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NOTES

Synthetic Biology: State Regulation in the Biomedical Context

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Abstract

Synthetic biology is an emerging, interdisciplinary research field with much promise for biomedicine. Broadly defined as "the design and construction of new biological systems to perform specific tasks," researchers and clinicians are using synthetic biology to develop targeted treatments for cancer, coronaviruses, and so forth. Because of the experimental nature of synthetic biology, regulation is necessary. Current federal frameworks, such as the Food, Drug, and Cosmetics Act, The Toxic Substances Act of 1976, Institutional Review Boards, and self-regulation are not enough. As a result, states have a unique opportunity to develop statutory and regulatory frameworks to develop a pathway for regulating synthetic biology. In developing legislation, state lawmakers should look to build a comprehensive framework that addresses businesses selling technology for synthesizing DNA codes, monitors orders for synthetic DNA, and develops statewide documentation systems. Additionally, public health information on treatments using synthetic biology can help to educate the public and reduce the prevalence of misconceptions about the technology. In the absence of federal regulation, states should step into the synthetic biology regulatory space to ensure that their citizens are not harmed by therapies developed using synthetic biology.

Introduction

Biology as a scientific discipline has existed for many centuries. From Hippocrates' study of medicine in Ancient Greece[1] to James Watson and Francis Crick's discovery of the structure of DNA in 1953,[2] humans have been continually fascinated by the intricacies of the human body. As technology and our understanding of the human body have advanced, scientists have created a new area of study: synthetic biology. Synthetic biology is "an emerging interdisciplinary research field" in which scientists design and create "novel artificial biological pathways, organisms, or devices" or redesign "existing biological systems," often with the goal of addressing health, energy, materials, or environmental issues.[3] While synthetic biology has led to progress in solving difficult medical problems, it also presents significant biosafety, biosecurity, and cyberbiosecurity concerns.[4] This Note focuses on the concerns raised by medical therapies and drugs that employ synthetic biology; the current lack of relevant regulation in this area; and options states have for introducing comprehensive, state-based regulation.

[1]Michael Boylan, *Hippocrates (c. 450 – c. 380 B.C.E.)*, Internet Encyclopedia of Phil., https://iep.utm.edu/hippocra/ [https://perma.cc/BG6S-K8S9] (last visited Nov. 17, 2022).

[2]Profiles in Science, *The Discovery of the Double Helix, 1951-1953*, U.S. Nat'l Libr. Of Med., https://profiles.nlm.nih.gov/spotlight/sc/feature/doublehelix [https://perma.cc/BDR9-XUXL].

[3]Jing Li, Huimiao Zhao, Lanxin Zheng & Wenlin An, 9 *Advances in Synthetic Biology and Biosafety Governance*, Frontiers in Bioengineering & Biotechnology, Apr. 30, 2021, at 2.

[4]*Id.*

While foreign countries have more comprehensive systems for regulating synthetic biology[5], the U.S. currently has a patchwork of federal laws, policies, regulations, and guidance addressing the field and accompanying biosecurity concerns.[6] This approach "relies heavily on federal administrative agencies empowered by statute to oversee issues within their jurisdictional mandates through rules and regulations."[7] As these federal agencies apply old laws to new technology, concerns about public health and welfare continue to grow.[8]

Synthetic biology as used in the biomedical context is not regulated as a technology in the U.S.[9] Pursuant to the 1986 Coordinate Framework for Regulation of Biotechnology ("CFRB"), "synthetic biology, like earlier generations of biotechnology products…will be regulated based on particular product categories and particular uses."[10] As a result, the U.S. Food and Drug Administration ("FDA") is the federal regulatory agency with primary oversight of products developed using biotechnology, including synthetic biology, as they relate to drugs.[11] The FDA regulates drugs produced using synthetic biology with existing laws and guidance; most notably the Food, Drug, and Cosmetic Act of 1938 ("FDCA") and its subsequent amendments.[12] Although the FDCA has been repeatedly applied to new technologies, synthetic biology and how it influences medical therapies presents an entirely new concern: organisms used in synthetic biology are often intended to multiply and can evolve while delivering treatment.[13] Further, some medical therapies developed using synthetic biology techniques are intended to reproduce within the body in order to deliver the desired treatment.[14] This raises questions as to how we should respond if a therapy developed using synthetic biology mutates into a pathogen. Current federal regulation is inadequate because it (1) is piecemeal and does not provide clear guidance on agency responsibilities, (2) does not adequately address pre-clinical trial concerns, (3) does not regulate all relevant laboratories or research facilities, and (4) does not fully address biomedical concerns that an organism made from nonpathogenic sources could display pathogenicity once introduced into a patient.[15]

As concerns around the use of synthetic biology outpace international guidance and the federal government's ability to pass legislation, develop regulations, and issue guidance and executive orders, the field will need to turn to other forms of oversight. While industry self-regulation has been utilized in the past to oversee the biotechnology industry, it may not address all potential regulatory gaps relevant to synthetic biology.[16] State governments have an open opportunity to address concerns raised by synthetic biology and should consider developing their own guidance for organizations within their jurisdiction. In 2021, California responded to biosecurity concerns by introducing the

[5]*See, e.g.*, *Biosecurity Act 2015* (Cth) (Austl.) [(中华人民共和国生物安全法) [Biosecurity Law of the People's Republic of China] (promulgated by the Standing Comm. Of the Nat'l People's Cong., Oct. 17, 2020, effective Apr. 15, 2021) P.R.C. Laws 56, *translated in* lawinfochina.com, http://www.lawinfochina.com/display.aspx?lib=law&id=33962 [https://perma.cc/Q9ZP-2YUT].

[6]*See, e.g.*, 7 U.S.C. § 3351 [Proper statute cite according to R.12.2]; Ctrs for Disease Control & Prevention, Nat'l Institute of Health, Biosafety in Microbiological and Biomedical Laboratories (6th ed.) (2020).

[7]Leili Fatehi & Ralph F. Hall, *Synthetic Biology in the FDA Realm: Toward Productive Oversight Assessment*, 70 Food & Drug L. J. 339, 349 (2015).

[8]Jordan Paradise & Ethan Fitzpatrick, *Synthetic Biology: Does Re-Writing Nature Require Re-Writing Regulation?*, 117 Penn St. L. Rev. 53, 54-55 (2012).

[9]Gregory N. Mandel & Gary E. Marchant, *The Living Regulatory Challenges of Synthetic Biology*, 100 Iowa L. Rev. 155, 173 (2014).

[10]*Id.*

[11]Deepti Kulkarni, *The Age of Innovation in Food: Is Our Regulatory System Ready?*, 80 Md. L. Rev. 41, 42 (2021).

[12]Paradise & Fitzpatrick, *supra* note 8, at 63.

[13]Mandel & Marchant, *supra* note 9, at 158.

[14]Paradise & Fitzpatrick, *supra* note 8, at 61. This approach has been used in cancer treatments. Researchers have altered bacteria and cells so that they gather at a tumor site, multiple, and eventually release the desired therapy. Ming-Ru Wu, Barbara Jusiak & Timothy K. Lu, *Engineering Advanced Cancer Therapies with Synthetic Biology*, 19 Nature Rev. 187, 188 (2019).

[15]*See* discussion *infra* Section II(b).

[16]Gardnar Arnason, *Synthetic Biology between Self-Regulation and Public Discourse: Ethical Issues and the Many Roles of the Ethicist*, 26 Cambridge Q. of Healthcare Ethics 246, 248 (2017).

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Gene Synthesis Providers bill, making it the first state to introduce a bill specifically governing synthetic biology.[17] The Maine State Legislature passed a law that establishing an advisory panel to study the risks and opportunities posed by synthetic biology to the citizens of the state.[18] States have a myriad of opportunities to regulate synthetic biology use in drug development. States can look to other supervisory models and apply them to their own regulation.

Part I of this Note defines synthetic biology, outlines a brief history of the discipline, and distinguishes it from biotechnology. Part II discusses some of the current uses and threats of the discipline, particularly as they pertain to drugs and vaccines. Part III discusses the FDA, the history of the FDCA, and how it currently oversees synthetic biology and acknowledges other regulatory mechanisms. Part IV outlines why the FDCA in its current form is inadequate to regulate drugs produced using synthetic biology and why self-regulation of the field is inadequate. Part V evaluates proposed state bills as they currently relate to synthetic biology as well as other models that can be considered when drafting legislation. Part VI looks at other potential models for regulation. Lastly, Part VII makes recommendations for future state legislation and opportunities at the state level for regulating the field based upon current legal issues and international legislation and guidance.

Synthetic biology: definition, a history, and current applications

Synthetic biology is an emerging, interdisciplinary research field with much promise for biomedicine. Based in fundamental genetics, gene-editing technology is a powerful tool to address diseases, climate change, food shortages, and other global considerations. Synthetic biology differs from traditional biotechnology and requires additional attention from lawmakers.

Definition

Synthetic biology can be broadly defined as "the design and construction of new biological parts, devices, and systems that do not exist in the natural world and also the redesign of existing biological systems to perform specific tasks."[19] Although the field has been described as a type of engineering (namely because it applies engineering principles[20]), synthetic biology is modeled after genetics.[21] The discipline stems from the long-held understanding that genetic sequences "can be assembled together like building blocks."[22] Synthetic biologists and other researchers use basic elements to "build" genetic sequences in labs, assembling everything from bacteria to viruses.[23] The field allows scientists to build gene sequences that are capable of cell behavior.[24]

[17]Gregory D. Koblentz, *Another Voice: California Biosecurity Bill Safeguards Bioeconomy and Public Health*, Sacramento Bus. J. (Sept. 23, 2021), https://www.bizjournals.com/sacramento/news/2021/09/23/another-voice-california-biosecurity-bill.html [https://perma.cc/P5SE-Q3WR]. *See also* A.B. 70, 2021 Cal. Leg., (Cal. 2021) [hereinafter Gene Synthesis Providers Bill]. The bill passed the Legislature, but was vetoed by the Governor. *AB-70 Gene synthesis providers*, Cal. Legis. Info., https://leginfo.legislature.ca.gov/faces/billStatusClient.xhtml?bill_id=202120220AB70 [https://perma.cc/59XB-HHGC] (last visited Nov. 23, 2022) [hereinafter Governor Veto].

[18]H.P. 1332, 130th Leg. (Me. 2022) [hereinafter Genome-Editing Resolution].

[19]Jing Li et al., *supra* note 3; Jim Thomas, Extreme Genetic Engineering: An Introduction to Synthetic Biology 1 (2007) https://www.etcgroup.org/files/publication/602/01/synbioreportweb.pdf [https://perma.cc/W9CV-DDR8].

[20]Tzu-Chieh Tang et al., *Materials Design by Synthetic Biology*, 6 Nature 332, 332 (2021).

[21]Paradise & Fitzpatrick, *supra* note 8, at 56.

[22]Mandel & Marchant, *supra* note 9, at 159.

[23]Brendan Parent, *Reproduction-Powered Industry: Coordinating Agency Regulations for Synthetic Biology*, 15 N.C. J.L. & Tech. 307, 311-12 (2014).

[24]George M. Church et al., *Realizing the Potential of Synthetic Biology*, 15 Nature Re. Molecular Cell Biology 289, 289 (2014).

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Synthetic biology: a brief history as a field

Despite being a relatively new field, synthetic biology is rooted in basic genetics and biological systems. The discipline has expanded from basic manipulation of DNA to being used in the development of vaccines, medical therapies and treatments, biofuels, etc.

The early years: 1869-1999

Understanding the power of synthetic biology requires a brief description of basic genetics and its history. In 1869, Swiss scientist Johann Friederich Miescher discovered nucleic acids.[25] Nucleic acids are large molecules found in a cell with the core function of storing and expressing genetic information. The two most relevant nucleic acids to this analysis are deoxyribonucleic acid ("DNA") and ribonucleic acid ("RNA").[26] The sequences of DNA and RNA are the genetic blueprint for life on Earth.

In 1953, James Watson and Francis Crick furthered our understanding of DNA when they published their ground-breaking report detailing the double-helix structure of DNA composed of a 5-carbon sugar, a phosphate, and a nucleobase.[27] In a biological process known as transcription, the DNA double-helix is separated into two chains and then copied into a complimentary chain of RNA, known as a messenger RNA ("mRNA") molecule.[28] mRNA is used by cells for a number of functions, including to create chains of amino acids called proteins.[29] Proteins perform most of the work within a cell.

In 1961, scientists Francois Jacob and Jacques Monod posited the theory that "new regulatory systems" could be assembled from molecular components.[30] In the early 1970s, scientists Stanley Cohen and Herbert Boyer conducted experiments demonstrating "that DNA from different sources could be deliberately" cut and "recombined into patterns distinct from those in nature."[31] The DNA could then be reintroduced into cells where it would be naturally replicated via the transcription process.[32] By the mid-1990s, technological advances allowed scientists to "scale-up" the process identified by Cohen and Boyer.[33] Gradually, researchers came to recognize that biological systems could be manipulated and organized, forming "the basis of a formal biological engineering discipline."[34]

2000-Present

The significance of synthetic biology garnered increasingly greater recognition in the early 2000s. As the field expanded, so too did the scope of actors involved. The first international conference for the field was held in 2004 at the Massachusetts Institute of Technology, bringing together researchers from biology, chemistry, physics, engineering, and computer science to discuss future initiatives.[35] By 2010, researchers had created the first self-replicating cell completely controlled by synthetic genes.[36]

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[25]Ralf Dahm, *Friederich Misecher and the Discovery of DNA*, 278 Developmental Biology 274, 276-77 (2005).

[26]*Nucleic Acid*, Nat'l Hum. Genome Rsch. Inst., https://www.genome.gov/genetics-glossary/Nucleic-Acid [https://perma.cc/278K-637W] (last updated June 9, 2022).

[27]James D. Watson & Francis H.C. Crick, *Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid*, 171 Nature 737, 737 (1953). The five nucleobases are adenine (A), guanine (G), cytosine (C), thymine (T) and Uracil (U). Nat'l Hum. Genome Rsch. Inst., *supra* note 26. DNA and RNA share the nucleobases adenine (A), guanine (G), and cytosine (C). RNA contains Uracil (U) while DNA contains thymine (T). *Id.*

[28]*Transcription*, Nat'l Hum. Genome Rsch. Inst., https://www.genome.gov/genetics-glossary/Transcription [https://perma.cc/YNP3-8GS7] (last updated May 24, 2022).

[29]*Id.*

[30]D. Ewen Cameron, Caleb J. Bashor & James J. Collins, *A Brief History of Synthetic Biology*, 12 Nature 381, 381 (2014).

[31]Stanley N. Cohen et al., *Construction of Biologically Functional Bacterial Plasmids* in Vitro, 70 Proc. Nat'l Acad. Sci. U.S.A. 3240, 3244 (1973).

[32]*Id.*

[33]Cameron et al., *supra* note 30.

[34]*Id.* (citing D. Bray, *Protein Molecules as Computational Elements in Living Cells*, 276 Nature. 307, 307-12 (1995)).

[35]*Id.* at 382-83.

[36]Press Release, J. Craig Venter Inst., First Synthetic Self-Replicating Bacterial Cell (May 20, 2010), https://www.jcvi.org/sites/default/files/assets/projects/first-self-replicating-synthetic-bacterial-cell/press-release-final.pdf#:~:text=ROCKVILLE%2C%20MD%20and%20San%20Diego%2C%20CA%E2%80%94May%2020%2C%202010%E2%80%94Researchers,self-replicating%20cell%20controlled%20only%20by%20the%20synthetic%20genome [https://perma.cc/9UHM-QS28].

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Recently, scientists have generated dramatic progress in the field. Scientists use synthetic biology to engineer multiple genes to work together as a gene circuit.[37] These gene circuits are then "uploaded" into cells with "programmable abilities allowing for the precise control of cellular behavior."[38] Today, scientists can employ synthetic biology to solve a number of problems, including to engineer gene circuits and place them in cells or bacteria that are then used to diagnose and treat diseases, such as cancer,[39] enable rapid production of vaccines,[40] create diesel fuel[41] and renewable energies, monitor pollutants in water,[42] produce entire genomes made of novel, synthetic genes,[43] and more.

Synthetic biology has substantially impacted—and is anticipated to continue impacting—the sectors and industries subject to oversight by the FDA, including dietary supplements and human and animal drugs.[44] Synthetic biology research is enabling scientists to "understand and control the genetic, genomic, protein, viral, metabolic, and other pathways that contribute to disease susceptibility and onset, as well as to effective treatment."[45]

Synthetic biology is fundamentally different from other biotechnology

Before addressing regulation of synthetic biology, it is important to further discuss why synthetic biology warrants regulation beyond that already in place. Synthetic biology builds upon current regulated scientific and medical technologies, but the field is marked by several major differences such as larger scale and sophistication and differences in end-products.

Synthetic biology allows for larger-scale and sophistication

Synthetic biology allows scientists to modify genetic material on a significantly larger and more sophisticated scale than they were previously capable.[46] Past methods used to develop medical therapies have traditionally only been able to modify a single gene.[47] Synthetic biology allows scientists to take advantage of the naturally occurring transcription and replication processes in organic cells, enabling rapid and mass replication of synthetic gene circuits. Additionally, while the processes for creating synthetic cells have grown in scale and sophistication, the cells remain relatively easy to use and can be stored at room temperature, making them more readily accessible in areas without refrigeration.[48]

[37]Warren C. Ruder et al., *Synthetic Biology Moving into the Clinic*, 333 Sci. 1248, 1248 (2011).

[38]*Id.*

[39]Tal Danino et al., *Programmable Probiotics for Detection of Cancer in Urine*, Sci. Translational Med., May 2015, 1. Synthetic biology can be used to interrupt the normal gene networks of a pathogen, thereby preventing the spread of infectious diseases. *See* Paradise & Fitzpatrick, *supra* note 8, at 59.

[40]Wilfried Weber & Martin Fussenegger, *Emerging Biomedical Applications of Synthetic Biology*, 13 Nature Revs. Genetics 21, 23 (2012).

[41]D. Ryan Georgianna & Stephen P. Mayfield, *Exploiting Diversity and Synthetic Biology for the Production of Algal Biofuels*, 488 Nature 329, 331 (2012).

[42]Jing Li et al., *supra* note 3, at 3-5.

[43]Paradise & Fitzpatrick, *supra* note 8, at 59.

[44]Fatehi & Hall, *supra* note 7, at 339.

[45]*Id.* (*citing* Ahmad S. Khalil & James J. Collins, *Synthetic Biology: Applications Come of Age*, 11 Nature Reviews Genetics 367, 371-374 (2010)).

[46]Paradise & Fitzpatrick, *supra* note 8, at 60.

[47]*Id.* (*citing* Subin Mary Zacharia & Leena K. Pappachen, *A Study of Genetic Engineering Techniques in Biotechnology Based Pharmaceuticals*, 3 Internet J. Nanotech. 1 (2009)).

[48]August Brookwell, Javin P Oza, & Filippo Caschera, *Biotechnology Applications of Cell-Free Expression Systems*, Life, Dec. 2021, at 1, 13.; Kira Sampson, Carlise Sorenson, & Kate Adamala, *The FDA Needs to Get Ready to Evaluate Synthetic Cells, the Next Generation of Therapeutics*, STAT (July 26, 2022), https://www.statnews.com/2022/07/26/fda-develop-framework-evaluate-synthetic-cells/ [https://perma.cc/4R2Z-FX8Q].

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Synthetic biology results in fundamentally different end-products

While traditional therapies based in genetic-modification techniques create a genetically altered organism, the drug produced is far removed from that organism.[49] For example, a technique known as recombinant DNA (rDNA) technology has been employed to modify *E. coli* genetically, manipulating them into producing human insulin.[50] This insulin is then used by patients with conditions such as diabetes. The modified *E. coli* is not itself used as the therapy.

In contrast, the products made using synthetic biology are active. These organisms manipulated with synthetic biology would be used as the therapy itself, as is done when scientists modify bacteria to target cancerous tumors and deliver treatment.[51] The organism "would be engineered to live, at least temporarily, inside the patient's body."[52] This difference creates much of the uncertainty around how the organism will react to the body and what will happen if excretion into the environment should occur. Further, whether the organism's DNA will be passed on to direct offspring and how that will impact future generations descended from a person receiving the treatment is unknown.

Some researchers and bioethicists argue that synthetic biology is not distinct enough from other biotechnology to warrant enhanced oversight.[53] However, evidence suggests that current biotechnology regulations are insufficient to regulate innovations in biotechnology, let alone synthetic biology.[54] While cells are generally well-understood, there is no definitive toolbox for creating one and it is difficult to anticipate how they will interact with their environments.[55] Overall, synthetic biology represents a large leap in human knowledge and ability to treat diseases, as well as a leap into uncharted territory.

Current uses and risks in the medical field

Synthetic biology has led to biomedical breakthroughs and continues to hold great promise for overcoming modern day medical challenges. Currently used to study diseases, researchers are hopeful that synthetic biology can lead to improved vaccine production and cancer treatments.[56] However, powerful technology like this is not used without risk. Researchers, bioethicists, politicians, and others have raised concerns regarding the risks associated with synthetic biology. Synthetic biology's utility and the accompanying risks are discussed below.

Current biomedical uses for synthetic biology

Synthetic biology has allowed researchers to better understand diseases and develop treatments for those diseases.

Reconstruction of diseases by synthesis and increased understanding of disease mechanisms

Synthetic biology allows researchers to assemble genetic sequences for proteins or viral and bacterial genomes rapidly.[57] Such rapid assembly aids them in understanding disease responses to certain

[49]Paradise & Fitzpatrick, *supra* note 8, at 61).

[50]*Id.*

[51]*Id.*; Wu et al., *supra* note 14.

[52]Paradise & Fitzpatrick, *supra* note 8, at 61.

[53]Parent, *supra* note 23, at 333 (*citing* Michael Rodemeyer, Woodrow Wilson Int'l Ctr. for Scholars, New Life, Old Bottles: Regulating First-Generation Products of Synthetic Biology 18 (2009)).

[54]*See* Terje Traavik, *An Orphan in Science: Environmental Risks of Genetically Engineered Vaccines*, Report to the Directorate for Nature Management, Norway, 21, 27, 49 (1999) (finding that some live rDNA vaccines can revert to full virulence at random).

[55]Sampson, Sorenson & Adamala, *supra* note 48.

[56]Rodemeyer, *supra* note 53, at 7, 18.

[57]Weber & Fussenegger, *supra* note 40, at 22-23; *see generally* Alan Villalobos et al., *Gene Designer – A Synthetic Biology Tool for Constructing Artificial DNA Segments*, BMC Bioinformatics, June 2006.

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treatments.[58] Researchers have employed this technology to understand viruses, including H1N1 and the coronavirus zoonoses responsible for the severe acute respiratory syndrome ("SARS") pandemic in 2002 and 2003.[59] They have used this information to develop vaccines currently in use or undergoing clinical trials.[60] Scientists also employed synthetic biology by reconstructing the SARS-CoV-2 (also known as the coronavirus or COVID-19) genome to facilitate rapid medical responses to the pandemic.[61] Researchers anticipate using similar techniques to prepare for and respond to future pandemics.[62]

Innovation in cancer treatments

Significant scientific work is already underway exploring how synthetic biology can be used or provide and produce therapies for a range of diseases, infections, and conditions, including cancer.[63] Cancer therapies are required to target and eliminate cancerous cells selectively.[64] Designing effective therapies that selectively target cancer cells while leaving healthy tissue undamaged has historically been a serious challenge.[65] Synthetic biology can be used to engineer "tumor-invading" non-pathogenic *E. coli* or *Salmonella* bacteria that release cytotoxic compounds once present in the tumor, thereby killing only the cancerous cells.[66] Researchers have also used this process to release "reporter proteins" for non-invasive follow-up monitoring.[67] These treatments are often delivered orally or through intravenous injection.[68]

Synthetic biology can also be used to make current cancer treatments more effective for more types of cancer. Recently, scientists have had great success using chimeric antigen receptor T ("CAR-T") cell therapy for treating blood cancers after all other treatment options had been exhausted.[69] However, researchers have reported issues using the therapy to treat other cancers.[70] In response, synthetic biologists are working to modify CAR-T cells to better control their activation and program them to target specific locations in the body.[71]

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[58]Fatehi & Hall, *supra* note 7, at 354.

[59]Weber & Fussenegger, *supra* note 40, at 23. A zoonosis (plural: zoonoses) "is an infectious disease that has jumped from a non-human animal to humans. Zoonotic pathogens may be bacterial, viral, or parasitic… ." *Zoonosis*, World Health Org. (July 29, 2020), https://www.who.int/news-room/fact-sheets/detail/zoonoses [https://perma.cc/YFZ9-KGN5].

[60]Xiao Tan, Justine H. Letendre, James J. Collins & Wilson W. Wong, *Synthetic Biology in the Clinic: Engineering Vaccines, Diagnostics, and Therapeutics*, 184 Cell 881, 883 (2021).

[61]Tran Thi Nhu Thao et al., *Rapid Reconstruction of SARS-CoV-2 using a Synthetic Genomics Platform*, 582 Nature 561 (2020). Because of their size and "occasional instability," coronaviruses are difficult to clone and manipulate using traditional methods. *Id.* Researchers used a "yeast-based synthetic genomics platform" to reconstruct SARS-CoV-2, facilitating rapid responses. *Id.* at 563-5.

[62]*Id.* at 565.

[63]Fatehi & Hall, *supra* note 7, at 355; Paradise & Fitzpatrick, *supra* note 8, at 59-60.

[64]Weber & Fussenegger, *supra* note 40, at 28.

[65]Fatehi & Hall, *supra* note 7, at 354.

[66]*Id.* Studies in mice have shown that oral introduction of engineered *Salmonella* bacteria, in combination with injection of a chemotherapeutic agent, can prolong survival. N. Omar Din et al., *Synchronized Cycles of Bacterial Lysis for in vivo Delivery*, 536 Nature 81 (Aug. 2016).

[67]Din et al., *supra* note 66.

[68]*Id.* Traditionally administered in hospitals, Medicare officials have recently corrected a "billing glitch" that will now allow physician's practices to administer and bill for CAR-T therapy. This is expected to make CAR-T therapy more accessible. John Wilkerson, *Medicare Paves the Way for CAR-T in Doctors Offices*, STAT (Jan. 12, 2023), https://www.statnews.com/2023/01/12/medicare-paves-the-way-for-car-t-in-doctors-offices/#:~:text=WASHINGTON%20%E2%80%94%20Medicare%20officials%20have,for%20increasingly%20common%20cancer%20types. [https://perma.cc/WSG4-KB2Z].

[69]Angus Chen, *Scientists are Making Car-T Cells More Clever. Here's What the Next Generation Could Look Like*, STAT (Jan. 14, 2022), https://www.statnews.com/2022/01/14/cancer-cart-cell-therapy-research/ [https://perma.cc/C6U5-2U4P]. In this treatment, a patient's T cells are harvested and engineered to express a tumor-antigen recognizing protein called a CAR, creating CAR-T cells. Wu, *supra* note 14, at 187. The CAR-T cells are reintroduced into the patient, "where they can recognize and destroy cancer cells expressing the antigen of interest." *Id.*

[70]Chen, *supra* note 69.

[71]*Id.* (*citing* Yiqian Wu et al., *Control of the Activity of CAR-T Cells Within Tumours Via Focused Ultrasound*, 5 Nature Biomedical Eng'g 1336 (2021)); Wu, *supra* note 14, at 188.

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Current biomedical risks of synthetic biology

While synthetic biology holds a lot of promise for positive scientific progress, it also presents very real threats and has spurred concern about bioterrorism and the intentional creation of biological weapons; crossing bioethical lines; and biomedical risks, such as the unintended mutation of a treatment into a malignant specimen while in the body.

Bioterrorism and black biology

Much has been written on synthetic biology as a tool for bioterrorism, "black biology," and biological warfare.[72] As early as 2002, researchers used synthetic biology to create a lab-built polivirus that was "almost indistinguishable from the original."[73] In 2018, a Canadian scientist spent less than $100,000 using synthetic DNA to recreate the extinct horsepox virus—a close relative to smallpox.[74] This has sparked fears throughout the community and amongst regulators that researchers or bad faith actors will recreate dangerous, but largely dormant, viruses and will accidentally or intentionally release them to infect the general population.

Others have expressed fear specifically over the prevalence of BioBricks™: a free and open library of synthetically created and genetic biological components that a number of researchers have contributed to with the purpose of encouraging individuals to develop solutions to problems.[75] Some believe nefarious actors can take advantage of the easy access to this database and utilize the genetic components to create bioweapons.[76] Today, "anyone with a laptop computer can access public DNA sequence databases via the Internet, access free DNA design software, and place an order for synthetized DNA for delivery."[77]

Biomedical risks

The risks associated with synthetic biology and the biomedical field are more about "bio-error" than bioterror.[78] This Note acknowledges these risks and discusses regulation to mitigate the risks posed by introducing synthetically produced organisms into humans for medical therapies and treatment, as in cancer therapies.[79] Unlike past biotechnology modifying single genes, synthetic biology "involves engineering entire synthetic circuits of genes that control a range of cellular behaviors."[80] In the medical context, "a microbe engineered using synthetic biology techniques would be used as the 'drug' itself," such as in cancer treatments where bacteria are engineered to target tumors.[81]

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[72]*See, e.g.*, Braden Leach, *Necessary Measures: Synthetic Biology & the Biological Weapons Convention*, 25 Stan. Tech. L. Rev. 141, 144 (2021) (referring to biological weapons developing using new, accessible synthetic biology techniques as "the poor man's atom bomb."); Nicole H. Kalupa, *Black Biology: Genetic Engineering, the Future of Bioterrorism, and the Need for Greater International and Community Regulations of Synthetic Biology*, 34 Wis. Int'l L.J. 952, 960 (2017) (discussing potential uses of synthetic biology to develop pathogenic viruses). "Black biology" is "the use of genetic engineering to enhance the virulence of a pathogen." Lawrence F. Roberge, *Black Biology- A Threat to Biosecurity and Biodefense*, Biosafety (2013), https://www.longdom.org/open-access/black-biologya-threat-to-biosecurity-and-biodefense-2167-0331.1000e139.pdf.

[73]Jennifer Couzin, *Active Poliovirus Baked from Scratch*, 297 Sci. 174 (2002).

[74]Kai Kupferschmidt, *How Canadian Researchers Reconstituted an Extinct Poxvirus for $100,000 Using Mail-Order DNA*, Sci. (July 6, 2017), https://www.science.org/content/article/how-canadian-researchers-reconstituted-extinct-poxvirus-100000-using-mail-order-dna [https://perma.cc/B8TR-5DGV].

[75]Fatehi & Hall, *supra* note 7, at 353.

[76]*See* Leach, *supra* note 72, at 142 (describing BioBricks as "tearing down barriers to entry").

[77]Michele S. Garfinkel et al., *Synthetic Genomics: Options for Governance*, 3 Industrial Biotech. Biosec. And Bioterrorism: Biodef. Strategy, Prac., and Sci., 359 333, 336 (2007); *see also* Parent, *supra* note 23, at 321 (separating potential harms into two categories: "intentional" and "unintentional").

[78]Mandel & Marchant, *supra* note 9, at 157-58.

[79]*See supra* Part I, at 4.

[80]Fatehi & Hall, *supra* note 7, at 356.

[81]Paradise & Fitzpatrick, *supra* note 8, at 61; Wu et al., *supra* note 14.

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Scientists are uncertain as to the long-term impacts of synthetically engineered organisms on humans. Major "uncertainty arises with the possibility of horizontal gene transfer between synthesized organisms and naturally occurring organisms."[82] One researcher described modified cells as "teenage kids," stating "[y]ou can maybe watch, but you can't really control them."[83] Other authors have expressed fear of lab leaks or excretion of synthetically created bacteria and viruses from a patient into their environment.[84] Bacteria and viruses mutate rapidly and may be uncontrollable into the broader environment, disturbing ecological balances carefully cultivated by thousands of years of evolution.[85] This difference in how the therapy is created leads to more uncertainty regarding how it will interact with the human body's cells and the environment.

Further, researchers cannot eliminate the risk that an organism made from nonpathogenic sources could display pathogenicity once introduced into a patient.[86] As stated in the 2010 Presidential Commission for the Study of Bioethical Issues, "[N]ovel organisms developed with synthetic biology to treat illness may trigger unanticipated adverse effects in patients. The use of cell therapies of bacterial, or potentially, mixed microbial origin may cause infections or unexpected immune responses."[87] Further, even cells modified to contain "off-switches" may harm healthy tissue surrounding the areas they are meant to target.[88]

Although synthetic biology has deep roots in the study of genetic material, it is still a relatively new field that poses many unanswered questions. As researchers develop the study, laws and regulations must not only address lingering questions; they must also keep pace with the new questions that synthetical biology will inevitably generate.

Bioethical concerns raised by synthetic biology

In addition to bioterror and biomedical risks, some have raised ethical concerns regarding the widespread use of synthetic biology. While many researchers argue that they are "not trying to imitate nature" but merely "supplement nature,"[89] others, including bioethicists, have express concern that synthetic biology is "playing God" or interfering with nature in ways that we should not.[90] In a similar, secular vein of thought, some worry that synthetic biology provides humans with a false sense of security, causing them to overestimate "their ability to control complex ecosystems" and putting the population at risk.[91] Ultimately, some view the field as allowing humans to move from modifying life to creating life.[92] While synthetic biology holds much promise for possibly preserving species at risk of extinction and preserving essential biodiversity potentially lost due to climate change, it also produces complex ethical challenges.[93] Concerns about "playing God" are not new or specific to the field of biology. While addressing the ethical implications will no doubt play a major role in the specific wording and content of legislation, further discussion of the bioethical implications of synthetic biology is beyond the scope of this discussion.

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[82]Parent, *supra* note 23, at 332-33.

[83]Chen, *supra* note 69.

[84]Fatehi & Hall, *supra* note 7, at 357; *see also* Parent, *supra* note 23, at 331.

[85]Parent, *supra* note 23, at 332-33. The rapid mutation of the COVID-19 virus has only bolstered concerns regarding a virus's ability to mutate and the risks associated with synthetic biology.

[86]*See* Rodemeyer, *supra* note 53, at 28.

[87]Amy Gutmann et al., Presidential Comm'n for Study of Bioethical Issues, New Directions: The Ethics of Synthetic Biology and Emerging Technologies 67-68 (2010).

[88]Chen, *supra* note 69.

[89]Parent, *supra* note 23, at 314.

[90]*Id.* at 324. Concerns about "playing God" or usurping the role of a higher power are not new to science. Similar concerns have been raised with regards to other areas of biotechnology, including gene editing technology. *See* Thomas Douglas & Julian Savulescu, *Synthetic Biology and the Ethics of Knowledge*, 36 J. Med. Ethics 687, 688 (2010).

[91]Douglas & Savulescu, *supra* note 90, at 688.

[92]*Id.*

[93]Chris Gyngell, *Synthetic Life and Biodiversity*, Univ. Oxford: Practical Ethics (Apr. 25, 2017), http://blog.practicalethics.ox.ac.uk/2017/04/synthetic-life-and-biodiversity/#_ftn1 [https://perma.cc/2NE5-SZHW]. Creating organisms not currently found may be a way to preserve biodiversity lost through climate change and habitat destruction. *Id.*

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Synthetic biology is already successfully used in several biomedical contexts. However, the technology is still relatively new. Lawmakers should look to introduce regulation to ensure that the field is regulated and continually monitored as synthetic biology is used to address more problems.

Regulating synthetic biology

Synthetic biology as used in the biomedical context is regulated as a drug and is therefore subject to a patchwork of federal statutes, regulations, and administrative guidance. These are discussed below.

A brief history of federal drug regulation

At the turn of the 20th century, the U.S. market for drugs was a treacherous one full of dangerous products marketed as safe and effective cures for diseases and no federal regulations.[94] Efforts at a form of self-regulation in the mid-1800s by educating pharmacists through the publication of the U.S. Pharmacopeia and the establishment of the first American colleges of pharmacy were not enough to stop the stream of unsafe products flooding the market.[95]

The movement to regulate drugs in the U.S. at the federal level began in earnest in the late 1800s with scientists, particularly Dr. Harvey W. Wiley, campaigning for federal law on drug regulation.[96] 1902 marked the beginning of federal food and drug regulation when Congress passed the Biologics Control Act to ensure purity and safety of vaccines, drugs, and serums.[97] In 1906, the Pure Food and Drugs Act was passed by Congress, prohibiting the sale of "misbranded and adulterated foods, drinks, and drugs" using interstate commerce, effectively outlawing "false therapeutic claims."[98] The FDA was created to enforce the 1906 Pure Food and Drugs Act.[99]

It was not until 1938, in response to intense lobbying and the death of over one hundred people from "Elixir Sulfanilamide," that comprehensive regulation was enacted in the form of the FDCA.[100] The FDCA extended the FDA's oversight to additional products, authorized factory inspections, and mandated that drugs be shown to be safe before they are available for sale and advertising.[101] Subsequent guidance, such as a 1939 twenty-six-point guidance document on drug labeling further strengthened the FDCA.[102]

[94]Michelle Meadows, *Promoting Safe & Effective Drugs for 100 Years*, FDA Consumer, January-February 2006, at 15, 15. For example, "medicines" containing opium, morphine, and cocaine were sold indiscriminately, often in packaging featuring false claims. Wallace F. Janssen, *Outline of the History of U.S. Drug Regulation and Labeling*, 36 Food Drug Cosm. L. J. 420, 422 (1981). Without regulations, the U.S. was "the world's dumping ground for substandard and contaminated drugs." *Id.*

[95]Janssen, *supra* note 94, at 422-23.

[96]In 1899, Wiley and his Bureau of Chemistry analyzed tablets a postal inspector suspected were being illegally vended at the request of the Postmaster General. *Id.* at 424. Wiley continued his relationship with the Postal Service by testing drugs into the early 1900s. *Id.*

[97]*Milestones of Drug Regulation in the United States,* U.S. Food & Drug Admin., https://www.fda.gov/media/109482/download [https://perma.cc/F8CW-TNC5] (last visited Nov. 25, 2022) [hereinafter Milestones].

[98]Pure Food and Drug Act, Pub. L. No. 59-384, 34 Stat. 768 (1906); Janssen, *supra* note 94, at 427. In 1911, the Act faced a serious setback when the Supreme Court held that the law did not prohibit false claims, only false statements made on a label regarding ingredients. *U.S. v. Johnson*, 221 U.S. 488 (1911). Congress remedied this loophole with the 1912 Sherley Amendment that prohibited anyone from labeling medicines with false therapeutic claims intended to defraud a purchaser. Milestones, *supra* note 97.

[99]*The Food and Drug Administration: The Continued History of Drug Advertising*, Weill Cornell Med., https://library.weill.cornell.edu/about-us/snake%C2%A0oil%C2%A0-social%C2%A0media-drug-advertising-your-health/food-and-drug-administration-continued [https://perma.cc/2FHP-K5U5].

[100]In 1933, the FDA assembled a "graphic display of shortcomings in pharmaceutical and other regulation under the 1906." The exhibit was dubbed "the Chamber of Horrors" and was displayed nationwide to help increase support for reform. In 1937, 107 persons, including a number of children, died after ingesting Elixir Sulfanilamide which contained the poisonous solvent diethylene glycol. This incident further illustrated the need for comprehensive regulation. Milestones *supra* note 97; Janssen, *supra* note 94, at 429.

[101]Weill Cornell Med., *supra* note 99.

[102]Janssen, *supra* note 94, at 431.

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From the FDCA came a flood of additional regulation. In 1941, the FDA started regulating individual drugs with the introduction of the Insulin Amendment.[103] The FDA also revised their manufacturing quality controls.[104] Soon after, drug labeling amendments for the first time requires a prescription for certain drugs and devices.[105] In 1962, the Kefauver-Harris Amendments were passed, marking the first-time drug manufacturers were required to prove effectiveness of their products to the FDA prior to marketing them.[106] In 1986, the White House's Office of Science and Technology Policy released the Coordinated Framework for Regulation of Biotechnology. Under this policy, "genetically engineered products should be regulated instead of processes" and current laws and regulations were considered sufficient.[107] The 1997 FDA Modernization Act increased patient access to experimental drug and devices.[108] In 2002, the FDA announced the current Good Manufacturing Practice ("cGMP") initiative intended to "ensure that process and product quality standards do not impede innovation."[109]

The U.S. has a long history of regulating new drugs and medical therapies for the purpose of ensuring consumers have access to safe and effective treatments. While the FDCA and its subsequent amendments, regulations, and guidelines have effectively regulated past drugs, they do not fully cover synthetic biology. Understanding the history of federal regulation and current federal infrastructure governing synthetic biology is key to understanding why new regulations are necessary.

Synthetic biology and current federal regulation

Currently, federal drug regulation is executed under a patchwork of policies, laws, regulations, and administrative guidance governing the many different facets of synthetic biology.[110] Federal agencies and actors that regulate synthetic biology include the FDA, the Environmental Protection Agency ("EPA"), and the U.S. Department of Agriculture ("USDA"). Without several effective regulatory safeguards, troubling gaps still exist. Notably, experts have expressed concern that the current biotechnology regulatory structure cannot properly regulate the synthetic microorganisms created for therapeutic treatments.[111]

Synthetic biology, as a drug, is primarily regulated by the FDCA

In the biomedical space, synthetic biology is regulated as a drug rather than as a technology.[112] Pursuant to the 1986 Coordinate Framework for Regulation of Biotechnology ("CFRB"), "synthetic biology, like earlier generations of biotechnology products…will be regulated based on particular product categories and particular uses."[113] As a result, the FDA has primary oversight of products developed using biotechnology, including synthetic biology, as they relate to drugs.[114] Currently, the FDA does not regulate products produced using biotechnology, including synthetic biology, any differently then they regulate other products.[115] The FDA regulates drugs produced using synthetic biology with existing laws

[103]Milestones, *supra* note 97.
[104]*Id.*
[105]Janssen, *supra* note 94, at 433. The main purpose of these amendments was to prevent the sale of drugs that were safe only when used under medical supervision. *Id.*
[106]*Id.* at 348. The law was upheld by the U.S. Supreme Court in 1973. *Id.* at 439.
[107]Parent, *supra* note 23, at 347.
[108]Weill Cornell Med., *supra* note 99.
[109]Milestones, *supra* note 97.
[110]Jing Li et al., *supra* note 3, at 7.
[111]*See* Rodemeyer, *supra* note 53, at 29, 47 n.2.
[112]Mandel & Marchant, *supra* note 9, at 173.
[113]*Id.*
[114]Kulkarni, *supra* note 11, at 42.
[115]Modernizing the Regulatory System for Biotechnology Products: Final Version of the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology, U.S. Env't. Prot. Agency 20 (2017).

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and guidance, such as the FDCA.[116] Although the FDA has repeatedly applied the FDCA to new technologies, synthetic biology and how it influences medical therapies presents entirely new concerns because of differences in its scale and the unpredictability of the end-product.[117]

The FDCA defines a "drug" as

> "(A) articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or an supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man…; and (C) articles (other than food) intended to affect the structure or any function of the body of man…; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).[118]

Medical therapies developed using synthetic biology are "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man" and therefore fall under this classification.[119]

Chapter V of the FDCA establishes FDA oversight of human drugs.[120] Under Chapter V, the FDA has oversight of "identification, synthesis, and purification of an active pharmacological ingredient," preclinical testing, clinical trials, final approval, and performance once released into the market.[121] At its most basic level, the FDCA requires developers show that "new drugs be shown safe before marketing."[122] Once a drug moves to the manufacturing stage, the FDA still has authority "to ensure good manufacturing practices."[123]

Prior to entering the market, new human drugs are reviewed extensively by the FDA to establish safety and efficacy.[124] This is often done through The New Drug Application ("NDA") Process.[125] The NDA Process is intended to allow the FDA to gather "substantial evidence" to demonstrate that:

1. The drug is safe and effective in the proposed use(s) and the benefits outweigh the risks;
2. The drug's proposed labeling is appropriate; and
3. The manufacturing methods and controls used to maintain the drug's quality are adequate.[126]

Documentation submitted to the FDA must detail what happened during clinical trials, what the ingredients of the drug are, results from animal studies, how the drug behaves in the body, and manufacturing and packaging processes.[127] Review is regarded as quite rigorous: it can take up to fifteen years and cost tens of millions of dollars to bring a new drug to market.[128] Per the Food and Drug Administration Amendments Act of 2007 ("FDAAA"), the FDA is also able to request or require post-approval nonclinical or clinical studies.[129]

[116]Paradise & Fitzpatrick, *supra* note 8, at 63. The FDCA establishes the FDA's regulatory authority. Fatehi & Hall, *supra* note 7, at 358.

[117]Mandel & Marchant, *supra* note 9, at 158; *See* discussion *infra* Section I(c)(i)-(ii).

[118]21 U.S.C. § 321(g)(1)(2021).

[119]*Id.*

[120]21 U.S.C. §§ 351-360ccc-2 (2021).

[121]21 U.S.C. § 355 (2021); Paradise & Fitzpatrick, *supra* note 8, at 66.

[122]Milestones, *supra* note 97; Parent, *supra* note 23, at 351.

[123]Parent, *supra* note 23, at 351.

[124]21 U.S.C. § 355(a) (2021).

[125]*New Drug Application (NDA)*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/types-applications/new-drug-application-nda (last updated Jan. 21, 2022) [hereinafter New Drug Application (NDA)]. The FDCA also provides for an abbreviated process that does not require preclinical and clinical data to establish safety and efficacy for drugs that the developer can demonstrate are "bioequivalent" and perform similarly to already approved drugs. *See* Paradise & Fitzpatrick, *supra* note 8, at 66.

[126]21 U.S.C. § 355(d)(5); New Drug Application (NDA), *supra* note 125.

[127]New Drug Application (NDA), *supra* note 125.

[128]Paradise & Fitzpatrick, *supra* note 8, at 66.

[129]21 U.S.C. §§ 355(o) (2021).

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Some have questioned whether synthetic biology should be addressed as a device rather than a drug.[130] Although manufactured, many therapies developed using synthetic biology cannot be classified as a "device" under the FDCA because they achieve their "primary intended purposes through chemical action within or on the body of man."[131] However, researchers have argued synthetic biology creates "devices" that "physically disrupt or embed in the host's network."[132] This matters because drug regulations are often stricter, require more clinical trial subjects, and demand more time for approval than do device regulations.[133]

Of note, some companies have produced cosmetics using synthetic biology techniques.[134] Although cosmetics are regulated by the FDA under the FDCA,[135] they will not be discussed for purposes of this Note because "a cosmetic product will be subject to the drug approval requirements if it ventures into the realm of a 'drug' given the marketing and advertising claims promoted by the manufacturer."[136] This Note focuses exclusively on drugs.

Institutional Review Boards ("IRBs") and biomedical research

IRBs are federally mandated, independent boards established to review "biomedical and behavioral research involving human subjects conducted at or supported by" an entity which receives funding from the U.S. Department of Health and Human Services ("DHHS") through a federal grant, contract, or cooperative agreement.[137] IRBs review clinical trials to determine they are ethical, ensure researchers and clinical investigators do not have any prohibitory biases, and evaluate compliance with all laws and regulations protecting human subjects.[138] IRB review helps to assure drug developers are protecting the rights and welfare of those participating in human trials.[139]

The goal of IRB review is to protect and assure the rights and welfare of all participants.[140] While IRB review will occur for products developed using synthetic biology, it focuses on research protocols and related materials, such as informed consent documents rather than the "bio-error" risks discussed above.[141] Therefore, IRB review will not adequately address the concerns posed in this Note.

The environmental protection agency (epa) and accidental release of genetically engineered organisms

A potential harm posed by synthetic biology is the negative environmental and health impacts caused by accidental release of synthetic biology microorganisms such as bacteria and viruses into the environment.[142] "Accidental release" is not limited to laboratories: as humans interact with their environment, they shed cells and other biomaterial.

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[130]Fatehi & Hall, *supra* note 7, at 360.

[131]*Importing Medical Devices*, Food & Drug Admin., https://www.fda.gov/industry/regulated-products/medical-device-overview#What%20is%20a%20medical%20device [https://perma.cc/Z9L4-9CGD] (last updated Sept. 14, 2018).

[132]Fatehi & Hall, *supra* note 7, at 360; *see also* W. John Koolage & Ralph Hall, *Chemical Action: What is it, and Why Does it Really Matter?*, 13 J. Nanoparticle Rsch. 1401, 1403-04 (2011).

[133]Fatehi & Hall, *supra* note 7, at 360.

[134]*See* Deanna Utroske, *Synthetic Biology Has a New Ally in the US*, cosmeticsdesign.com (Apr. 14, 2021), https://www.cosmeticsdesign.com/Article/2021/04/14/Synthetic-Biology-has-a-new-ally-in-the-US [https://perma.cc/S6FU-TEVQ].

[135]21 U.S.C. § 321(i) (2021).

[136]Paradise & Fitzpatrick, *supra* note 8, at 71.

[137]42 U.S.C. § 289(a); *see also Institutional Review Boards (IRBs) and Protection of Human Subjects in Clinical Trials*, U.S. Food & Drug Admin. (Sept. 11, 2019), https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/institutional-review-boards-irbs-and-protection-human-subjects-clinical-trials [https://perma.cc/323S-J5TC].

[138]Christine Grady, Commentary, *Institutional Review Boards: Purpose and Challenges*, 148 CHEST 1148 (2015).

[139]U.S. Food & Drug Admin., *supra* note 137.

[140]Grady, *supra* note 138, at 1149.

[141]*Id.*

[142]Parent, *supra* note 23, at 330.

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The EPA has "authority to require reporting, record-keeping and testing requirements, and restrictions relating to chemical substances and/or mixtures" under the Toxic Substances Act of 1976 ("TSCA").[143] In 1997, the EPA brought genetically engineered organisms "under the umbrella of the 'new chemicals' regulation" of the TSCA.[144] Chemical substances regulated by the TSCA do not include drugs.[145] This can, understandably, lead to confusion. To date, medical therapies using synthetic biology have been regulated as drugs under the FDCA. It remains an open question whether the EPA should have a hand in regulating these medical therapies, particularly as they are entering the environment through human contact. Others question whether the TSCA provides a better framework for addressing potential spread of organisms created by synthetic biology. Answers to these questions are beyond the scope of this Note, however they do highlight the need for more comprehensive regulation of synthetic biology.

At the time of writing, there are a number of stalled federal initiatives to regulate synthetic biology and other technology areas.[146] Some of these bills, such as the House of Representatives' Endless Frontier Act, focus more on increasing America's international competitiveness without creating a comprehensive regulatory structure.[147] Others focus on the use of synthetic biology for bioterror, rather than "bio-error."[148] While reform in these areas is important and should not be discounted, it does not address the regulatory issues at the crux of this Note.

In addition to stalled attempts at legislation, President Trump abandoned an attempt to regulate synthetic biology and other aspects of the country's bioeconomy through executive order.[149] The stated purpose of the proposed order was to promote scientific research while reinforcing the safety and security of the country and developing standards consistent with "American principles and values."[150] The executive order was intended to "coordinate a national strategic effort to promote a bioeconomy innovation ecosystem…promote access to Federally-funded biological data, models, and computing resources," and support research into new areas with the goal of protecting the American people.[151] Central to the executive order was the creation of a multidisciplinary "Bioeconomy Interagency Committee" ("BIC") tasked with creating a clear, comprehensive strategy for the bioeconomy while ensuring coordination across all agencies.[152] If this executive order had moved forward, BIC's findings would have been an excellent starting point for state and local governments to move forward in their own initiatives and create comprehensive plans responding to concerns raised by synthetic biology.

[143] *Summary of the Toxic Substances Control Act*, U.S. Env't Prot. Agency, https://www.epa.gov/laws-regulations/summary-toxic-substances-control-act (last updated Oct. 4, 2022).

[144] Parent, *supra* note 23, at 349. This decision by the EPA was based on the premise that non-natural arrangement of nucleic acids are new chemicals. *See id. (citing* Michael Rodemeyer, *New Life, Old Bottles: Regulating First Generation Products of Synthetic Biology*, 17 Woodrow Wilson Int'l Ctr. for Scholars (2009)).

[145] *About the TSCA Chemical Substance Inventory*, U.S. Env't Prot. Agency, https://www.epa.gov/tsca-inventory/about-tsca-chemical-substance-inventory (last updated on June 29, 2022).

[146] *See, e.g.*, Endless Frontier Act, S. 1260, 117th Cong. (2021) [hereinafter Endless Frontier Act] (A proposed bill that divides regulation of "key technology focus areas" (including synthetic biology) among the Secretary of Energy as it pertains to biofuel and "environmental remediation," the National Aeronautics Space Administration (NASA) as it pertains to "Earth and space sciences, aeronautics, space technology, and space exploration," and the Secretary of Agriculture); Bioeconomy Research and Development Act of 2021, S. 1418, 117th Cong. (2021); Biological Weapons Policy Act of 2021, S. 2912, 117th Cong. (2021) [hereinafter Biological Weapons Policy Act] (A proposed bill targeting China's use of U.S. funds in the field of synthetic biology).

[147] *See* Endless Frontier Act, *supra* note 146.

[148] *See* Biological Weapons Policy Act, *supra* note 146.

[149] Nicholas Florko, *Abandoned Trump Order on the Bioeconomy Highlights a Path Forward for Biden – But with Mixed Reviews*, STAT (May 17, 2021), https://www.statnews.com/2021/05/17/abandoned-trump-eo-on-the-bioeconomy-highlights-a-path-forward-for-biden-but-with-mixed-reviews/ [https://perma.cc/6L75-JLRC].

[150] Proposed Exec. Ord., The Off. of the Pres. of the U.S., Promoting and Protecting the American Bioeconomy, https://www.documentcloud.org/documents/20709009-trump-bioeconomy-eo?responsive=1&title=1 [https://perma.cc/U86D-5GM9].

[151] Florko, *supra* note 149.

[152] *Id.*

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Regulatory issues

Despite the existence of relevant laws and regulations, the avenues currently relied upon to regulate synthetic biology are imperfect and piecemeal. Current laws and regulations leave numerous regulatory gaps. Self-regulation or leaving regulation to the market is inconsistent with the country's current stance on drug regulation and subjects' potential consumers to too much risk.

Current laws are not enough to regulate synthetic biology

FDCA oversight of synthetic biology is ultimately inadequate to regulate synthetic biology for biomedical uses. FDA oversight of drugs typically begins after a chemical composition has already been created in a laboratory.[153] Laboratory procedures are mainly guided by the U.S. National Institute of Health's ("NIH") Guidelines for Researcher Involving Recombinant DNA Molecules.[154] The NIH has a limited role in managing synthetic biology: mainly setting biosafety standards and requirements.[155] The NIH guidelines for "constructing and handling recombinant DNA organisms" only apply to research conducted or funded by federal agencies and do not impact the private industry.[156] Because a lot of research employing synthetic biology, including drug research, is conducted by private institutions, the NIH cannot effectively regulate the field.[157] Additionally, BioBricks™ and similar technology allows small private entities and individual actors to enter the "synthetic biology market," only further decreasing the impact the NIH can have on regulation.[158]

Further, FDA oversight "technically begins at the initiation of clinical investigations" in clinical trials.[159] Unless and until the FDA is notified of research involving clinical trials, researchers and nefarious actors can illegally circumvent the FDA by simply choosing not to seek approval for trials.[160] Similarly, with the prevalence of DNA sequence databases, such as BioBricks™, widespread access to DNA design software, and the ability for anyone to place an order for synthesized DNA,[161] more innocent "curiosity-driven experimentation" is almost impossible to regulate.[162]

Ultimately, regulation at the federal level is inadequate because it (1) is piecemeal and does not provide clear guidance on agency responsibilities, (2) does not adequately address pre-clinical trial concerns, (3) does not regulate all relevant laboratories or research facilities, and (4) does not fully address biomedical concerns that an organism made from nonpathogenic sources could display pathogenicity once introduced into a patient.

Self-regulation is not enough to regulate synthetic biology

Legal scholars and regulators believe in a more hands-off approach in which researchers involved in synthetic biology should be responsible for self-regulating their laboratories to "prevent major

[153]Paradise & Fitzpatrick, *supra* note 8, at 73.

[154]*Id.*

[155]Mandel & Marchant, *supra* note 9, at 192; Gutmann, *supra* note 87, at 81.

[156]Mandel & Marchant, *supra* note 9, at 192.

[157]*Id.*; Dep't Health & Human Servs., NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) § I-C-1 (2013).

[158]Mandel & Marchant, *supra* note 9, at 193; *see also* Sarah R. Carter et al., *Synthetic Biology and the U.S. Biotechnology Regulatory System: Challenges and Options* 41 (2014) (asserting that "[t]he lack of a relevant regulatory agency with jurisdiction over non-commercial genetically engineered microbes could hinger important basic research by preventing controlled field trials.").

[159]Paradise & Fitzpatrick, *supra* note 8, at 74.

[160]*Id.*

[161]*See* Garfinkel, *supra* note 77, at 336.

[162]*See* Carter et al., *supra* note 158. This concern is somewhat mitigated by the fact that many "do-it-yourself" biologists, particularly those working in community labs, have chosen to pursue commercial applications for their work, making this research subject to oversight. As a result, many of these researchers practice and document biosafety procedures. *Id.* at n.45. While encouraging, this does not eliminate all risks, including lack of knowledge of procedures and regulation of those who do not pursue commercial applications.

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risks."[163] Although self-regulation of rDNA technology has been successful,[164] attempts at self-regulation in the field of synthetic biology have failed.[165] For example, in 2006 at the second International Meeting on Synthetic Biology, organized by the BioBricks Foundation, actors attempted to introduce a code of conduct intended to prevent the misuse of synthetic biotechnology.[166] Even before the conference, the proposed code faced significant opposition.[167] Some argued that without proper channels through which dangerous experiments could be reported, the code was useless.[168] Others felt that researchers could not be trusted to regulate themselves.[169]

Today, fears concerning the lack of a designated reporting body may be somewhat assuaged by the existence of the International Gene Synthesis Consortium ("IGSC"). The IGSC, founded in 2009, is "an industry-led group of gene synthesis companies and organizations formed to design and apply a common protocol to screen both the sequences of synthetic gene orders and the customers who place them."[170] The IGSC has developed a comprehensive database of regulated pathogens that they use to monitor orders.[171] Additionally, the IGSC already represents a large number of commercial gene synthesis organizations world-wide.[172] Synthetic biologists and adjacent researchers should consider reintroducing a revised code of conduct with membership or permission to be monitored by the IGSC as a requirement of doing business. Researchers can look to past successes as a model.[173] Such a requirement would address current federal gaps by providing all relevant laboratories with clear guidance and standards.

Self-regulation by a uniform set of standards may help address concerns about piecemeal regulation by providing a cohesive standard all organizations and actors in the profession agree to abide by. However, without an international or national regulatory body such as the IGSC, it will be almost impossible to enforce this standard. Additionally, self-regulation does not fully address the biomedical concerns around pathogenicity. Ultimately, it is largely unreasonable to hold scientists solely responsible for regulating themselves. Regulators must turn to other means of regulation.

Synthetic biology and state-based regulation

Current federal regulations as they relate to synthesis of organisms using synthetic biology in a lab and use of said organisms in the human body are not wholly adequate to address the unique concerns raised by synthetic biology. As regulators begin to recognize the problem, some have moved to recommend other avenues that will produce stricter regulation. One such avenue is an increase in state regulation.

[163]Parent, *supra* note 23, at 333 (*citing* Amy Gutmann et al., New Directions: The Ethics of Synthetic Biology and Emerging Technologies, Report of the Presidential Commission for the Study of Bioethical Issues v (2010), https://bioethicsarchive.georgetown.edu/pcsbi/sites/default/files/PCSBI-Synthetic-Biology-Report-12.16.10_0.pdf).

[164]Paul Berg, *Asilomar 1975: DNA Modification Secured*, 455 Nature 290 (Sept. 2008). The 1975 Asilomar Conference set standards that allowed geneticists to "push research to its limits without endangering public health." *Id.*

[165]Arnason, *supra* note 16, at 248.

[166]*Id.*

[167]*Id.* (stating "[a] group of 35 civil society organizations, including Greenpeace International and Genewatch, strongly opposed the plan and called for 'inclusive public debate, regulation, and oversight of the rapidly advancing field of synthetic biology.'"); Peter Aldhous, *Synthetic Biologists Reject Controversial Guidelines*, New Scientist (May 2006), https://www.newscientist.com/article/dn9211-synthetic-biologists-reject-controversial-guidelines/.

[168]Aldhous, *supra* note 167.

[169]*Id.* (quoting Sue Mayer, director of GeneWatch: "Scientists creating new life forms cannot be allowed to act as judge and jury.").

[170]*About IGSC*, Int'l Gene Synthesis Consortium, https://genesynthesisconsortium.org/ [https://perma.cc/BPX7-FT38] (last visited Nov. 26, 2022) [hereinafter About IGSC]. *See also Harmonized Screening Protocol*$^{(c)}$ *v2.0: Gene Sequence & Customer Screening to Promote Biosecurity,* Int'l Gene Synthesis Consortium (Nov. 19, 2017), https://genesynthesisconsortium.org/wp-content/uploads/IGSCHarmonizedProtocol11-21-17.pdf [https://perma.cc/M2SR-BUCV].

[171]About IGSC, *supra* note 170.

[172]*Id.*

[173]*See* Berg, *supra* note 164.

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Although introducing more state regulation may only further the piecemeal nature of regulation of synthetic biology, states are in a unique position to create a system for properly screening all labs that the federal government is currently unable to reach through the NIH. Increased state regulation may act as a catalyst for more comprehensive federal regulation.[174] Additionally, states can introduce a number of regulations targeted at synthetic biology laboratories that will address pre-clinical trial and end-product concerns around mutation and pathogenicity. Several states have already introduced legislation that will acknowledge different concerns raised by synthetic biology.[175]

Barriers do exist to introducing state regulation. First, federal preemption of state laws is major concern that could put the strength, legitimacy, and consistency of state efforts at substantial risk for failure. Second, state laws may be found unconstitutional as regulating interstate commerce, thereby infringing on Congress's express right to regulate interstate commerce under the Commerce Clause.[176]

State regulation as a pathway to federal regulation

Although not the most common pathway, there have been cases in which increased state regulation acts as a catalyst for federal regulation. The most recent example of this is Congress's passage of GMO Food Labeling legislation in 2016. In 2013, Connecticut became the first state to enact a mandatory labeling law for foods containing genetically modified organisms ("GMOs").[177] The Connecticut law required that all food "produced with genetic engineering" be clearly labelled.[178] The Connecticut law stipulated that it would not go into effect until four additional states also passed mandatory labeling laws and one of those four states bordered Connecticut.[179] The goal behind the clause was to ensure Connecticut did not face a lawsuit alone.[180] In January 2014, Maine passed a substantially similar law.[181]

On May 8, 2014, Governor Peter Shumlin of Vermont signed a bill making the state the first to require labeling genetically modified organisms ("GMOs").[182] The purpose of the law was to "allow consumers…to make informed decisions about the food they" purchase.[183] Vermont's law included a penalty of up to $1,000 per day, per product for companies that failed to comply with the law.[184] The law pushed major food and beverage companies, such as Campbell Soup and General Mills, to add labels to their products.[185] Industry trade groups quickly challenged the law on constitutional grounds in federal district court, arguing that Vermont's law set "a de facto food-labeling policy for the rest of the country.[186]

[174]*See* Section 5(a).

[175]*See, e.g.,* Gene Synthesis Providers Bill, *supra* note 17; Genome-Editing Resolution, *supra* note 18.

[176]U.S. Const. art. 1, § 8, cl. 3; *Gibbons v. Ogden*, 22 U.S. 1 (1824) (finding that no area of interstate commerce is reserved for state control).

[177]Marne Coit & Kim Bousquet, *GMO Labeling: An Emerging Food Labeling Issue*, 23 Drake J. Agric L. 21, 22 (2018).

[178]Id. (citing Conn. Gen. Stat. § 21a-92c (2013), *repealed by* 7 U.S.C. § 1639b (Supp. IV 2017).

[179]Id. (citing Conn. Gen. Stat. § 21a-92c(e) (2013), *repealed by* 7 U.S.C. § 1639b (Supp. IV 2017)).

[180]Id. at 23.

[181]Id. (citing Me. Rev. Stat. Ann. tit. 22, § 2593 (2014), *repealed by* 7 U.S.C. § 1639b (Supp. IV 2017)).

[182]Jenny Hopkinson, *How Vermont Beat Big Food*, Politico (Mar. 17, 2016), https://www.politico.com/agenda/story/2016/03/vermont-gmo-labeling-law-national-standard-000067/ [https://perma.cc/37V8-Z3PX]. Vermont's law is considered the first because, unlike Maine and Connecticut, it did not have a trigger clause.

[183]Coit & Bousquet, *supra* note 176, at 23 (*citing* Vt. Stat. Ann. tit. 9, §§ 3041-3048 (2014), *repealed by* 7 U.S.C. § 1639b (Supp. IV 2017)).

[184]*Id.* at 24.

[185]*Id.* (*citing* Stephanie Strom, *G.M.O.s in Food? Vermonters Will Know*, N.Y. Times (June 2016), https://www.nytimes.com/2016/07/01/business/gmo-labels-vermont-law.html).

[186]Maria DeGiovanni, *The Future of GMO Labeling: How a New Federal Labeling Scheme Will Alter Public Discourse*, 95 Wash. U. L. Rev. 705, 712 (2017) (citing *Grocery Mfrs. Ass'n v. Sorrell*, 102 F. Supp. 3d 583 (D. Vt. 2015)); Hopkinson, *supra* note 182. Hopkinson asserts that this is exactly what occurred with a California egg production law that effectively jumpstarted the "cage-free" movement. *Id.*

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Ultimately, state regulation of synthetic biology can be used as a pathway to federal legislation. Policymakers can use concerns around piecemeal legislation to bolster their arguments in support of federal legislation. The recent GMO Food Labeling legislation can serve as a campaign model.[187] Should this be the goal, states must consider federal preemption. According to the constitution's Supremacy Clause, when state and federal law conflict in an area in which the federal government has authority, federal law always preempts state law.[188] Regarding synthetic biology, federal law would likely either expressly preempt state law or be upheld in courts as validly preempting state law.[189] Further, the biomedical field is no stranger to preemption.[190] A major risk of preemption is that federal regulation will be a "watered-down compromise" that removes many of the effective protections imposed by states.[191] States will therefore be limited in what they are able to do to regulate synthetic biology.[192] As a result, when drafting legislation, policymakers should consider preemption as a possible disruption to state-based regulation.

State legislation: defeated and passed

The U.S. has a long history of regulating drugs at the state level.[193] In the absence of federal regulation, state level legislation, regulation, and guidance may be a viable option for ensuring drugs and medical therapies produced using synthetic biology do not remain underregulated. Several states have already introduced legislation that would regulate synthetic biology or build the foundation for drafting comprehensive regulation. This movement towards legislation is very much in the early stages of development, with California proposing the first bill regulating the field in 2021.[194]

California Assembly Bill No. 70: Gene Synthesis Providers

In 2021, California introduced Assembly Bill No. 70 in response to concerns about synthetic biology being used to create a biological weapon.[195] If enacted, it would have been the first "legally binding

[187]Notably, the absence of evidence demonstrating how GMOs are harmful did not prevent federal legislation from being enacted. *See* DeGiovanni, *supra* note 186, at 716.

[188]U.S. Const. art. VI., § 2.

[189]Synthetic biology, as part of the biomedical industry, would certainly cross state lines and involve instrumentalities of interstate commerce, placing is squarely under the federal government's purview. *Gibbons v. Ogden*, 22 U.S. 1 (1824); *Champion v. Ames*, 188 U.S. 321 (1903).

[190]In 1976, Congress enacted the Medical Device Amendments to the FDCA and expressly preempted any state laws. 21 U.S.C. § 360k(a); *see also* Laura Henze Russell, *Congress Needs to Turn its Attention to Medical Device Safety*, STAT (Dec. 21, 2016), https://www.statnews.com/2016/12/21/medical-devices-safety-congress/ [https://perma.cc/2R3G-NCPW].

[191]Detractors, including Vermont Senators Pat Leahy and Bernie Sanders, denounced the Act, nicknaming it the "DARK Act" (Deny Americans the Right to Know). *DARK Act Approved in the House*, Nat'l Sustainable Agric. Coalition, NSAC's Blog (July 23, 2015), https://sustainableagriculture.net/blog/dark-act-passes-house/ [https://perma.cc/Y5NB-AFGX]. Leahy and Sanders asserted that the bill would replace existing state legislation with softer, less-effective legislation. Omri Ben-Shahar, *The GMO Labeling Fight Has Nothing to do With Information – On Either Side*, Forbes (March 21, 2016), https://www.forbes.com/sites/realspin/2016/03/21/the-gmo-labeling-fight-has-nothing-to-do-with-information-on-either-side/?sh=7213ec54691e [https://perma.cc/NC79-J89V]. Opponents wanted Congress to leave Vermont's law intact rather than enact federal legislation. *Id.*

[192]"While preemptive laws at the…federal levels can provide important protections that reach many people" preemption poses a substantial threat to state and local policymaking and public health. ChangeLab Solutions, Fundamentals of Preemption 5(2019).

[193]Edward Kremers, *Kremers & Urdang's History of Pharmacy*, 158 (4th ed. 1976). In 1736 the Colony of Virginia's legislature passed on act addressing the dispensing of more drugs than was necessary or useful. *Id.* Other early laws include the 1808 act passed in the Louisiana Territory requiring pharmacists obtain a diploma and pass an exam before being permitted to dispense drugs and further prohibitions in the Louisiana Territory on the sale of deteriorated drugs and poisons. *Id.* at 182-84, 214. South Carolina and Georgia enacted similar legislation in 1817 and 1825, respectively. *Id.* at 214, 216.

[194]Koblentz, *supra* note 17. *See also* Gene Synthesis Providers Bill, *supra* note 17.

[195]Koblentz, *supra* note 17.

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biosecurity measure for the synthetic biology industry" in the U.S..[196] The bill acknowledged that California already has laws establishing an advisory committee to advise "the Legislature and the Governor on human cloning and other issues relating to human biotechnology."[197] This bill required the California State Department of Public Health ("DPH") to "develop a process…to verify that gene synthesis providers and manufacturers of gene synthesis equipment" screen both their customers and their sequence orders."[198] DPH will develop this process with input from the IGSC and other industry stakeholders.[199] Screening protocols must be equivalent to, or stronger than, the Harmonized Screening Protocol put forward by the IGSC.[200] Further, beginning January 1, 2025, providers and manufacturers of gene synthesis equipment operating in California must be current members of the IGSC or verified by the DPH as adhering to screening protocols. Any recipient of state funding that purchases gene synthesis products or equipment must also be current members of the IGSC or verified by DPH.[201] Failure to comply may result in imposition of a penalty.[202]

Supporters of the bill argued it would make Californians safer by increasing biosecurity measures and signal to synthetic biology companies that California's already growing bioeconomy is open and ready for business.[203] Assembly member Rudy Salas asserted that the pandemic only made the need for such legislation more pressing.[204] Despite widespread, bipartisan support from legislators,[205] Governor Gavin Newsom vetoed the bill on October 5, 2021, citing the structure of the program as "not implementable."[206] The governor wrote that further "consideration should be given to whether a patchwork of state and federal regulations on biosecurity is the most effective way to approach an issue of international magnitude."[207] Consideration of the Governor's veto occurred on January 3, 2022. The Governor's veto was sustained on February 3, 2022.[208]

A.B. 70 was mostly focused on the bio-terror concerns raised by synthetic biology.[209] The bill fails to address the equally pressing risks posed by introducing synthetically produced organisms into humans for medical therapies and treatment, as in cancer therapies.[210]

Maine House Bill No. 1771: To Establish an Advisory Panel to Study the Implications of Genome-Editing Technology for the Citizens of the State

Although not specific to synthetic biology, Maine House Bill No. 1771 will directly impact the discipline in the state. The bill establishes an Advisory Panel to "study the implications of genome-editing technology" on the citizens of Maine.[211] The panel is charged with studying "the implications of genome-editing technology and the legislative, administrative or other steps that the State should take

[196]*Id.*
[197]Gene Synthesis Providers Bill, *supra* note 17.
[198]*Id.*
[199]*Id.*
[200]*Id.*
[201]*Id.*
[202]*Id.*
[203]Koblentz, *supra* note 17.
[204]Megan Molteni, *California Could Become First State to Mandate Biosecurity Screening by Mail-Order DNA Companies*, STAT+ (May 20, 2021), https://www.statnews.com/2021/05/20/california-could-become-first-state-to-mandate-biosecurity-screening-by-mail-order-dna-companies/ [https://perma.cc/9K49-7C33] (quoting Salas, "We started this pre-pandemic, but if anything, the last year has shown how dangerous a virus can be. We shouldn't be giving people building blocks to create them without guardrails for keeping people safe.").
[205]Cal. A.B. 70 Vote Analysis (October 5, 2021), https://app.fiscalnote.com/bills/11862545 [https://perma.cc/RX7G-K8PP].
[206]Governor Veto, *supra* note 17.
[207]*Id.*
[208]Cal. A.B. Bill 70 Timeline (February 3, 2022), https://app.fiscalnote.com/bills/11862545 [https://perma.cc/5SLC-XV4N].
[209]Koblentz, *supra* note 17; Kupferschmidt, *supra* note 74.
[210]*See* discussion *infra* Section I.
[211]Genome-Editing Resolution, *supra* note 18.

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to capitalize on the potential and avoid the hazards of genome-editing technology."[212] The panel must hear testimony from experts in, among other subjects, ethics, clinical medicine, public health, bioscience research, environmental protection, and the history of race, ethnicity, and eugenics.[213] The bill passed the Maine State Legislature in April 2022 and was signed by Governor Janet Mills on May 3, 2022.[214]

While Maine's bill is preparatory in nature, rather than reactive to the concerns raised by synthetic biology, it reflects a general desire to understand synthetic biology and other gene editing techniques for the purpose of potentially drafting regulation in the near future. Other states with growing biotechnology industry may follow Maine's example and implement similar statutes. Synthetic biology is a rapidly expanding field, particularly as it pertains to biomedical research. As drugs employing synthetic biology become more common, these preparatory initiatives will increase in importance and value.

Other potential sources of model legislation and regulation – regulating tissue banks as a model for state-based regulation of synthetic biology

As Governor Newsom pointed out in his veto message, national legislation would likely be the most efficient way to achieve comprehensive regulation of synthetic biology.[215] But the absence of national legislation does not mean that states should ignore the pressing concerns synthetic biology presents to the U.S. and the world. State-based regulation of tissue banks offers a model which states can use when considering how to design regulation of biomedical products and therapies using synthetic biology.

A number of similarities between the human tissue industry and synthetic biology exist. Both are billion-dollar industries with significant upward potential.[216] Both face criticism related to ethics.[217] In response to concerns regulating the human tissue industry, California, Maryland, New York, and Florida have all implemented laws and oversight programs to "inspect and license tissue banks in and out of their states."[218] In New York, all tissue banks must submit to state inspections and obtain a license to operate.[219] All tissue banks in the state must be in compliance with FDA regulations.[220] Further, banks must report any adverse events or outcomes to the state, effectively establishing a kind of tracking system.[221]

Florida takes its law a step further than New York, requiring that all tissue banks (1) "collect, keep, and make available to the Governor and the Legislature information regarding the numbers and disposition of organs, tissues, and eyes procured by each certified procurement organization and (2) monitor procurement organizations for program compliance.[222] Further, all tissue banks must adopt rules and protocols in accordance with Florida law as well as federal law and "existing standards and guidelines" of

[212] *Id.*

[213] *Id.*

[214] *Summary of LD 1771*, Me. State. Leg. https://legislature.maine.gov/LawMakerWeb/summary.asp?ID=280081979 [https://perma.cc/A49Z-YYU8] (last visited October 25, 2022). An identical bill failed to pass in 2021.

[215] Governor Veto, *supra* note 17.

[216] Laura A. Buck, *Regulating Human Tissue Banks*, 20 St. Thomas L. Rev. 121, 122 (2007). By the end of 2003, the tissue transplantation industry was expected to reach one billion dollars. *Id.* In 2020, the global market for synthetic biology was estimated to be at $6.4 billion. ResearchAndMarkets.com, *Global Synthetic Biology Market Trajectory & Analytics Report 2021*, Businesswire (Jan. 18, 2022, 10:21 AM), https://www.businesswire.com/news/home/20220118005899/en/Global-Synthetic-Biology-Market-Trajectory-Analytics-Report-2021---ResearchAndMarkets.com#:~:text=Amid%20the%20COVID-19%20crisis%2C%20the%20global%20market%20for,a%20CAGR%20of%2028.1%25%20over%20the%20analysis%20period.

[217] *Compare* Buck, *supra* note 216, at 122 (discussing concerns about commodifying the human body), *with* Parent, *supra* note 23, at 324 (discussing concerns that synthetic biology is "playing God.").

[218] Buck, *supra* note 216,at 134.

[219] N.Y. Pub. Health § 4364 (2001).

[220] N.Y. Comp. Codes R. & Regs. tit. 10, § 52-3.1 (2000).

[221] N.Y. Pub. Health § 4364-66 (2003).

[222] Fla. Stat. § 765.541 (2006).

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specific professional groups, such as the American Association of Tissue Banks and the North American Transplant Coordinators Organization.[223]

Both the New York and Florida tissue bank statutes are comparable to California's synthetic biology bill. All three require compliance with federal laws and/or the standard set out by professional organizations in the field.[224] All three also require some sort of tracking or monitoring system to ensure that consumers and the wider public do not come to harm.[225] Given the similarities, states may look to regulation of tissue banks as a model when designing regulation for therapies using synthetic biology.

Recommendations for comprehensive state-based legislation regulating synthetic biology

States are a crucial part of the national health care system.[226] In the absence of federal legislation, states should step into the synthetic biology space and regulate it for the safety of all. States should first consider legislation substantially similar to the legislation proposed in Maine. Specifically, the legislation should require the state to form a task force responsible for monitoring the effects of medical treatments and therapies utilizing synthetically created DNA. The task force should consist of medical professionals, bioscience and synthetic biology researchers, lawmakers, members of the state's health and/or public health departments, industry stakeholders, including persons with expertise in biomedical ethics, and potential consumers of the treatment or therapy.[227] The task force may also include input from the IGSC.[228] The task force should "study the implications of" synthetic biology and genome-editing technology.[229] Within one year of formation, the task force should be required to issue a report detailing state-specific hazards of synthetic biology technology and making specific recommendations regarding security measures.[230]

When drafting additional legislation, lawmakers should consider including the following provisions:

- Definitions for "synthetic biology," "gene synthesis," "genome editing," "the biomedical risks associated with synthetic biology," "biosecurity," and all relevant terms.
- Require all businesses selling technology for synthesizing DNA codes or products created using synthetic biology techniques to implement comprehensive biosecurity systems. These systems must include regular risk assessments and internal monitoring systems for all research and manufacturing processes.[231] Regulations should require that the business monitor all orders and ensure that no one orders DNA sequences that can be manipulated or used for a pathogenic function.[232]
- Require all businesses in the synthetic biology industry, including researchers, manufacturers, and distributors, to become members of an international synthetic biology consortium, such as the IGSC.[233]

[223]*Id.*

[224]*Id.*; Gene Synthesis Providers Bill, *supra* note 17; N.Y. § 4364.

[225]Fla. Stat. §765.541; N.Y. § 4364.

[226]Isaac D. Buck, *The Drug (Pricing) Wars: States, Preemption, and Unsustainable Prices*, 99 N.C.L. Rev. 167, 172 (2020).

[227]*Id.*; Genome-Editing Resolution, *supra* note 18.

[228]Gene Synthesis Providers Bill, *supra* note 17.

[229]Genome-Editing Resolution, *supra* note 18.

[230]*See id.*

[231]Xiaomei Zeng et al. *Regulation and Management of Biosecurity for Synthetic Biology*, 7 Synthetic & Sys. Biotech. 784, 788 (2022).

[232]Jason Kelly, *Our Work on Biosecurity*, Ginkgo Bioworks (June 26, 2018), https://www.ginkgobioworks.com/2018/06/26/our-work-on-biosecurity/ [https://perma.cc/A8AN-WVH5].

[233]Gene Synthesis Providers Bill, *supra* note 17. IGSC screens all orders to regulate pathogen and other potentially dangerous sequences and vets customers. About IGSC, *supra* note 170. Requiring membership and review through a third-party, expert organization will help business actors keep costs down while ensuring comprehensive review.

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- Implementation of a statewide database documenting use of medical therapies that employ synthetic biology.[234] This database should also include documentation of all adverse events or unplanned reactions to and changes in treatments employing synthetic biology. These events may include all unplanned mutations or all adverse reactions to the treatment or therapy.
- Creation of a statewide, public facing platform and database that provides the general public with information, including all relevant risks, regarding medical treatments and therapies utilizing synthetic biology and data. Alternatively, legislation could require researchers to submit their data to an external public database.[235] Public health information supports shared decision-making and improved health care quality and patient outcomes.[236]
- Require regulatory bodies to regularly evaluate and incorporate scientific guidance into administrative regulations and guidance. This may involve establishing a body responsible for issuing regular guidance opinions on the subject.[237]

In addition to enacting their own legislation, states may wish to consider forming regional consortiums or other similar agreements with strategic partnerships to increase the impact of their regulations. States have many options when drafting, enacting, and enforcing synthetic biology legislation, regulation, and guidance. In the absence of federal regulation, states should pursue enacting legislation, regulations, and guidance that include, if not the majority, all of the above recommendations.

Conclusion

Synthetic biology is a rapidly growing scientific field with a seemingly infinite number of applications. Rooted in the foundational principles of genetics, the field has opened a number of doors to new and promising medical treatments and therapies, such as cancer treatments and vaccines. But organisms altered by synthetic biology techniques pose risks: dangerous mutations, uncontrollable proliferation, and disruption of or interference with the natural environment. Current laws, regulations, and guidance do not address the field directly and synthetic biology is regulated by various agencies and governing bodies that do not overlap. States have an opportunity to step into this space and develop rules researchers, producers, manufacturers, distributors, and all other actors must follow. California and Maine have already taken steps to do so by introducing bills specifically targeting gene-synthesis and genome-editing technology. When developing comprehensive legislation, states should first do due diligence by assessing their individual, synthetic biology landscape and how it impacts its' citizens. States should ensure legislation and regulation considers all stakeholder concerns, particularly those related to scientific, biomedical, environmental, and public health. States must ensure that regulations are updated regularly to keep pace with the rapidly advancing industry. Ultimately, states should step into the synthetic biology space to ensure that their citizens are not harmed by products created using synthetic biology.

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[234] *See* Fla. Stat. § 765.541.

[235] Hanzhi Yu et al., *Toward Inclusive Global Governance of Human Genome Editing*, PNAS, Nov. 17, 2021, at 1, 4.

[236] *Why Health Information Technology is Important*, Nat'l Am. Univ., https://www.national.edu/2021/03/10/why-health-information-technology-is-important/ [https://perma.cc/2HSG-YPED] (last accessed Nov. 22, 2022).

[237] About IGSC, *supra* note 170.

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