences for pathogens, select agents and other virulent strains.

Artificial Gene Synthesis and the Future of Biology

The best measure against bioterrorism is wide proliferation and promotion of genome synthesis technology and education in the biological sciences. Educating students and industry professionals about the risks and benefits of synthetic biology allows for a deeper understanding of the field and a heightened awareness of the risks. Increased funding for synthetic genomic research, particularly in academia and federal biosafety bureaus, will ensure that the leading edge

of this field is pursued by those scientists with the intentions of advancing human knowledge and safety. This strategy provides a statistical advantage; by promoting research in synthetic biology, it is far more likely that the thousands of scientists endeavoring to make use of this technology for purposes to serve human knowledge will be able to out-innovate and out-engineer those few individuals aiming to use this technology as a weapon.

While today it may be difficult to predict the direction artificial gene synthesis will take as the technology matures, it is important to strive to prevent misuse or corruption. In an era in which nations are constantly on alert for terror threats, it is crucial to acknowledge the serious risks posed by biological weapons and strive to attenuate them. It is critical to not undervalue this technology’s potential—for harm, but also for hope. In providing humans with the power to control and command the most intricate of nature’s chemical reactions, gene synthesis presents the extraordinary opportunity to engineer the future of biology. If channeled towards education and research, the promise of artificial gene synthesis can promote a more nuanced knowledge of the molecular world and serve to enrich the health of humankind. ■

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