

**REPRODUCTION-POWERED INDUSTRY: COORDINATING AGENCY  
REGULATIONS FOR SYNTHETIC BIOLOGY**

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*The products of synthetic biology may improve medicine, national security, environmental protection, and the economy, but under-regulated development could catastrophically compromise these endeavors. Considering the dangers exhibited by existing microorganisms and public access to tools of synthetic biology construction, the field's untested novelty implicates human health and safety. Further, social justice concerns are raised by the resources required to sustain a shift from a fossil fuel-based economy to a biofuel-based economy. Current regulations are insufficient to address these risks. Accordingly, regulations must be modified through amendments coordinated between the National Institutes of Health, the Environmental Protection Agency, and the Food and Drug Administration. Interagency regulation provides the strongest prospect for supporting beneficial developments while protecting against hazards unique to the field. This Article provides a brief history of synthetic biology and examines its public and private development. This Article also examines its potential benefits and risks and current applicable regulations, both national and international. It concludes with propositions for regulatory modification, and attention is given to domestic interagency regulation.*

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**TABLE OF CONTENTS**

I.	<b>INTRODUCTION</b> .....	309
II.	<b>DEFINITION AND BRIEF HISTORY</b> .....	310
III.	<b>PUBLIC VS. PRIVATE MODELS OF DEVELOPMENT</b> ...	315
	A. <i>Public Development</i> .....	316
	B. <i>Private Development</i> .....	318
IV.	<b>POTENTIAL HARMS</b> .....	321
	A. <i>Intentional Malicious Dangers</i> .....	322
	B. <i>Unintentional Dangers</i> .....	324
	1. <i>Symbolic Concern</i> .....	324
	2. <i>Threats to Social Justice</i> .....	326
	3. <i>Physical Dangers</i> .....	330
V.	<b>ARGUMENTS DISMISSING THE DANGERS OF SYNTHETIC BIOLOGY</b> .....	333
VI.	<b>CURRENT REGULATIONS</b> .....	338
	A. <i>The Presidential Commission's Report</i> .....	339
	B. <i>International Regulation</i> .....	342
	C. <i>U.S. Agency Regulations</i> .....	346
VII.	<b>SUGGESTIONS FOR MODIFICATION</b> .....	352
	A. <i>NIH Modification</i> .....	353
	B. <i>EPA and TSCA Modification</i> .....	353
	C. <i>FDA and FDCA Modification</i> .....	355
VIII.	<b>CONCLUSION</b> .....	356

## I. INTRODUCTION

A new phase of production innovation is touting potential for cheap and effective fuel, medicine, and virtually any other essential product or device. The machines of this production are literally more intelligent—they are living. Synthetic biology involves programming and building bacteria and viruses to produce diesel gas or synthetic fibers, or perform as poison sensors or pollution eaters. The excitement stems from both the seemingly limitless possibilities of exploiting genetic code and from the potential for self-renewing production through cellular reproduction. But, there is a complication with using cells as machines. While the best production machines reliably generate identical results with little maintenance, microorganisms constantly change their forms and functions without warning. Microorganisms adapt on their own terms, and the best scientists have little clue how to control this.

Science and industry are at a pivotal juncture where promises of clean, efficient, and sustainable bio-energy could overshadow the dangers in manipulating cellular machinery for environmental and human application. Those responsible for the research, development, and packaging of synthetic biology disregard the breadth and severity of these dangers.<sup>1</sup> Health and social justice concerns need to be publicized and addressed by authoritative powers. Financial constraints and pre-established regulatory roles

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<sup>1</sup> Instead of taking measured steps to examine risks, synthetic biology's primary proponents are using resources and actualizing products in ways that increase the risk of unjust land use and public exposure to dangerous agents. See Denise Caruso, *Synthetic Biology: An Overview and Recommendations for Anticipating and Addressing Emerging Risks*, SCI. PROGRESS 5, 5–6 (2008); *Synthetic Solutions to the Climate Crisis: The Dangers of Synthetic Biology for Biofuels Production*, FRIENDS OF THE EARTH, 37 (Sept. 2010), available at [http://libcloud.s3.amazonaws.com/93/59/9/529/1/SynBio-Biofuels\\_Report\\_Web.pdf](http://libcloud.s3.amazonaws.com/93/59/9/529/1/SynBio-Biofuels_Report_Web.pdf). Craig Venter, a leading pioneer of synthetic biology called development of synthetic biology “wise, warranted and restrained, which will help to ensure that this young field of research will flourish in a positive manner.” See Andrew Pollack, *U.S. Bioethics Commission Gives Green Light to Synthetic Biology*, N.Y. TIMES (Dec. 16, 2010), <http://www.nytimes.com/2010/12/16/science/16synthetic.html>.

for governing genetically engineered organisms prevent the development of a new domestic supervisory entity from being a realistic consideration. Instead, existing regulations of biotechnology need to be modified and supplemented through amended regulations coordinated between the National Institutes of Health (“NIH”), the Environmental Protection Agency (“EPA”), and the Food and Drug Administration (“FDA”) to support beneficial developments and protect against safety and social justice hazards unique to synthetic biology. This Article proceeds accordingly: Part II will provide a brief history of synthetic biology. Part III will examine its public and private development. Part IV examines its potential risks. Part V characterizes arguments that dismiss the risks of synthetic biology and provides counter arguments. Part VI discusses current national and international regulations. Part VII proposes domestic interagency regulation to promote the field’s benefits and protect against its dangers. Finally, Part VIII concludes by discussing the reasons that make interagency regulation the best option.

## II. DEFINITION AND BRIEF HISTORY

Understanding the principles of synthetic biology and its commercial underpinnings is essential to the justification of a new regulatory framework. Synthetic biology is “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.”<sup>2</sup> Scientists in this burgeoning field intend to “create a programmable microorganism from scratch,”<sup>3</sup> and some claim “the horizon is ‘the industrialisation of biology.’”<sup>4</sup> These aspirations are made possible by recombinant

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<sup>2</sup> See JIM THOMAS, *EXTREME GENETIC ENGINEERING: AN INTRODUCTION TO SYNTHETIC BIOLOGY 1* (2007), available at <http://www.etcgroup.org/sites/www.etcgroup.org/files/publication/602/01/synbioreportweb.pdf>.

<sup>3</sup> Arjun Bhutkar, *Synthetic Biology: Navigating the Challenges Ahead*, 8 J. BIOLAW & BUS. 2, 20 (2005).

<sup>4</sup> Dorothee Browaeys, *The Industrialisation of Biology*, LE MONDE DIPLOMATIQUE—ENGLISH EDITION (Oct. 2010), available at <http://mondediplo.com>.

DNA technology, or “gene splicing,” which over the past thirty-five years has influenced health outcomes,<sup>5</sup> the design of cosmetics,<sup>6</sup> agricultural practices,<sup>7</sup> and the potential for biowarfare.<sup>8</sup> The identification of genes that encode for practical functions like production of bioluminescence, pesticide, and insulin led to the development of tools that can isolate, cut, transfer, and insert these genes from one organism to another.<sup>9</sup> Genetic technology has greatly improved over time; for example, scientists no longer have to extract desirable genetic sequences from organisms, but can

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com/2010/10/11biology (quoting Richard Kitney, head of the department of biological and medical systems at Imperial College London).

<sup>5</sup> See Paul Berg, Herbert W. Boyer, and Stanley N. Cohen, CHEM. HERITAGE FOUND. (2010), <http://www.chemheritage.org/discover/online-resources/chemistry-in-history/themes/pharmaceuticals/preserving-health-with-biotechnology/berg-boyer-cohen.aspx>.

<sup>6</sup> See Robert Fedič et al., *The Silk of Lepidoptera*, 71 J. INSECT BIOTECH. & SERICOLOGY 1, 3 (2002) (explaining that silk worms have been genetically engineered to produce better silk-based additives for cosmetics).

<sup>7</sup> Keith R. Schneider & Renee Goodrich Schneider, *Genetically Modified Food*, INST. OF FOOD AND AGRIC. SCI., UNIV. OF FLA. (2002), <http://edis.ifas.ufl.edu/fs084>. All genetically modified foods are the product of gene splicing. *Id.*

<sup>8</sup> See generally Lawrence F. Roberge, *Black Biology—A Threat to Biosecurity and Defense*, 2 BIOSAFETY 1 (2013), available at <http://www.omicsgroup.org/journals/black-biologya-threat-to-biosecurity-and-biodefense-2167-0331.1000e139.pdf> (explaining that “Black biology is the use of genetic engineering to enhance the virulence of a pathogen,” an increasingly easy method for terrorist groups and lone individuals to use as weapons).

<sup>9</sup> Memorable pieces of this history include: 1) Rats that glow in the dark, see Matthew Herper, *Biotech’s Glowing Breakthrough*, FORBES (July 26, 2001), <http://www.forbes.com/2001/07/26/0726gfp.html>; 2) Bt delta endotoxin-resistant corn (“Bt corn”), see Richard Hellmich et al., *Use and Impact of Bt Maize*, 10 NATURE EDUC. KNOWLEDGE 4, 4 (2012), available at <http://www.nature.com/scitable/knowledge/library/use-and-impact-of-bt-maize-46975413>; and 3) laboratory-manipulated bacteria that provide an essential hormone for diabetics, see Suzanne Junod, *Celebrating a Mileston: FDA’s Approval of First Genetically Engineered Product*, FDA (Apr. 2009), available at <http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SelectionsFromFDLIUpdateSeriesonFDAHistory/ucm081964.htm>.

synthesize them in a lab.<sup>10</sup> By 2005, leading researchers had assembled whole genomes of the poliovirus and the 1918 Spanish influenza virus entirely from lab-synthesized nucleic acid sequences.<sup>11</sup> Only three years later, Craig Venter<sup>12</sup> of the J. Craig Venter Institute (“JCVI”) advanced from viruses to bacteria by assembling the first 600,000 base-pair length genome of *M. Genitalium*.<sup>13</sup> In 2010, after many years of unsuccessful trials, JCVI took their lab-assembled *M. Mycoides* genome, inserted it into an emptied *M. Capricolum* cell, and created the first self-replicating cell completely controlled by synthetic genes.<sup>14</sup>

JCVI’s achievement was not recognized for producing a unique or useful bacterium, but it provides a valuable forecast for future endeavors. Without carefully examining the DNA, their lab-created bacteria would appear virtually identical to naturally occurring *M. Mycoides*. The only genetic differences were excised pathogenic genes and a few inserted “genetic watermarks”

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<sup>10</sup> See generally Alan Villalobos et al., *Gene Designer—A Synthetic Biology Tool for Constructing Artificial DNA Segments*, 7 *BIOINFORMATICS* 285 (June 2006).

<sup>11</sup> See Gabrielle Samuel et al., *Back to the Future: Controlling Synthetic Life Sciences Trade in DNA Sequences*, 66 *BULLETIN OF THE ATOMIC SCIENTISTS* 5, 10 (2010).

<sup>12</sup> Venter is one of the most celebrated scientists in contemporary genomic research. He has founded several companies for the research of genomics and the development of genomic technologies. He is known for pushing scientific boundaries that raise serious ethical issues about human and environmental safety and about the proper role of humans in the creation and manipulation of life. See *Biographies: J. Craig Venter*, J. CRAIG VENTER INST., [http://www.jcvi.org/cms/about/bios/jcventer/?em\\_x=22](http://www.jcvi.org/cms/about/bios/jcventer/?em_x=22) (last visited Oct. 3, 2013); Susan Okie, *Is Craig Venter Going to Save the Planet? Or is This More Hype from One of America’s Most Controversial Scientists?*, WASH. POST (Aug. 11, 2011), [http://articles.washingtonpost.com/2011-08-11/lifestyle/35269880\\_1\\_synthetic-genomics-algae-craig-venter](http://articles.washingtonpost.com/2011-08-11/lifestyle/35269880_1_synthetic-genomics-algae-craig-venter).

<sup>13</sup> See MICHAEL RODEMEYER, *NEW LIFE, OLD BOTTLES: REGULATING FIRST GENERATION PRODUCTS OF SYNTHETIC BIOLOGY* 17 (Woodrow Wilson Int’l Ctr. for Scholars 2009).

<sup>14</sup> See Press Release, J. Craig Venter Institute, *First Synthetic Self-Replicating Bacterial Cell* (May 20, 2010), available at <http://www.jcvi.org/cms/press/press-releases/full-text/article/first-self-replicating-synthetic-bacterial-cell-constructed-by-j-craig-venter-institute-researcher/>.

representing Venter's and his Colleagues' names and James Joyce quotes.<sup>15</sup> Although genetic engineering endeavors had produced viable organisms with excised genes for several years,<sup>16</sup> this was different. The excitement over JCVI-syn1.0, as Venter describes in press conferences, is that "[its] parent is a computer."<sup>17</sup> The ability to create a living cell without harvesting naturally occurring genes substantially widens design prospects.<sup>18</sup> To understand the implications of this feat, it must be considered in context of other contemporary genetic engineering endeavors.

There are several companies across the globe that are redesigning bacteria for specific purposes,<sup>19</sup> but the point at which the science behind their practices moves from conventional genetic engineering to synthetic biology is not clear. These companies are modifying bacteria using laboratory-synthesized genes to produce desired functionality, which is certainly the basis for the new field. However, it is uncertain how much synthetic DNA is required to deem the organism synthetic. One company heading down the synthetic path is Amyris, which has engineered yeast to produce Artemisinin, a chemical used in the treatment of Malaria

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<sup>15</sup> See Robert Lee Hotz, *Scientists Create Synthetic Organism*, WALL ST. J. (May 21, 2010), <http://online.wsj.com/article/SB10001424052748703559004575256470152341984.html>.

<sup>16</sup> Knockout mice are an example of organisms with excised genes; these animals simplify studying causes and effects of specific genes. See *Knockout Mice*, NAT'L HUMAN GENOME RESEARCH INST., <http://www.genome.gov/12514551> (last visited Oct. 3, 2013).

<sup>17</sup> See Nicholas Wade, *Researchers Say They Created a 'Synthetic Cell'*, N.Y. TIMES (May 20, 2010), <http://www.nytimes.com/2010/05/21/science/21cell.html>.

<sup>18</sup> Using existing genes limits the designer to the functions for which the genes encode; designing original genes ostensibly allows the designer to encode for previously unknown functions or immensely improved functions. See *Hidden Genetic Code for Better Designer Genes*, SCIENCE DAILY (Sept. 26, 2013), <http://www.sciencedaily.com/releases/2013/09/130926143236.htm>.

<sup>19</sup> See *Number of Synthetic Biology Firms Tripled Over Last Four Years*, GENOME WEB (May, 2, 2013), <http://www.genomeweb.com/number-synthetic-biology-firms-tripled-over-last-four-years>.

previously only found in Sweet Wormwood.<sup>20</sup> Another company approaching synthetic biology is Joule Unlimited, which has modified cyanobacteria to convert sunlight and carbon dioxide into alkane, a component of diesel fuel.<sup>21</sup> Many researchers and companies support the endeavor, proclaiming they are “not trying to imitate nature,” but rather they are “trying to supplement nature.”<sup>22</sup> Furthermore, they claim they are “building the modern chemical factories of the future.”<sup>23</sup> In light of these sentiments, the objectives of genetic engineers become clear: in harnessing the power of genetics, scientists intend to create wholly original organisms to supplement, enhance, and ultimately replace current commercial production methods. Venter’s cell sets the precedent for scientific confidence in ground-up design of these biological factories, which scientists intend to customize and control with precision. For some, the goals go even further: Drew Endy of Stanford speculates that within twenty years, human genomes will be synthesized completely from scratch.<sup>24</sup>

Emerging examples of synthesized genomes and engineered organisms, fantasies of biology-based economies, contractual partnerships relying on these fantasies, and public access to genetic information and tools should all be considered in the context of preserving health, relationships, and environmental integrity. The ways in which synthetic biology presents unique threats to these

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<sup>20</sup> See ERIK PARENS ET AL., ETHICAL ISSUES IN SYNTHETIC BIOLOGY: AN OVERVIEW OF THE DEBATES 1, 14 (Woodrow Wilson Int’l Ctr. for Scholars 2009).

<sup>21</sup> See Matthew L. Wald, *Biotech Company to Patent Fuel Secreting Bacteria*, N.Y. TIMES (Sept. 13, 2010), <http://www.nytimes.com/2010/09/14/science/earth/14fuel.html>.

<sup>22</sup> See Andrew Pollack, *Scientists Are Starting to Add Letters to Life’s Alphabet*, N.Y. TIMES (July 24, 2001), <http://www.nytimes.com/2001/07/24/science/scientists-are-starting-to-add-letters-to-life-s-alphabet.html?pagewanted=all&src=pm> (quoting Floyd E. Romesburg of the Scripps Research Institute).

<sup>23</sup> Robert Sanders, *Keasling and Cal: A Perfect Fit*, U.C. BERKELEY NEWS (Dec. 13, 2004), [http://www.berkeley.edu/news/media/releases/2004/12/13\\_keasling.shtml](http://www.berkeley.edu/news/media/releases/2004/12/13_keasling.shtml) (quoting Jay Keasling of the U.C. Berkeley’s California Institute for Quantitative Biomedical Research, and of Amyris Biotechnologies).

<sup>24</sup> See THOMAS, *supra* note 2, at 10.



assets should guide implementation of new domestic and international biotechnology regulations.

### III. PUBLIC VS. PRIVATE MODELS OF DEVELOPMENT

Researchers at discrete edges of synthetic biology are designing competing models for development—public and private—that bear different risks that need to be addressed by regulation. This section addresses these models and their risks. This Article will refer to the “Open Source” model, which is propounded by Drew Endy and Tom Knight through the Biobrick Registry<sup>25</sup> and International Genetically Engineered Machine (“iGEM”) competition.<sup>26</sup> Under this framework, unrestricted access to tools, materials, and information could have the potential to promote creation and sharing among established scientists as well as do-it-yourselfers. This is juxtaposed to start-ups that are hoarding patents in private partnerships with major corporations.<sup>27</sup> Assisted by their contracted researchers, these start-up companies likely intend to be the proprietors of synthetic biology-based fuels, rubber, cosmetics, and vaccines. In the future, case law and agency-issued guidelines and regulations must reconcile these divergent paths by determining what aspects of synthetic biology should be encouraged in public development and which may be safely left to market forces. Currently, there is insufficient oversight of both public and private sectors.

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<sup>25</sup> See *Our Philosophy*, REGISTRY OF STANDARD BIOLOGICAL PARTS, <http://parts.igem.org/Help:Philosophy> (last visited Oct. 3, 2013).

<sup>26</sup> The iGEM competition grew out of a month-long summer bacterial design course at MIT and has become Endy and Knight’s annual undergraduate competition. See *Synthetic Biology Based on Standard Arts*, iGEM, <http://igem.org/About> (last visited Oct. 3, 2013) [hereinafter iGEM].

<sup>27</sup> Corporate examples include Exxon, BP, and Dupont. See Alok Jha, *Gene Scientist to Create Algae Biofuel with Exxon Mobil*, GUARDIAN U.K. (July 14, 2009), <http://www.guardian.co.uk/environment/2009/jul/14/green-algae-exxon-mobil>; Robert Sanders, *BP selects U.C. Berkeley to lead \$500 Million Energy Research Consortium with Partners Lawrence Berkeley National Lab, University of Illinois*, U.C. BERKELEY NEWS (Feb. 1, 2007); THOMAS, *supra* note 2, at 20.

### A. *Public Development*

The Open Source movement is the core of public development; it places disconcerting power in the hands of amateurs. Biobricks and the iGEM competition are pillars of Open Source development.<sup>28</sup> Now entering its eighth year, 223 teams will be competing in iGEM using “biobricks”<sup>29</sup> to design unique bacteria to be compared in several categories. Previous winning entries included toxin-sensing cyanobacteria and “light-emitting cells” that acted as a bio-screen emulating movement.<sup>30</sup> The database from which the genetic components are drawn is the Biobrick registry, another contemporarily developed Endy/Knight endeavor.<sup>31</sup> The registry was designed as a public access central repository for information regarding “standardized genetic materials and associated functional information.”<sup>32</sup> This system has been compared to the Linux software model where collective efforts of thousands of developers contribute to an ever-improving platform encouraging broad design participation.<sup>33</sup> DNA strand-synthesis technology is becoming ubiquitous in reasonably well-equipped genetic research laboratories, but for those without such equipment, companies like Integrated DNA Technologies make custom strands to order.<sup>34</sup> The production price of DNA has

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<sup>28</sup> See Alla Katsnelson, *Open Source Synthetic Biology*, THE SCIENTIST (Nov. 3, 2007), <http://www.the-scientist.com/?articles.view/articleNo/25646/title/Open-source-synthetic-biology/>.

<sup>29</sup> Biobricks are “a standard for interchangeable parts, developed with a view to building biological systems in living cells . . . [they] can be assembled to form useful devices, through a process often referred to as ‘Standard Assembly.’ BioBrick™ parts are composable; allowing endless numbers of Biobrick™ parts to be pieced together to form complex systems.” See *Help: An Introduction to Biobricks*, REGISTRY OF STANDARD BIOLOGICAL PARTS, [http://parts.igem.org/Help:An\\_Introduction\\_to\\_BioBricks](http://parts.igem.org/Help:An_Introduction_to_BioBricks) (last visited Oct. 3, 2013).

<sup>30</sup> See Andrew Torrance, *Synthesizing Law for Synthetic Biology*, 11 MINN. J. L. SCI. & TECH. 629, 630–31 (2010).

<sup>31</sup> See iGEM, *supra* note 26.

<sup>32</sup> See *The BioBrick™ User Agreement Version 1.0*, BIOBRICKS FOUND., <https://biobricks.org/bpa/users/agreement/> (last visited Oct. 14, 2013).

<sup>33</sup> See THOMAS, *supra* note 2, at 34.

<sup>34</sup> See *gBlocks Gene Fragments*, INTEGRATED DNA TECH. <http://www.idtdna.com/pages/products/genes> (last visited Oct. 3, 2013).

dropped substantially, from thirty dollars per base pair to one dollar per base pair in the last ten years.<sup>35</sup> As a result, the public database of gene functions and access to DNA synthesis give researchers at any level the ability to swiftly test gene combinations in the modification of organisms.

Synthetic biology activity in the nonprofessional realm is substantial. “Biopunk” is a culture of do-it-yourselfers, or “biohackers,” with significant web presence.<sup>36</sup> Usability of the biobrick registry is increased by other free web-based information, such as the *Synthetic Biology Primer*, written by Scott Mohr, a chemist at Boston University specializing in Nucleic Acid interactions.<sup>37</sup> Web forums for sharing information about biohacks include biopunk.org, biohack.sf.net, and openwetware.org, where tinkerers can share links to contemporary news, ask and answer questions about gene splicing, and share their genetic hacks for simple light-up bacteria and even health treatments. For example, on biopunk.org a teenager agitated by a friend’s complaints about having celiac disease provided a series of links. The contributor, who spent twenty minutes doing this research, claimed to be providing the means to design gastrointestinal bacteria that will “cure” the friend’s condition. In the writer’s words, “Problem Freakin’ Solved.”<sup>38</sup>

An institutionally-approved version of biohacking is the iGEM competition, which demonstrates the intersection between public

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<sup>35</sup> RODEMEYER, *supra* note 13, at 16.

<sup>36</sup> See *Biopunk*, BIOPUNK, <http://www.biopunk.org/> (last visited Oct. 3, 2013); *Biopunks Tinker with the Building Blocks of Life*, NAT’L PUB. RADIO (May 19, 2011), <http://www.npr.org/2011/05/22/136464041/biopunks-tinker-with-the-building-blocks-of-life>.

<sup>37</sup> Scott Mohr, *Primer for Synthetic Biology*, OPENWETWARE (July 18, 2007), available at [http://openwetware.org/images/3/3d/SB\\_Primer\\_100707.pdf](http://openwetware.org/images/3/3d/SB_Primer_100707.pdf); Scott Mohr, BOS. UNIV., <http://www.bu.edu/chemistry/faculty/mohr/> (last visited Nov. 3, 2013).

<sup>38</sup> Andrew Maynard, *Synthetic Biology, Ethics and the Hacker Culture*, 2020 SCIENCE (June 13, 2008), <http://2020science.org/2008/06/13/8613-synthetic-biology-ethics-and-the-hacker-culture/> (citing Kanzure, *On the State of BioDIY/Biopunk Culture*, BIOPUNK (Mar. 19, 2008), <http://www.biopunk.org/on-the-state-of-biodiy-biopunk-culture-t36.html>).

and private development. The rapid growth of the contest, from twelve teams in 2004 to over 200 internationally in 2013, is a testament to the growth of synthetic biology's Open Source development.<sup>39</sup> Even though many of the competition projects appear to be novelties testing the limits of biological manipulation, venture capitalists and companies are expressing great interest in the student creations that demonstrate more practical applications.<sup>40</sup> This appears to be the manifestation of Endy's intentions—to build simplicity and accessibility into the field of synthetic biology and ultimately encourage participation at all levels.<sup>41</sup> However, Endy's stated goals are difficult to reconcile with the fact that he was once co-founder of a now-defunct all-service synthetic biology company, Codon Devices. Codon Devices once held an extensive patent portfolio and advertised that the company's policy is to “aggressively pursue patent protection for most of our proprietary technology, and protect other aspects of our proprietary technology as trade secrets.”<sup>42</sup>

#### B. *Private Development*

Several companies and universities have been granted proprietary genetic ownership and are capitalizing on businesses' hunger for profit innovation while ignoring safety and equality concerns.<sup>43</sup> Researchers, on behalf of their companies and universities, hold patents on bacterial genes, including representatives of University of California, Harvard University, Temple University, Egea Biosciences, and Genencor.<sup>44</sup> Several labs are using their exclusive technology rights as leverage to barter for development deals with industry leaders. For example,

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<sup>39</sup> See *Projected Growth in iGEM Through 2015*, iGEM, [http://2011.igem.org/Regions/iGEM\\_Growth](http://2011.igem.org/Regions/iGEM_Growth) (last visited Oct 3, 2013).

<sup>40</sup> See THOMAS, *supra* note 2, at 17.

<sup>41</sup> See *id.* at 34.

<sup>42</sup> Sapna Kumar & Arti Rai, *Synthetic Biology: The Intellectual Property Puzzle*, 85 TEX. L. REV. 1745, 1761 (2007) (quoting *Intellectual Property*, CODON DEVICES, <http://codondevices.com/science.aspx?id=118>).

<sup>43</sup> See THOMAS, *supra* note 2, at 35.

<sup>44</sup> See *id.*

Exxon has invested \$600 million with Craig Venter's Synthetic Genomics, and BP has invested \$500 million in Lawrence Berkeley Labs to develop biofuels.<sup>45</sup> Solazyme has signed a deal with Unilever to replace palm oil with an algal-based oil and another deal with the United States Navy to deliver 150,000 gallons of algal-based biofuel to supplement the military branch's primarily used fuel.<sup>46</sup> Genencor is working under chemical manufacturer Dupont and is engineering *E. coli* to produce key components of a "spandex-like fib[er]."<sup>47</sup> Synthetic Genomics Vaccines, Inc.<sup>48</sup> recently announced a three-year collaboration with Novartis to develop influenza seed strains for vaccine manufacturing.<sup>49</sup>

The budding technology's proven applications must cover vast ground to catch up with the hype. For several years now, the U.S. Department of Energy, the U.S. Department of Defense, and others have sunk hundreds of millions of public and private dollars into research, but not a single commercial project has come to fruition.<sup>50</sup> Several companies have gone bankrupt because they were unable to keep up the rouse of viable production being "just around the corner" during the investment skepticism of the recent

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<sup>45</sup> Jha, *supra* note 27; Sanders, *supra* note 27.

<sup>46</sup> *Join The Navy and Free the World: A Special Report on Military Biofuels*, BIOFUELS DIGEST (Sept. 15, 2010), <http://biofuelsdigest.com/bdigest/2010/09/15/join-the-navy-and-free-the-world-a-special-report-on-military-biofuels/>; Paul Sonne, *To Wash Hands of Palm Oil Unilever Embraces Algae*, WALL ST. J. (Sept. 15, 2010), <http://online.wsj.com/article/SB100011424052748703720004575477531661393258.html>.

<sup>47</sup> THOMAS, *supra* note 2, at 20.

<sup>48</sup> Synthetic Genomics Vaccines, Inc. is one of Craig Venter's enterprises. *About Us*, SYNTHETIC GENOMICS, <http://www.syntheticgenomics.com/about/> (last visited Oct. 11, 2013).

<sup>49</sup> Press Release, Synthetic Genomics, Inc., SGVI Announces Collaboration With Novartis on the Development of Influenza Vaccines Using Synthetic Genomics Technologies (Oct. 7, 2010), *available at* <http://www.syntheticgenomics.com/media/press/100710.html>.

<sup>50</sup> See generally Paul Voosen, *Synthetic Biology Comes Down to Earth*, CHRON. REV. (Mar. 4, 2013), <http://chronicle.com/article/Synthetic-Biology-Comes-Down/137587/> (explaining that \$1.84 billion has been invested in synthetic biology, but no significant breakthroughs have been made).

market crash.<sup>51</sup> In short, the field is young and bio-based commercial production is possible, but it is likely that expectations are too high for such a poorly understood science.

Regulation is also weak. As will be discussed in Part VI, no current laws require synthetic biology production methods to guarantee safety or efficacy. It is also difficult to believe that the concerns of civil society could cause Venter to pause when a trial phase of fuel-excreting algae produces less than predictable results. Manufacturers, thus, have limited incentive to acknowledge and address production risks. When faced with a \$600 million check riding on a looming deadline, bacteria that appear to be doing its designed job, even in an unanticipated manner or rate, may be deemed sufficient for production and ultimately consumer use. “Economic imperative and lack of coordinated regulatory structure beyond basic laboratory compliance have propelled this field at an unprecedented rate without substantial discussion of the risks and benefits . . . .”<sup>52</sup>

The potential concentration of power is also a serious concern. For example, Venter applied for patents on the construction process of Synthia, the first synthetic-genome controlled cell.<sup>53</sup> Although the creation is a “proof of concept,” the patent office may find the process demonstrating sufficient utility in light of advances in gene splicing to grant ownership.<sup>54</sup> If this is the case, JCVI will have exclusive rights to the field of synthetic biology.

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<sup>51</sup> Kristie Prinz, *Biotech Companies Filing for Bankruptcy in Bad Economy*, CAL. BIOTECH L. BLOG (Nov. 21, 2008), <http://californiabiotechlaw.com/archives/biotech-industry-news/biotech-companies-filing-for-bankruptcy-in-bad-economy/>.

<sup>52</sup> Brendan Parent, *Report on the Unintentional Physical Dangers of Synthetic Biology* delivered to the Presidential Comm’n for the Study of Bioethical Issues (Oct. 1, 2010) (on file with author) (citing Denise Caruso, *Synthetic Biology: An Overview and Recommendations for Addressing and Anticipating Emerging Risks*, SCI. PROGRESS (2008), available at <http://www.scienceprogress.org/wp-content/uploads/2008/11/syntheticbiology.pdf>).

<sup>53</sup> *Will J. Craig Venter’s Patents Protect Novel Life Forms?*, IP FRONTLINE (May 26, 2010), <http://www.ipfrontline.com/depts/article.asp?id=24290&deptid=6>.

<sup>54</sup> *Id.*

This kind of monopoly would be devastating for the numerous companies and investors trying to advance the technology and would put a definitive cap on Open Source contributions. The risks of development posed by established genetic engineering pioneers as well as garage do-it-yourselfers could be both deep and broad. Thus, the burden of responsible development seems too great to place in one corporation's hands.

#### IV. POTENTIAL HARMS

Potential harms of synthetic biology that should be addressed through regulation can be divided roughly into "intentional" and "unintentional" categories. Intentional harms can develop from the malicious use of virulently designed pathogens. Unintentional harms can further be divided into what the Hastings Center describes as "physical" and "nonphysical" harms.<sup>55</sup> Non-physical harms include long-term unequal access to the technology and socioeconomic displacement through eliminating jobs and occupying land.<sup>56</sup> These harms would arise from the prioritization of development over the protection of people and communities where development takes place. These harms could manifest even if synthetic biology generates safe and beneficial products.<sup>57</sup> Another non-physical harm is the symbolic concern of humanity's relationship with nature as implicated in the ability to design and own living beings.<sup>58</sup> Unintentional physical harms are often referred to as "bioerror."<sup>59</sup> These "bioerrors" include potential for accidental release of organisms from a laboratory and commercial release from production facilities that result in the modified

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<sup>55</sup> David Rejiski, *Preface*, in PARENS, *supra* note 20.

<sup>56</sup> *Id.*

<sup>57</sup> See Press Release, ETC Group, *Synthia Is Alive . . . And Breeding: Panacea or Pandora's Box?* (May 20, 2010) available at [http://www.etcgroup.org/sites/www.etcgroup.org/files/publication/pdf\\_file/ETCVenterSynthiaMay202010.pdf](http://www.etcgroup.org/sites/www.etcgroup.org/files/publication/pdf_file/ETCVenterSynthiaMay202010.pdf).

<sup>58</sup> *Effects on Development in Synthetic Genetics, Hearing Before the H. Comm. on Energy & Commerce*, 111th Cong., 46–49 (2010) (statement of Dr. Gregory Kaebnick, Research Fellow at The Hastings Center).

<sup>59</sup> See Andrew Leonard, *ETC Group Warns Against "Bio-error"*, SALON (Jan. 19, 2007, 3:54 PM), [http://www.salon.com/2007/01/19/etc\\_responds\\_to\\_endy/](http://www.salon.com/2007/01/19/etc_responds_to_endy/).

organisms interacting with the environment so as to create negative ecological or health consequences. All of these harms require serious consideration in the implementation of the appropriate regulatory infrastructure.

A. *Intentional Malicious Dangers*

The use of synthetic biology to cause intentional harm requires access to both information and tools. Such access is difficult to regulate. In the digital age, even young children in remote regions of the world have the capacity to transfer vast amounts of information across the globe with minimal clicking. Information is far more difficult to regulate than is the use and sale of equipment. As genetic understanding improves, the tools for assembling genomes and building cells might become easier to make, such that the parts for building DNA synthesis machines soon might become as easy to order as gene fragments are today. Accordingly, regulatory attention must be dedicated to both synthetic biology information and tools to prevent bio-terror.

The ease of synthesizing pathogens has been demonstrated repeatedly. Viruses have significantly shorter genomes, so stability issues are less prevalent when assembling their gene fragments. Furthermore, building such organisms is becoming less complicated. In 2002, researchers synthesized the poliovirus in a lab; in 2005 the researchers reconstructed the 1918 Spanish flu; and in 2008 researchers created a bat version of SARS—which is closely related to the human infection.<sup>60</sup> Eckard Wimmer of SUNY at Stony Brook, responsible for generating the poliovirus from mail-ordered genes, explains that the ease of access and design is a “wake up call”<sup>61</sup> because he has recreated the experiment six times and each time the work is “easier and faster.”<sup>62</sup> The sequence for the 1918 flu virus was published in

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<sup>60</sup> See Samuel et al., *supra* note 11, at 10.

<sup>61</sup> THOMAS, *supra* note 2, at 23 (quoting Joby Warrick, *Custom-Built Pathogens Raise Bioterror Fears*, WASH. POST (July 31, 2006), available at <http://www.washingtonpost.com/wp-dyn/content/article/2006/07/30/AR2006073000580.html>).

<sup>62</sup> THOMAS, *supra* note 2, at 23.



*Nature* and details of the virus reconstruction were published in *Science*.<sup>63</sup> This feat was met with criticism from both watchdog civil society members as well as voices sympathetic to biotechnology. Ray Kurzweil and Bill Joy, both avid self-proclaimed “transhumanists”<sup>64</sup> called the publication of the flu virus reconstruction “foolish” and similar to publishing the precise designs for the atomic bomb.<sup>65</sup>

Concerns regarding intentional use dangers are the most obvious and commonly voiced, but sufficient protections are not close to being implemented. Some DNA segment manufacturers, like Blue Heron, voluntarily screen orders for potentially dangerous combinations.<sup>66</sup> This kind of self-regulation is a small step, but without collaboration between gene providers, it is of little value. A 2005 study by *New Scientist* showed that five of twelve gene manufacturers performed some regulatory screening, with only five screening every sequence that they receive.<sup>67</sup> Even if most of these companies began screening their own products in

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<sup>63</sup> Andreas von Bubnoff, *The 1918 Flu Virus is Resurrected*, 437 *NATURE* 794, 794–95 (2005); Terrence M. Tumpey et al., *Characterization of the Reconstructed 1918 Spanish Flu Pandemic Virus*, 310 *SCIENCE* 77, 77 (2005).

<sup>64</sup> Transhumanism, more recently known as “Humanity Plus,” is a social and cultural movement embracing science and technology as means to directly improve mental and physical capacities. See *About*, HUMANITY+, <http://humanityplus.org/about> (last visited Oct. 29, 2010). Another prominent transhumanist figure is Larry Page, co-founder of Google. See Nathan Ingraham, *Larry Page wants to ‘set aside a part of the world’ for unregulated experimentation*, *THE VERGE* (May 15, 2013), <http://www.theverge.com/2013/5/15/4334356/larry-page-wants-to-set-aside-a-part-of-the-world-for-experimentation>; Ashlee Vance, *Merely Human? That’s So Yesterday*, *N.Y. TIMES* (June 12, 2010) (describing Page’s co-founding of the Singularity University, an institution which promotes achieving superhuman abilities and defying death).

<sup>65</sup> THOMAS, *supra* note 2, at 24 (quoting Ray Kurzweil & Bill Joy, *Recipe for Destruction*, *N.Y. TIMES* (Oct. 17, 2005), [http://www.nytimes.com/2005/10/17/opinion/17kurzweiljoy.html?\\_r=0](http://www.nytimes.com/2005/10/17/opinion/17kurzweiljoy.html?_r=0)).

<sup>66</sup> CRAIC COMPUTING, *BLACKWATCH: SOFTWARE TO IDENTIFY SEQUENCES FROM HAZARDOUS BIOLOGICAL AGENTS* 3 (2003), available at [http://biotech.craic.com/blackwatch/BlackWatch\\_Datasheet.pdf](http://biotech.craic.com/blackwatch/BlackWatch_Datasheet.pdf).

<sup>67</sup> See Peter Aldhous, *The Bioweapon is in the Post*, *NEW SCIENTIST* 8 (Nov. 12, 2005).

the last eight years, “distributive purchasing” could circumvent red flags triggered by suspect gene combinations ordered from an individual provider. Ultimately, it will be impossible to prevent all malicious or harmfully careless do-it-yourself projects when any consumer can order from multiple sources.

Publicized pathogen design plans, easily ordered genetic sequences, and manuals like Mohr’s *Primer for Synthetic Biology* should call attention to major regulatory gaps.<sup>68</sup> Accordingly, a centralizing effort akin to a DNA clearinghouse should be entertained, where a single facility screens *all* DNA orders from *all* providers.<sup>69</sup> Public dissemination of gene information such as the biobrick registry should be appropriately constrained until monitoring technology is sufficient to implement this type of unified regulation.

## B. *Unintentional Dangers*

Unintentional dangers of synthetic biology are comprised of harms that producers overlook while pursuing the creation of beneficial products, processes, and/or profit. These harms are not generally the result of malicious actors, unlike intentional dangers discussed in the subsequent section. Three forms of unintentional dangers will be discussed here: symbolic concern, threats to social justice, and physical dangers.

### 1. *Symbolic Concern*

Of the unintentional use dangers, the impact of nonphysical harms would be least immediate. For example, those who believe the creation of life should solely be the province of greater powers might view engineering organisms as “playing God.” Synthetic biology, thus, unintentionally conflicts with their values.<sup>70</sup>

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<sup>68</sup> See generally Howard Wolinsky, *Kitchen Biology*, 10 EMBO REPORTS 683, 684–85 (2009), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2727445/pdf/embor2009145.pdf> (describing the concern that “amateur science [synthetic biology] is moving faster than regulators and legislators”).

<sup>69</sup> See Samuel et al., *supra* note 11, at 15.

<sup>70</sup> This conflict is unintentional because it is highly unlikely that any synthetic biology practice is undertaken with the goal of subverting religious beliefs.

Although this concern is substantial, addressing it with regulatory changes will be difficult because this particular harm does not *directly* manifest in health, economic, or environmental consequences. Affronts to personal beliefs are generally left for sorting out among individuals in the private sphere beyond the reach of the law.<sup>71</sup>

There is also the possibility that the normalization of manipulating life at the synthetic cell level could lead to undesirable social changes. There may be decreased respect for the natural development of life, as individuals feel entitled to assert greater control over the biological development of humans.<sup>72</sup> But this fear can be alleviated if careful attention is paid to more immediate concerns. Refining synthetic biology regulation efforts to protect human dignity by preempting social justice concerns (i.e., tailoring development to avoid disparity increases in human treatment and access to resources)<sup>73</sup> will almost certainly prevent long-term negative social consequences posed by “playing God.” Policies enacted to protect communities from the negative effects of synthetic biology on the environment would likely indicate social sentiment against using synthetic biology to design humans. However, all concerns should remain secondary to the risks of physical harms. It would be irresponsible to solely address symbolic and social justice concerns before enacting regulations that can guarantee safety of synthetic biology products and

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<sup>71</sup> If the development of synthetic biology interferes with basic tenets of respected faiths—and thus daily social life—such development may need to be examined for First Amendment violations.

<sup>72</sup> Recall claims from synthetic biology proponents about supplementing nature and synthesizing human genomes from scratch. See Pollack, *supra* note 22 (“We’re not trying to imitate nature; we’re trying to supplement nature . . . .”) (quoting Dr. Floyd Romesburg); see also THOMAS, *supra* note 2, at 10 (speculating that “within 20 years human genomes will be synthesized from scratch” (quoting Drew Endy)).

<sup>73</sup> See Jeff Conant & Eric Hoffman, *Synthetic Biology and the “Bioeconomy”*: *Feeding Fuel to the Fire of Landgrabs and Biodiversity Loss*, FRIENDS OF THE EARTH (Feb. 18, 2013), <http://www.foe.org/news/archives/2013-02-synthetic-biology-and-the-bioeconomy-feeding-fuel-to>.

processes, as intended by the regulatory suggestions later in this Article.

## 2. *Threats to Social Justice*

The threats to social justice<sup>74</sup> are pressing in light of the extraordinary resource transformation and redistribution that would need to occur to support the biofactory/biofuel-based economy envisioned by researchers and their investment partners. Although synthetic biology promises cheaper and more efficient production, cultivation of synthetic cells for biofuel will require land, energy, and labor.<sup>75</sup> The most prominent dilemma is that the scale of transition from current fuels to biofuels would be enormous. The new extraction, maintenance, and upkeep methods would likely require different labor and energy inputs. This shift will place immense burdens on strained economies that rely on employment and sustenance from practices that would be displaced, and many residential areas will be forced to accommodate changes in the use of their land and water.<sup>76</sup> Even if biofuels prove more efficient in the long run, the transition itself and the loss of food agricultural practices could be irreparably destabilizing.

Much attention is directed to synthetic biology because of recent U.S. Government mandates requiring that 36 billion gallons of fuel for transport be derived from biofuel, largely ethanol, by the year 2022.<sup>77</sup> Current ethanol production practices are far from

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<sup>74</sup> Social justice concerns of resource/labor displacement and unequal access should not literally be interpreted as “nonphysical.” These issues become physical when they impact the health and well-being of large populations. The term is used here for the sake of consistency with the terms used in Erik Parens’s *Ethical Issues in Synthetic Biology*. See PARENS ET AL., *supra* note 20, at 4.

<sup>75</sup> See *Synthetic Solutions to the Climate Crisis: The Dangers of Synthetic Biology for Biofuels Production*, FRIENDS OF THE EARTH, 37 (Sept. 2010), [http://libcloud.s3.amazonaws.com/93/59/9/529/1/SynBio-Biofuels\\_Report\\_Web.pdf](http://libcloud.s3.amazonaws.com/93/59/9/529/1/SynBio-Biofuels_Report_Web.pdf).

<sup>76</sup> See *id.* at 15.

<sup>77</sup> *Renewable Fuel Standard (RFS)*, U.S. ENVTL. PROT. AGENCY (Aug. 6, 2013), <http://www.epa.gov/otaq/fuels/renewablefuels/index.htm>

sufficient to meet this demand.<sup>78</sup> The primary method begins by breaking down corn and sugarcane starches into sugars to be fermented into ethanol, but this process is energy intensive and requires between a third and a half-gallon of fuel per bushel of corn.<sup>79</sup> Land, energy, and water could all be seriously strained by the amount of corn that would be required to supplement the 36 billion gallons of biofuel.<sup>80</sup> It is likely that reaching this target through conventional corn methods would require massive resource redistribution.

A second approach for ethanol production is to break down cellulose from discarded plant material, which would greatly diminish the primary stock problem because of plant-waste abundance.<sup>81</sup> However, cellulose is significantly harder to break down than starch, requiring 50–57% more energy from fossil fuels

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<sup>78</sup> See U.S. Dep't of Energy Office of Sci., *Breaking the Biological Barriers to Cellulosic Ethanol: A Joint Research Agenda*, 13 (June 2006), available at <http://www.genomicscience.energy.gov/biofuels/2005workshop/b2blowres63006.pdf> (“Traditional cellulosic biorefineries have numerous complex, costly, and energy-intensive steps that may be incompatible or reduce overall process efficiency.”).

<sup>79</sup> Michael Pollan, *The Great Yellow Hope*, N.Y. TIMES (May 24, 2006), <http://pollan.blogs.nytimes.com/2006/05/24/the-great-yellow-hope/> (“Every bushel of corn grown in America has consumed the equivalent of between a third and a half gallon of gasoline.”).

<sup>80</sup> See Randy Schnepf & Brent Yacobucci, *Renewable Fuel Standard (RFS): Overview and Issues*, CONG. RESEARCH SERV. 19, 22–23 (Mar. 14, 2013), available at <http://www.fas.org/sgp/crs/misc/R40155.pdf> (explaining that corn produced for biofuel already uses an enormous share of overall corn production of 40%, and it is uncertain that crop area can continue to expand with demand because corn is energy intensive).

<sup>81</sup> See generally Amanda Peterka, *Fla. plant begins producing ethanol from waste*, GREENWIRE (July 2013), <http://www.eenews.net/greenwire/stories/1059985389> (referencing the use of 250,000 raw tons of bio-waste material); *INEOS Bio Produces Cellulosic Ethanol at Commercial Scale*, ENVIRONMENTAL LEADER (Aug. 2, 2013), <http://www.environmentalleader.com/2013/08/02/ineos-bio-achieves-cellulosic-ethanol-production-at-commercial-scale/> (describing that INEOS has converted several types of waste including vegetative and yard waste, citrus, oak, pine, and pallet wood waste).

than the process generates in usable output energy.<sup>82</sup> One biotech company has engineered a fungus that can break down cellulose, but the cost of developing the appropriate processing facility would be five times greater than building a conventional corn ethanol processing plant.<sup>83</sup> It is likely that no pioneering manufacturer has adopted this company's technology because it would not generate swift enough dividends. Thus, an attractive marketing goal is to engineer a microorganism that can perform the full gamut of fuel-production on its own. The winning organism would most likely perform all tasks from breaking down cellulose and glucose to converting the biomass to usable biofuel. Another company has begun commercial production of ethanol from biowaste using a strain of *Clostridium*,<sup>84</sup> and claims it will be able to produce eight million gallons of ethanol per year.<sup>85</sup> The company claims high efficiency yield of ethanol and low environmental impact,<sup>86</sup> but data supporting these facts have not been released.

Even if production methods of companies like the one described above work as advertised, they could still create a severe strain on resources such as land, water, and labor. The plant material for cellulose is generated by perennial feedstocks, which are bulky and slow to establish.<sup>87</sup> To compensate for the long growth period and crop size, it is likely that overall land use would have to increase substantially. Furthermore, their harvest period is

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<sup>82</sup> See David Pimentel & Tad Patzek, *Ethanol Production Using Corn, Switchgrass, and Wood: Biodiesel Production Using Soybean and Sunflower*, 14 NATURAL RESOURCES. RES. 65 (Mar. 2005).

<sup>83</sup> This company is called Iogen, and it is based in Ottawa, Canada. See Jamie Shreeve, *Redesigning Life to Make Ethanol*, MIT TECH. REV., 2 (July 1, 2006), <http://www.technologyreview.com/energy/17052/>.

<sup>84</sup> See *Cambridge Website for Synthetic Biology Resources*, UNIV. OF CAMBRIDGE (2013), <http://www.synbio.org.uk/index/958-ineos-goes-down-the-fischer-tropsch-route-to-ethanol-from-municipal-waste.html>.

<sup>85</sup> See Peterka, *supra* note 81.

<sup>86</sup> See *INEOS Bio Produces Cellulosic Ethanol at Commercial Scale*, YAHOO FINANCE (July 31, 2013), <http://finance.yahoo.com/news/ineos-bio-produces-cellulosic-ethanol-135600723.html>.

<sup>87</sup> Schnepf & Yacobucci, *supra* note 80, at 24.

seasonal, so year-round biofuel production would require immense transportation and storage resources.<sup>88</sup> This risk of resource-strain is not just domestic: The 2005 U.S. Energy Act requires the U.S. Department of State to transfer “climate friendly” technologies to developing countries.<sup>89</sup> If synthetic biology is among the transferred technologies, it could increase pressures on scarce resources and worsen water shortages. If the plant material is grown directly, this could require large plots of land likely already in use for other valuable commodities, including marginalized local sustenance. Some have hinted at potential locations for this land. At the Asia Pacific Partnership Conference, held in April 2006, Dr. Steven Chu of Berkeley noted that Sub-Saharan Africa and Latin America in particular have conditions suitable for biomass production.<sup>90</sup>

In the end, the fuel produced will likely be distributed according to the financial terms of the developer. Rural populations might lose land benefits when their agricultural practices are replaced by biofuel production for which they will have far less need. Organizations like the World Trade Organization, which set international standards for protection of local economies and prevention of coercive overseas business transactions, should adopt rules specifically for the commercialization of synthetic biology. However, because international law creates minimal regulatory pressure, domestic law should set a global example through strong legal commitments to safety and equality. This Article makes suggestions for this kind of domestic regulation.<sup>91</sup>

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<sup>88</sup> *See id.*

<sup>89</sup> Energy Policy Act of 2005, Pub. L. No. 109-58, §§ 1611, 119 Stat. 594 (2005).

<sup>90</sup> *See* DIANA BRONSON, HOPE SHAND, JIM THOMAS & KATHY JO WETTER, ETC GROUP, *EARTH GRAB: GEOPIRACY, THE NEW BIOMASSTERS AND CAPTURING CLIMATE GENES 70* (Pambazuka Press 2011).

<sup>91</sup> *See infra* Part VII.

### 3. *Physical Dangers*

The most immediate physical harms pertain to negative environmental and health impacts from accidental and intentional release of synthetic biology microorganisms. Bacteria and viruses are particularly adept at reproduction, mutation, and survival as they are the oldest, most numerous, diverse, difficult to track, and deadliest group of organisms on the planet.<sup>92</sup> Some of them mutate into completely new pathogens in a matter of days.<sup>93</sup> Only recently has scientific understanding of microbial mutation developed so as to allow researchers to track changes in virulent strains and tailor treatment and avoidance accordingly.<sup>94</sup> These methods are not foolproof—new microbial threats, including the 2009 swine flu, emerge regularly.<sup>95</sup> Furthermore, we cannot permanently treat infections we have known about for years, like Human Immunodeficiency Virus.<sup>96</sup> As effective as humans are at adapting,

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<sup>92</sup> See generally NAT'L INST. OF HEALTH, BIOLOGICAL SCIENCES CURRICULUM STUDY, UNDERSTANDING EMERGING AND RE-EMERGING INFECTIOUS DISEASES (2007), available at <http://www.ncbi.nlm.nih.gov/books/NBK20370/> [hereinafter UNDERSTANDING INFECTIOUS DISEASES] (discussing the different mechanisms by which various microorganisms reproduce and mutate); Ed Rybicki, *Where did viruses come from?*, SCI. AM. (Mar. 27, 2008), <http://www.scientificamerican.com/article.cfm?id=experts-where-did-viruses-come-fr> (explaining that because of the complex relationship between viruses and their host genome, “the origins of most viruses may remain forever obscure.”); Matthew Harper, *The Most Dangerous Bacteria*, FORBES (Mar. 11, 2006, 9:00 AM), [http://www.forbes.com/2006/03/01/antibiotics-pfizer-cubist-cx\\_mh\\_0301badbugs.html](http://www.forbes.com/2006/03/01/antibiotics-pfizer-cubist-cx_mh_0301badbugs.html) (highlighting that the problem of “Bug Wars” will only get worse as more common bacteria and fungi develop resistance to many of the drugs available).

<sup>93</sup> See John W. Drake & John J. Holland, *Mutation Rates Among RNA Viruses*, 96 PROC. NAT'L ACAD. SCI. USA 13910 (1999).

<sup>94</sup> See *New List Of HIV Mutations Vital To Tracking AIDS Epidemic*, SCIENCE DAILY (Mar. 13, 2009), <http://www.sciencedaily.com/releases/2009/03/090305204330.htm>.

<sup>95</sup> Seasonal influenza reoccurs at least annually. See *Seasonal Flu*, U.S. Dep't. of Health & Human Services, [http://www.flu.gov/about\\_the\\_flu/h1n1/index.html](http://www.flu.gov/about_the_flu/h1n1/index.html), (last visited Oct. 3, 2013) (“WHO announced that the world is in a post-pandemic period. However, H1N1 [swine flu] is still circulating.”).

<sup>96</sup> See *New List Of HIV Mutations Vital To Tracking AIDS Epidemic*, STAN. UNIV. MED. CTR. (March 2009), <http://www.sciencedaily.com/releases/>



microbes adapt more quickly and take advantage of immune system deficiencies.<sup>97</sup> The concern over the appropriate control and confinement of microbes is not to be taken lightly.

The environmental release of dangerous synthetic biology microorganisms could be accidental. Laboratory confinement mechanisms are not perfect, as evidenced by scientific theories that both the 1977 Russian flu<sup>98</sup> and 2009 H1N1 virus<sup>99</sup> escaped from high-end, high-security laboratories. Labs are generating harmful pathogens including poliovirus, SARS strains, and the Spanish Flu.<sup>100</sup> If inappropriately monitored or contained, these could cause massive disease infection. Even if regulations prohibit the production of certain uncommon or eradicated pathogens like those listed above, some pathogen production will need to be legal for vaccine development. To treat some reoccurring infections like seasonal influenza, the infecting agent itself must be created and maintained.<sup>101</sup> Although this development has been ongoing for decades, synthetic versions of virus seed stock might be generated in substantially greater quantities as the technology improves. The synthetic versions may also be less stable or predictable than conventional versions, thus leading to accidental escape and contamination. Even laboratories that maintain the highest containment standards should be subject to continuous review as technology shifts from traditional rDNA practices to synthetic biology. Also, as the ease of production increases and the

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2009/03/090305204330.htm; Vladimir Trifonov et al., *Geographic Dependence, Surveillance, and Origins of the 2009 Influenza A (H1N1) Virus*, 361 *NEW ENG. J. MED.* 115, 115–19 (2009).

<sup>97</sup> See UNDERSTANDING INFECTIOUS DISEASES, *supra* note 92.

<sup>98</sup> See Richard Harris, *New Strain May Edge Out Seasonal Flu Bugs*, *NAT'L PUB. RADIO* (May 4, 2009, 12:03 PM), <http://www.npr.org/templates/story/story.php?storyId=103711274&sc=emaf>.

<sup>99</sup> See Simeon Bennet, *Scientist Repeats Swine Flu Lab-Escape Claim in Published Study*, *BLOOMBERG* (Nov. 24, 2009), <http://www.bloomberg.com/apps/news?pid=newsarchive&sid=ajw2AS.d1wK8>.

<sup>100</sup> See Samuel et al., *supra* note 11, at 10.

<sup>101</sup> See *How Vaccines are Made, History of Vaccines*, *THE COLLEGE OF PHYSICIANS OF PHILADELPHIA* (2013), <http://www.historyofvaccines.org/content/how-vaccines-are-made>.

technology continues to be publicly available, insufficiently trained participants are performing microbial experiments in facilities not subject to laboratory guidelines.<sup>102</sup> Accidental release from these “amateur” facilities would be even more likely. Beneficent but careless production is the most likely cause of accidental release.

Some precautionary mechanisms that can be implemented include incorporation of toggle switches to disarm or kill the engineered microbes and engineering cells to demonstrate highly predictable behavior.<sup>103</sup> But the possibility for mutation has never been and probably cannot be eliminated, as researchers know very little about what causes mutation and how to prevent it.<sup>104</sup> Additionally, gene-environment interaction is important to microorganism behavior but is poorly understood.<sup>105</sup> Removing parts of an organism’s genome in the hopes of simplifying it might make the organism unviable or unpredictable.<sup>106</sup> Thus, it is likely that no method of “bioconfinement” will be completely effective.<sup>107</sup> Accordingly, a regulatory framework will need to set strict standards for monitoring and containment. Recommendations to this end are proposed in Part VII of this Article.

Even if synthetic organisms remain properly contained during development, major concerns remain when the “successfully designed” cells are intentionally released. Extraordinary

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<sup>102</sup> See discussion of do-it-yourself synthetic biology *supra* Part III.A.

<sup>103</sup> See Drew Endy, *Foundations for Engineering Biology*, 438 NATURE 449, 450, 452 (2005); Ahmad Khalil & James Collins, *Synthetic Biology: Applications Come of Age*, 11 NAT. REV. GENETICS 367, 367 (2010).

<sup>104</sup> See James F. Crow, *How Much Do We Know About Spontaneous Human Mutation Rates?*, 21 ENVTL. & MOLECULAR MUTAGENESIS 122, 122–29 (1993).

<sup>105</sup> See generally Jan-Willem Veening, Wiep Klaas Smits & Oscar P. Kuipers, *Bistability, Epigenetics, and Bet-Hedging in Bacteria*, 62 ANN. REV. MICROBIOLOGY 193 (2008) (explaining that there are multiple and complex ways in which epigenetics plays an essential role in the phenotypic variability of microorganisms).

<sup>106</sup> See Caruso, *supra* note 1, at 5–6.

<sup>107</sup> News Release, Nat’l Research Council, Committee on Biological Confinement of Genetically Engineered Organisms, *Biological Confinement of Genetically Engineered Organisms*, (Jan. 20, 2004), [http://www.nap.edu/webcast/webcast\\_detail.php?webcast\\_id=260](http://www.nap.edu/webcast/webcast_detail.php?webcast_id=260).

uncertainty arises with the possibility of horizontal gene transfer between synthesized organisms and naturally occurring organisms.<sup>108</sup> Consideration must also be given to the effects of disturbing the balance produced by organisms that have been responding to each other's evolutionary changes over hundreds of thousands of years.<sup>109</sup> Predicting outcomes becomes futile because the permutations of interaction between the synthesized organism and those naturally occurring are virtually infinite. Companies that hope to grow their "living factories" in the environment, or use cells as cleaning agents or pesticides, should be required to adhere to the strictest standards of tracking and control. If commercial organisms cannot be proven safe through guaranteed incorporated limitations on ability to mutate through horizontal and vertical gene transfer reproduction, they should be banned from production. The effects of allowing otherwise could be devastating.

#### V. ARGUMENTS DISMISSING THE DANGERS OF SYNTHETIC BIOLOGY

Three salient arguments that dismiss the dangers of synthetic biology deserve to be characterized and countered. These can be summarized as follows: (1) regulations are already in place for rDNA practices and synthetic biology is not distinct enough to require new oversight;<sup>110</sup> (2) researchers will self-regulate to prevent major risks;<sup>111</sup> and (3) regulation cannot prevent the creation of dangerous synthetic organisms, so it would serve no purpose. The latter argument is based on the general assertion that something difficult to prevent is not worth trying to prevent.

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<sup>108</sup> See Drake & Holland, *supra* note 93, at 13910–12.

<sup>109</sup> Maggie Zhou, Commentary, *Comments on Synthetic Biology* (Oct. 1, 2010), <http://www.climatesos.org/2010/11/comments-to-presidential-commission-on-synthetic-biology/> (addressing the Presidential Commission for the Study of Bioethical Issues).

<sup>110</sup> See RODEMEYER, *supra* note 13, at 27.

<sup>111</sup> See AMY GUTMANN & JAMES WAGNER, *NEW DIRECTIONS: THE ETHICS OF SYNTHETIC BIOLOGY AND EMERGING TECHNOLOGIES, REPORT OF THE PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES*, at v (2010), available at [http://bioethics.gov/sites/default/files/PCSBI-Synthetic-Biology-Report-12.16.10\\_0.pdf](http://bioethics.gov/sites/default/files/PCSBI-Synthetic-Biology-Report-12.16.10_0.pdf) [hereinafter *NEW DIRECTIONS*].

Responses to the first two points were addressed indirectly in previous sections,<sup>112</sup> but deserve more detail in light of historical harm caused by rDNA practices. The third point relies on the false premise that the possibility of harm is equivalent to the inevitability of harm, which overlooks the power of education and choice.

A belief that current rDNA regulations are sufficient to address synthetic biology risks assumes that: (1) current rDNA regulations are sufficient even for current rDNA practices and (2) compared to intergeneric organisms, which are products of rDNA technology, the uncertainty of whole genome synthesis does not lead to greater risk of pathogenic mutation or less controllability. Regarding the claim that rDNA regulations are sufficient, there are scientists and physicians who would disagree based on studies of genetically modified products. Several animal studies on consumption of genetically modified food show serious deleterious effects, including birth deformities and mortality,<sup>113</sup> liver atrophy,<sup>114</sup> and toxic effects on the pancreas, stomach, and blood systems.<sup>115</sup> Whether these effects translate to humans has yet to be adequately studied.<sup>116</sup> There are also several case studies of human and animal allergies and illnesses closely linked to transgenic crops<sup>117</sup> Theories that the H1N1 flu virus of 2009 was made in the lab and

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<sup>112</sup> See *supra* Part I (discussing the previous untested novelty of synthetic biology, the lack of existing oversight for research and development, and the corporate pressures on research to produce results that compromise researchers' ability to self-regulate).

<sup>113</sup> See Mae-Wan Ho, Joe Cummins, & Peter Saunders, *GM Food Nightmare Unfolding in the Regulatory Sham*, 19 MICROBIAL ECOLOGY IN HEALTH AND DISEASE 66, 66 (2007).

<sup>114</sup> See Arpad Pusztai, *Can Science Give Us the Tools for Recognizing Possible Health Risks of GM Food?*, 16 NUTRITION & HEALTH 73, 81 (2002).

<sup>115</sup> See Artemis Dona & Ioannis Arvanitoyannis, *Health Risks of Genetically Modified Foods*, 49 CRITICAL REVIEWS IN FOOD SCI. AND NUTRITION 164, 169–70 (2009).

<sup>116</sup> See *id.* at 164.

<sup>117</sup> See Ho, Cummins & Saunders, *supra* note 113, at 67 (describing allergies from exposure to Bt cotton, thousands of sheep deaths from grazing on Bt cotton residue, human illnesses from a protein in Bt maize, and several similar linkages).

escaped garnered significant scientific support.<sup>118</sup> Several live rDNA viruses produced for vaccines can revert to full virulence at random and scientists have yet to determine the cause.<sup>119</sup> These examples support the notion that current rDNA regulations may not be adequate to prevent substantial harm from current rDNA practices, let alone synthetic biology practices.

Even if protections against intergeneric organisms are sufficient, the additional uncertainty of synthetic biology weighs in favor of modified regulation. The relationship between uncertainty and risk should be demonstrated, but there is disagreement as to whether technology stakeholders or the public should provide such a demonstration. For example, those with a stake in the technology, such as researchers and investors, believe the burden falls on the wary party, usually civil society, to prove that the technology is *not* safe. Those concerned about harm believe the burden rests with the developers to prove it *is* safe. However, the only method for evaluating danger associated with the new practice, and thus with whom the burden should lie, is through comparison to past experiences.

While intergeneric organisms are the closest parallel, synthetic organisms do not benefit from environmentally tested stability.<sup>120</sup>

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<sup>118</sup> Richard Seah, *H1N1: Is it a manmade genetically engineered virus?*, FLU PREVENTION AND TREATMENT—NATURALLY (2010), <http://www.flu-treatments.com/h1n1-virus.html>.

<sup>119</sup> Terje Traavik, *An Orphan in Science: Environmental Risks of Genetically Engineered Vaccines*, REPORT TO THE DIRECTORATE FOR NATURE MANAGEMENT, NORWAY, 21, 27, 49 (1999), available at <http://www.biosafety-info.net/article.php?aid=515>. Currently, live vaccination practices are used for measles, mumps, and rubella, which were determined safe by trial and error. But this form of administration was discovered harmful for treating poliovirus. It is likely that several “vaccinated” people died of poliovirus while this determination was made. *Id.*

<sup>120</sup> Fully synthetic organisms that are not just copies of existing organisms, such as Venter’s Synthia, will not be the norm for quite a while. Current synthetic biology generally involves the insertion of some lab-synthesized genes into a pre-existing microbe. This is similar to rDNA practices, but lab-synthesis makes genes more available and will eventually make it easier to produce novel genes.

*E. coli* is an exemplar of intergeneric stability; researchers can use several strains of it for gene splicing because these organisms are hardy and less prone to pathogenic mutation.<sup>121</sup> However, as previously explained, mutation is not well understood and its complete prevention is currently impossible.<sup>122</sup> The mutation patterns of synthetic organisms will be more unfamiliar than those naturally occurring, which have been observed for several decades.<sup>123</sup> Furthermore, genetic stability cannot be built into a synthetic organism if the builder doesn't know what accounts for stability in the first place. Because of past harms demonstrated by rDNA organisms, natural pathogens, and the gravity of potential harm from unstable synthetic microbes, regulation should require those pursuing the research to prove that it is safe.

In conjunction with the reasons just stated, industry self-regulation will be insufficient to protect against synthetic biology harms. This is because it is not reasonable to hold researchers and investors solely responsible for preempting the field's dangers when their goals center on advancement of the field. Scientists invest their lives and livelihoods into this work under great pressure from industry and media, so it is foreseeable that they would prioritize the realization of synthetic biology promises over safety considerations.

An early example of failed self-regulation is the Asilomar Declaration of 1975, in which public rDNA fears facilitated the convention of several handpicked, elite scientists to discuss potential safety issues.<sup>124</sup> Civil society was unrepresented at the

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<sup>121</sup> See *General Information: Escherichia coli*, CTR. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/ecoli/general/index.html> (last visited Aug. 12, 2013); *National Center for Zoonotic, Vector-Borne, and Enteric Diseases*, CTR. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/nceid/> (last visited Aug. 12, 2013).

<sup>122</sup> See Veening et al., *supra* note 105.

<sup>123</sup> Comprehension of mutation patterns is largely the product of empirical evidence, which does not exist for novel synthetic organisms. See generally J. L. Martinez & F. Baquero, *Mutation Frequencies and Antibiotic Resistance*, 44 *ANTIMICROBIAL AGENTS & CHEMOTHERAPY* 1771 (2000) (describing the mutation rates of pathogens as related to the use of antibiotics over time).

<sup>124</sup> See THOMAS, *supra* note 2, at 46.

Asilomar meetings, and the discussion resulted in few temporarily relinquished experiments to assuage public concern while it completely overlooked broader social and ethical concerns.<sup>125</sup> Obviously, this Declaration set little preventative precedent with shortsighted genetic engineering endeavors like Monsanto's "Golden Rice" occurring twenty-five years later.<sup>126</sup> Currently, self-regulation attempts in synthetic biology are limited to a few obligatory quotes from scientists acknowledging there might be some risks, and few gene manufacturers self-screening for dangerous orders.<sup>127</sup>

Finally, it is not persuasive to argue that regulation serves no purpose because it cannot prevent the creation of dangerous organisms. The first inherent fallacy in this belief is that regulation would be ineffective. If this paper's recommendations in Part VII are followed, constraint of public information can be implemented swiftly and the ability to create pathogenic microbes can be isolated to research settings. If these settings are required to adhere to strict containment measures, the organisms created will have no access to the environment, thus neutralizing their dangerous attributes. Regulation can also prohibit the creation of particularly virulent and robust strains that are found to be too dangerous even for research. This kind of prohibition is demonstrated by the United Nations' 2005 Ban on Cloning, which determined that cloning was incompatible with human dignity and

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<sup>125</sup> *Id.*

<sup>126</sup> In 2000, Monsanto widely advertised its distribution of vitamin A enriched GE rice to the third world to compensate for malnutrition. The product could not provide adequate nutritional value to compensate for the deficiency, but the recipients relied on it heavily, forgoing other sources of Vitamin A. It is speculated that this overreliance aggravated health problems. See Vandana Shiva, *The Golden Rice Hoax—When Public Relations Replaces Science*, GENETIC ENGINEERING AND ITS DANGERS, <http://online.sfsu.edu/~rone/GEessays/goldenricehoax.html> (last visited Aug. 12, 2013); Paul Brown, *GE "Golden Rice" Propaganda Denounced as a Hoax*, ORGANIC CONSUMERS ASS'N (Feb. 10, 2001), <http://www.organicconsumers.org/corp/gericetooofar.cfm>.

<sup>127</sup> See Samuel et al., *supra* note 11, at 13.

the protection of human life.<sup>128</sup> A similar ban on human-animal hybrids exists in several states domestically.<sup>129</sup> As of this publication, there are no known examples of either prohibited practice.

This leads to the second inherent fallacy that regulation is useless even if the practice is difficult to prevent. Regulation creates several modes of deterrence beyond sanctions for noncompliance, including the representation of national sentiment. Particularly in a democratic government, positions taken by executive agencies and the legislature should reflect and reinforce the opinions of the majority. Combining the principle behind the regulation with educational support from nonprofits, schools, and media might be an effective method of informing public choice on how to engage with new technology. In this way, citizens, scientists, and amateurs can choose to abstain from dangerous experiments. This precautionary approach of ensuring safety is superior to waiting for human lives to be negatively impacted before reactionary regulation is catalyzed.

## VI. CURRENT REGULATION

The dangers previously discussed demonstrate that the development of synthetic biology cannot be left solely to market forces and scientific discretion. Regulations will have to protect against intentional malicious design of pathogens, address the potential for expansion of socioeconomic disparities, solidify safety and confinement measures, and preempt negative environmental impact from released modified organisms. Neither the United States nor international governments, however, have to start from scratch. Biotechnology regulations have developed around several genetic engineering products and are at least in part

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<sup>128</sup> See Press Release, *General Assembly Adopts United Nations Declaration on Human Cloning by Vote of 84-34-37*, General Assembly/10333, Fifty-Ninth General Assembly Plenary, 82nd Meeting (Aug. 3, 2005), available at <http://www.un.org/News/Press/docs/2005/ga10333.doc.htm>.

<sup>129</sup> Eric Bland, *Animal Human Hybrids Banned in Some States*, DISCOVERY NEWS (June 4, 2010, 3:00 AM), <http://news.discovery.com/tech/human-animal-hybrids-splice.html>.



responsible for respectable biosafety records in the United States and abroad.<sup>130</sup>

This section will begin by critiquing shortcomings of the Presidential Commission's Report on synthetic biology; second, it will examine international regulations that should apply to the development of the field; third, it will analyze applicable rules and operations of U.S. agencies; and it will conclude with suggestions for modification to agency rules and operations that would create comprehensive oversight.

#### A. *The Presidential Commission's Report*

Hopes for meaningful regulation of synthetic biology were briefly peaked in 2010 when, in response to the JCVI announcement regarding the creation of Synthia, President Obama asked his Commission for the Study of Bioethical Issues to examine the field's risks.<sup>131</sup> When the Presidential Commission's Report ("Report") was released, those hopes were quashed. The Report provides impressive detail on the development, potential advantages, and risks of synthetic biology, but provides no specific recommendations for oversight.<sup>132</sup>

The Presidential Commission, an advisory body composed of well-respected professionals from medicine, science, law, ethics, and engineering,<sup>133</sup> examined synthetic biology as its first

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<sup>130</sup> See RODEMEYER, *supra* note 13, at 13.

<sup>131</sup> Jeffrey Mervis, *Obama Orders Review of Synthetic Biology*, SCIENCE INSIDER (May 20, 2010, 6:57 PM), <http://news.sciencemag.org/2010/05/obama-orders-review-synthetic-biology>.

<sup>132</sup> See generally *NEW DIRECTIONS* *supra* note 111, at v (describing five categories of ethical considerations related to synthetic biology, but eschewing the recommendation of practical mechanisms to address the field's potential dangers).

<sup>133</sup> See *Presidential Commission for the Study of Bioethical Issues, History of the Bioethics Commission*, BIOETHICS, available at <http://bioethics.gov/history>. The Commission's chartered objectives include "advis[ing] the President on bioethical issues that may emerge as a consequence of advances in biomedicine and related areas of science and technology." *Id.* Versions of the Commission existed under previous administrations going back forty years and they have

undertaking. The Commission held hearings in which representatives from research and engineering, including Endy and Venter, touted promises of renewable energy, treatments, and vaccines.<sup>134</sup> University faculty, members of environmental protection groups, government agencies, and scholarly think tanks discussed benefits, risks, ethics, and oversight.<sup>135</sup> After two days of probing questions and informative panels, the Commission also solicited public comments to further guide their recommendations.<sup>136</sup>

The 175 page Report was published six months after the President's request and provides little guidance on effective regulation of synthetic biology. This is because the Commission merely found that "synthetic biology is capable of significant but limited achievements posing limited risks. Future developments may raise further objections, but the Commission found no reason to endorse additional federal regulations or a moratorium on work in this field at this time."<sup>137</sup>

The Report's recommendations support open-access development<sup>138</sup> and public funding for synthetic biology projects that promote the "public good."<sup>139</sup> The Report also encourages the federal government to periodically review the field, ensure consistent regulatory requirements, and update the public on findings.<sup>140</sup> However, at no point does the Report make specific suggestions for how the risks of synthetic biology should be

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advised the President on issues including human subject research, life-sustaining treatment, defining death, and stem cell research. *Id.*

<sup>134</sup> See Webcast, *Presidential Commission for the Study of Bioethical Issues, Meeting One: July 8–9, 2010 in Washington D.C.*, BIOETHICS, <http://www.tvworldwide.com/events/bioethics/100708/> (last visited Oct. 1, 2013).

<sup>135</sup> *See id.*

<sup>136</sup> Interested parties were able to submit feedback to the Commission via its website at [bioethics.gov](http://bioethics.gov) until September 1, 2010. *See NEW DIRECTIONS*, *supra* note 111, at 22.

<sup>137</sup> *See id.* at v.

<sup>138</sup> *Id.* at 7.

<sup>139</sup> *Id.* at 6–7.

<sup>140</sup> *Id.* at 8.

managed. This was clearly an intentional disregard as opposed to ignorance because the “Risks” section of the Report describes in detail many of the dangers covered in this Article’s analysis.<sup>141</sup>

The Commission considered and reported on the concerns voiced by members of civil society who spoke at the hearings, as well as those written in public comments by several organizations.<sup>142</sup> However, the final recommendations show little appreciation for their gravity, and instead issue vague warnings that caution might be warranted in the future.<sup>143</sup> Even though the Commission might have been genuine in its belief that self-regulation adequately protects against present synthetic biology dangers, there is a disconnect between this belief and the Report’s findings. It acknowledges the uncertain nature of harm from accidental release, and that not all research-implemented containment strategies will necessarily be adequate.<sup>144</sup> It further acknowledges the potential for land mass destruction and displacement of resources on which already-marginalized communities subsist.<sup>145</sup> It also tries to dismiss the threat of “bioterror” by saying the tools to grow pathogens are only in the hands of few people due to financial and technical requirements,<sup>146</sup> which is questionable in light of examples like the iGEM competition.

Even though the Commission might believe that actionable concern is unwarranted, many others remain unconvinced. In response to the Report’s publication, fifty-eight environmental, public interest, and religious groups issued a joint letter to the Commission criticizing the Report for “ignoring the precautionary principle, lacking adequate review of environmental risks, [and] placing unwarranted faith in . . . technologies that provide no

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<sup>141</sup> *See id.* at 62–67.

<sup>142</sup> *See id.* at 22 (explaining that the Commission listened to expert concerns and solicited public comments), 62–63, 67 (enumerating the risks of accidental release, intentional release, land mass conversion, and human application).

<sup>143</sup> *See id.* at 170–71.

<sup>144</sup> *Id.* at 63.

<sup>145</sup> *Id.*

<sup>146</sup> *Id.* at 72.

guarantee against the escape of synthetic organisms.”<sup>147</sup> Advocates and opponents would likely agree that the Report’s implicit message is that safety and environmental concerns pale in comparison to the promises of reproduction-powered industry. This evaluation is particularly hard to accept in light of the fact that safety has not been demonstrated over multiple generations of synthetic biology-based production, and potential harms include pandemic infection of food, land, livestock, and humans.

### B. *International Regulation*

Recent international efforts to regulate synthetic biology have begun to address unique safety and health risks, but these efforts are not sufficient to preempt dangers caused by unpredictable novel organisms. The Biological and Toxin Weapons Convention (“BWC”) was designed to prevent the creation and storage of biological weapons.<sup>148</sup> The Convention on Biological Diversity includes efforts to ensure regulation of international movement of Living Modified Organisms, including the requirement that member parties provide informed consent prior to receipt or delivery.<sup>149</sup> The United States is a party to the former Convention,<sup>150</sup> but has shirked its specified regulatory requirements.

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<sup>147</sup> *Groups Criticize Presidential Commission’s Recommendations on Synthetic Biology*, ETC. GROUP (Dec. 16, 2010), <http://www.etcgroup.org/content/groups-criticize-presidential-commission%E2%80%99s-recommendations-synthetic-biology>.

<sup>148</sup> *See Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction*, THE BIOLOGICAL AND TOXINS WEAPONS CONVENTION (Apr. 10, 1972), <http://www.opbw.org/convention/documents/btwctext.pdf> [hereinafter *BWC*].

<sup>149</sup> *About the Protocol*, CONVENTION ON BIOLOGICAL DIVERSITY <http://bch.cbd.int/protocol/background/> (last visited Aug. 7, 2013) [hereinafter *CBD*].

<sup>150</sup> *About the Biological and Toxin Weapons Convention*, THE BIOLOGICAL AND TOXIN WEAPONS CONVENTION, <http://www.opbw.org/> (last visited Aug. 8, 2013).

The United States is not a party to the latter Convention.<sup>151</sup> These instances of nonparticipation set a poor regulatory example for synthetic biology both domestically and internationally.

The intentional malicious release of synthetic microorganisms is regulated by the Biological and Toxin Weapons Convention (“BWC”),<sup>152</sup> but the effort is more likely symbolic than effective. This international treaty bans the development, production, stockpiling, and transfer of “[m]icrobial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes.”<sup>153</sup> As such, the BWC and the 1993 Chemical Weapons Convention prohibit the intentional development and production of toxin-producing organisms through the use of synthetic biology.<sup>154</sup>

Unfortunately, the ability to monitor and regulate against this kind of proliferation is seriously limited. Access to genetic information, gene fragments, and tools for production is not well-guarded; recall that college students have access to synthetic biology synthesis tools,<sup>155</sup> and any individual intending to design pathogens could order genes from multiple manufacturers, thereby circumventing suspect combination ordering that might otherwise be detected when ordering from a single gene manufacturer.<sup>156</sup>

Even though the United States is a signatory to the BWC, and thus subject to the Article IV requirement of taking national measures to prevent the misuse and means of delivery of biological agents,<sup>157</sup> it has been lax in its duty. Certainly the publication of

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<sup>151</sup> *Parties to the Protocol and signature and ratification of the Supplementary Protocol*, CONVENTION ON BIOLOGICAL DIVERSITY, <http://bch.cbd.int/protocol/parties/> (last visited Aug. 7, 2013).

<sup>152</sup> THOMAS, *supra* note 2, at 48.

<sup>153</sup> BWC, *supra* note 148 at art. I(1).

<sup>154</sup> THOMAS, *supra* note 2, at 48.

<sup>155</sup> See iGEM, *supra* note 26.

<sup>156</sup> See Aldhous, *supra* note 67.

<sup>157</sup> *About the Biological and Toxin Weapons Convention*, THE BIOLOGICAL AND TOXIN WEAPONS CONVENTION, <http://www.opbw.org/> (last visited Aug. 8, 2013).

virulent pathogen genomes and do-it-yourself synthetic biology culture together *enable* such misuse, yet participating journals and authors have only received public reprimands from peers, at most. The open-access mentality that pervades the field of synthetic biology and lack of regulatory infrastructure regarding gene fragment distribution further promote the potential misuse and delivery of malicious agents.

International regulatory efforts to address commercial use and environmental release of Living Modified Organisms (“LMO”)—a category that includes synthetic biology organisms—were established by the Convention on Biological Diversity, which was formed by United Nations parties interested in sustainable development.<sup>158</sup> In 2003, the Convention developed the Cartagena Protocol on Biosafety, which is an international treaty governing the movements of LMOs from one country to another.<sup>159</sup> The Cartagena Protocol provides mechanisms for developing countries to receive valuable information before agreeing to the import of LMOs.<sup>160</sup> The mechanisms include an Advance Informed Agreement to ensure that importing countries understand the risks inherent in LMO receipt<sup>161</sup> and make information available about LMOs through a bio-safety clearing house.<sup>162</sup> The Cartagena Protocol has 166 signatories, but the United States is not among them.<sup>163</sup> The U.S. Department of State explained that it was concerned instead about unnecessarily strict barriers to trade, referencing the

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<sup>158</sup> *History of the Convention*, CONVENTION ON BIOLOGICAL DIVERSITY, <http://www.cbd.int/history/> (last visited Aug. 7, 2013).

<sup>159</sup> *CBD*, *supra* note 149.

<sup>160</sup> *Id.*

<sup>161</sup> *See Advance Informed Agreement Procedure*, PROTOCOL ON BIOSAFETY TO THE CONVENTION ON BIOLOGICAL DIVERSITY (Jan. 29, 2000), [http://bch.cbd.int/protocol/NKL\\_text.shtml](http://bch.cbd.int/protocol/NKL_text.shtml).

<sup>162</sup> *Id.* at art. 20.

<sup>163</sup> The U.S. is not a party to the Convention on Biological Diversity, so it is not eligible for party status to the Cartagena Protocol. *See Parties to the Protocol and Signature and Ratification of the Supplementary Protocol*, *supra* note 151.

importance of food aid delivery during times of crisis.<sup>164</sup> Other parties, including those whose previous agreement efforts have been complicated by the United States, frame the United States' abstention as a subordination of environmental concerns in favor of free trade.<sup>165</sup>

Nonparticipation of the United States notwithstanding, the Protocol's efficacy in protecting against synthetic biology hazards is questionable due to broad room for interpretation. The Nagoya-Kuala Lumpur Protocol for Redress and Liability of LMOs—a supplementary agreement to the Cartagena Protocol—creates loose standards for accountability in the event of damage caused to the environment by LMOs.<sup>166</sup> This document employs three protective themes for parties to the Convention: (1) compensation; (2) capacity building; and (3) creation of domestic law.<sup>167</sup> Each theme delegates responsibilities. Entities (such as businesses exporting LMOs) that cause LMO harm must compensate the harmed nation; parties to the convention who host LMO producers must create domestic law to regulate LMO exports and implement monitoring schemes for LMO production; and parties to the Protocol with sufficient resources must assist less-developed parties with developing their own LMO regulatory frameworks.<sup>168</sup> Furthermore, Article 12 states that “[p]arties shall implement domestic law for rules and procedures that address responsibility for damages.”<sup>169</sup>

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<sup>164</sup> *Frequently Asked Questions on the Cartagena Protocol on Biosafety*, U.S. DEPT OF STATE (Feb. 23, 2004), <http://2001-2009.state.gov/g/oes/rls/or/2004/29751.htm>.

<sup>165</sup> Lavanya Rajamani, *The Cartagena Protocol—A Battle Over Trade or Biosafety?*, THIRD WORLD NETWORK, <http://www.twinside.org.sg/title/lavanya-cn.htm> (last visited Aug. 12, 2013).

<sup>166</sup> *See generally Liability and Redress for Damage Resulting from GMOs*, THIRD WORLD NETWORK (2012), [http://www.twinside.org.sg/title2/books/pdf/liability\\_and\\_redress.pdf](http://www.twinside.org.sg/title2/books/pdf/liability_and_redress.pdf).

<sup>167</sup> *See generally Text of the Nagoya—Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety* (Oct. 15 2010), [http://www.cbd.int/protocol/NKL\\_text.shtml](http://www.cbd.int/protocol/NKL_text.shtml) [hereinafter *NKLSPP*].

<sup>168</sup> *Id.* at art. 5.

<sup>169</sup> *See id.* at art. 12 (“Implementation and Relation to Civil Liability.”).

These measures appear protective at face value, but the Supplementary Protocol also simplifies circumvention. Causation must be shown between the microorganism and the harm caused in order for repercussions to take effect,<sup>170</sup> yet standards are not explicit for demonstrating causation. Furthermore, several exemptions to responsibility for causing harm are enumerated, including acts of God, war, or *any other exemption* a party deems fit through its own domestic laws.<sup>171</sup> Specific standards to keep countries accountable for harm caused by their distribution of LMOs are nonexistent. In order for the Protocol to have real deterrent value in the prevention of microbial mishaps, each article should provide more specific standards.

Unfortunately, the Conventions here described have not prevented or even slowed the creation of synthetic organisms that could lead to intentional misuse or commercial release. Their existence demonstrates global concern for harm that can stem from biological products, but the intensified dangers of synthetic biology go unrecognized, especially in the United States. The potential for self-replicating fuel, food, and other consumer products is blinding investors and nations to the potential for self-replicating pathogens and unjustifiable land conversion. The coordinated domestic regulatory framework proposed at the end of this Article should be implemented in conjunction with ratification of the Cartagena Protocol, and implementation of intentional release control measures as required by the Biological and Toxin Weapons Convention.

### C. *United States Agency Regulations*

Currently, the United States model for biotech regulation is product-oriented, in which the appropriate agencies are responsible for overseeing the risks posed by the products of genetic engineering currently under their purview.<sup>172</sup> The precedent for this was the “Coordinated Framework,” which came out of the

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<sup>170</sup> See *id.* at art. 4 (“Causation”).

<sup>171</sup> See *id.* at art. 6 (“Exemptions”).

<sup>172</sup> See RODEMEYER, *supra* note 13, at 31.



White House's Office of Science and Technology Policy in 1986.<sup>173</sup> This policy statement declared that organisms created with rDNA did not pose any unique risks in comparison to those conventionally created.<sup>174</sup> As such, genetically engineered *products* should be regulated instead of *processes*, and contemporary laws were deemed sufficient to address the risks.<sup>175</sup> The result has been an uncoordinated patchwork of coverage, which some critics claim over-regulates biotechnology, while others claim it under-regulates biotechnology.<sup>176</sup> An examination of some of the most relevant agency biotechnology acts and rules demonstrates that adjustments toward regulation of process, control of particularly dangerous information, and compliance incentive structures through inter-agency coordination can reasonably secure against the potential harms of synthetic biology.

*NIH and rDNA Guidelines:* The NIH has developed research standards that have been recently and specifically modified to consider synthetic biology.<sup>177</sup> Although useful, they are limited in coverage. In 1975, NIH established the Recombinant Advisory Committee ("RAC") as a body to "provide independent federal scientific oversight of proposed rDNA research and to establish standardized safety guidelines for researchers."<sup>178</sup> Recombinant DNA technology was new, and genetics was poorly understood, so the guidelines initially issued were conservative as compared to today's guidelines. As the technology proved valuable and reasonably safe over time, the RAC delegated oversight authority

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<sup>173</sup> See Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23, 302 (June 26, 1986).

<sup>174</sup> See RODEMEYER, *supra* note 13, at 35–36.

<sup>175</sup> See 51 Fed. Reg. at 23, 302.

<sup>176</sup> See RODEMEYER, *supra* note 13, at 13.

<sup>177</sup> The amendments include modification of the definition of "rDNA" molecule. Synthetic nucleic acids that can be created without joining segments are added to those created by standard joining techniques and those replicated by joining techniques. See Office of Biotechnology Activities, *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, NAT'L INST. OF HEALTH, § 1-B, available at [http://oba.od.nih.gov/rdna/nih\\_guidelines\\_oba.html](http://oba.od.nih.gov/rdna/nih_guidelines_oba.html).

<sup>178</sup> See RODEMEYER, *supra* note 13, at 20.

to local Institutional Biosafety Committees (“IBCs”), the establishment of which is one requirement for the receipt of NIH funding for rDNA experimentation.<sup>179</sup> Factors including pathogenicity, virulence, communicability, and environmental stability determine the level of IBC notification.<sup>180</sup> The highest risk requiring direct approval from the NIH and the degree of containment required, is laid out by “Biosafety Levels” in the research guidelines.<sup>181</sup> Under the recent amendments, these levels appear to reflect the dangers of synthesizing virulent pathogenic agents proportionately. The guidelines address the concern that predictive power regarding virulence, communicability, or the other criteria becomes weaker when the organism’s genes come from multiple sources.<sup>182</sup> The recommendation is that the “synergistic effect” of multiple risk groups be given serious consideration when determining the appropriate biosafety levels.<sup>183</sup>

The NIH’s guidelines are comprehensive and reasonably well-tailored to safe confinement of synthetic biology research. However, the guidelines do not address the intentional release of organisms for commercial purposes, nor does the NIH wield any control over organizations not receiving its funding.<sup>184</sup> The White House Office of Science and Technology Policy recognized the need to examine intentionally released organisms, and, thus, generated the Coordinated Framework. With regard to the

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<sup>179</sup> *See id.* at 30. IBCs function much like Institutional Review Boards, consisting of four to five members representing appropriate expertise for the field being reviewed. The individuals on the committee must be registered with NIH’s office of biotechnology, keep minutes, and open meetings to the public when reasonable. Problems or violations must be reported to the Office of Biotechnology activities within 30 days. *Id.*

<sup>180</sup> *See id.*

<sup>181</sup> *See id.* at 34 (citing § II–A–3).

<sup>182</sup> *See* Office of Biotechnology Activities, *Notice Pertinent to the March 2013 Revisions of the NIH Guidelines for Research Involving Recombinant DNA Molecules*, NAT’L INST. OF HEALTH, 13–15 (Sept. 2009), *available at* [http://oba.od.nih.gov/rdna/nih\\_guidelines\\_new.htm](http://oba.od.nih.gov/rdna/nih_guidelines_new.htm).

<sup>183</sup> *See id.* at 13.

<sup>184</sup> The NIH has no enforcement body, so its only enforcement mechanism is withdrawing funding.

confinement standards, the NIH's enforcement mechanisms against noncompliance are to refuse or withdraw funding and/or report research events that may be related to public health to state and local health departments.<sup>185</sup> These tools create reasonable deterrence, but they cannot prevent researchers from performing privately funded experiments under whatever degree of confinement they choose.

*The EPA and the Toxic Substances Control Act:* The amended Toxic Substances Control Act ("TSCA") includes some language providing a significant line of defense against genetically modified organisms, but needs further modification to cover synthetic biology.<sup>186</sup> The TSCA was passed by Congress in 1976 for the EPA to use in response to discontent with the health and environmental impact of chemicals like dioxin and asbestos.<sup>187</sup> The language of the Act allows the EPA to test existing chemicals and control those posing unreasonable risk, and to screen and track new chemicals before they enter the market.<sup>188</sup> Manufacturers are also required to notify the EPA of new chemicals not in their inventory within 90 days.<sup>189</sup> In 1997, the EPA finalized rules that brought genetically engineered organisms under the umbrella of the "new chemicals" regulation of TSCA by deciding that non-natural arrangements of nucleic acids be included in this category.<sup>190</sup> The rules require a special application for environmental release tests called a TSCA Experimental Release Application ("TERA").<sup>191</sup> They also have a notice requirement, or a Microbial Commercial Activity Notification ("MCAN"), that must be submitted 90 days before organisms are produced for a commercial purpose.<sup>192</sup>

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<sup>185</sup> See RODEMEYER, *supra* note 13, at 25.

<sup>186</sup> See *id.* at 35.

<sup>187</sup> See *id.*

<sup>188</sup> See *id.*

<sup>189</sup> See *id.*

<sup>190</sup> See Reporting Requirements and Review Processes for Microorganisms, 40 C.F.R. § 725 (1997).

<sup>191</sup> See RODEMEYER, *supra* note 13, at 35.

<sup>192</sup> See 40 C.F.R. § 725.1.

Although these are beneficial protections for conventionally engineered organisms, the EPA's rule modifications define "intergeneric microorganism" in a way that may preclude synthetic biology from the Act's regulatory scope. "Intergenic microorganism means a microorganism that is formed by the deliberate combination of genetic material originally isolated from organisms of different taxonomic genera."<sup>193</sup> On its face, this does not appear to cover organisms containing lab-synthesized DNA unless they also have gene donors from different taxonomic genera. Although the TSCA's original definition of "new chemical substances" may be broad enough to cover synthetic biology, the newer intergeneric organism rules may have unintentionally exempted *synthetic* organisms from regulation.

In addition, the TSCA's "new chemicals" regulation only covers substances designed for commercial purposes,<sup>194</sup> which would not cover noncommercial laboratory research. In fact, a section specifically exempts from regulation small amounts of chemicals produced for experimentation, analysis, and research for product development.<sup>195</sup> This language formulation clarifies that genetically engineered organisms were not considered in the development of the original Act. The drafter's assumption was likely that a limited amount of an inanimate chemical would have limited health and safety impact. Unlike inanimate chemicals, even a limited number of *organisms* may have extraordinarily broad health and safety implications. The newer intergeneric rules specifically cover laboratory research and development by acknowledging the danger posed by small amounts of organisms,<sup>196</sup> but as previously discussed, many cells containing synthesized DNA and not transgenic DNA would be outside this defined scope.

The EPA also needs to determine methods to sufficiently monitor the activity of companies over which it is supposed to have authority. This is because, currently, the overstretched

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<sup>193</sup> See 40 C.F.R. § 725.3.

<sup>194</sup> See RODEMEYER, *supra* note 13, at 36.

<sup>195</sup> See 15 U.S.C. § 2607(a)(1)(B)(ii) (2013).

<sup>196</sup> See 40 C.F.R. § 725.205 (1997).

agency relies on manufacturers to provide data in order to perform its risk analysis of new chemicals' toxicities.<sup>197</sup> If the company does not have enough information to perform a "reasoned evaluation" of health and safety risks, the company is only required to delay manufacture if it can show that the chemical presents an "unreasonable risk."<sup>198</sup> As Michael Rodemeyer explains, it is unlikely that the EPA can determine an unreasonable safety risk without enough information to perform a reasoned evaluation beforehand. This catch-22 limits the EPA's intervention, which has been demonstrated by the meager total of 16 MCANs submitted to the EPA in the past 10 years.<sup>199</sup>

*The FDA and the Food Drug and Cosmetics Act:* The role of the FDA's regulation of biotechnology concerns a broad range of products and will translate to synthetic organisms with little difficulty. This is because the agency has broad authority to regulate drugs, cosmetics, food, food additives, animal feed, biologics, and medical devices under provisions of the Food, Drug and Cosmetic Act ("FDCA").<sup>200</sup> The FDCA requires that drugs and medical devices be proven safe and effective by the developer before they can be marketed.<sup>201</sup> Once the drug or device moves into the manufacturing stage, the agency still has authority to ensure that current good manufacturing practices are used to prevent drug adulteration.<sup>202</sup> The manufacturer is also required to report to FDA for approval if it changes its manufacturing practices.<sup>203</sup> Thus, if a company trades conventional production for synthetic biology, the FDA will have to certify the switch. At this point, the agency has the authority to impose biosafety standards and measures for worker safety.<sup>204</sup> There is reason to believe they will do so. This is because in the early 1980s, the FDA explicitly

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<sup>197</sup> See RODEMEYER, *supra* note 13, at 37.

<sup>198</sup> See 15 U.S.C. § 2604(e)(1)(A) (2013).

<sup>199</sup> See RODEMEYER, *supra* note 13, at 40.

<sup>200</sup> See 21 U.S.C. § 301 (2013).

<sup>201</sup> See *id.*

<sup>202</sup> See RODEMEYER, *supra* note 13, at 41.

<sup>203</sup> See 21 U.S.C. § 356a (2013).

<sup>204</sup> See RODEMEYER, *supra* note 13, at 41.

recommended that drug and biologic manufacturers using rDNA technology should follow the NIH guidelines regarding biosafety measures.<sup>205</sup>

Although the FDA has no direct authority to require compliance with NIH guidelines for rDNA, it may have the greatest regulatory authority for the present concerns. When synthetic biology plays a commercial role in the development and production of drugs, vaccines, other biologics, or medical devices, the FDA has the power to instigate and enforce the appropriate precautionary measures. If manufacturers do not comply, their products will not be certified for market and if they still attempt to commercialize they can be fined and shut down.<sup>206</sup> The fact that the burden of proof for drug and biologic safety is on the developer is a great boon to the prevention of synthetic biology harms. The direct application of food and drugs to the human body requires the most stringent standards for health and safety; thus, the FDA acts as a filter that products must pass through to get from manufacture to consumption.

## VII. SUGGESTIONS FOR MODIFICATION

Together, the agencies discussed above have complimentary oversight capacity to ensure the safe and effective development of synthetic biology. However, their specific rules and operations need minor modifications to reach this goal. Subpart A will describe how the NIH must employ its powerful funding incentives to restrict financial assistance to well-planned and non-malicious synthetic biology research. Subpart B will describe methods for the EPA to improve auditing of commercial synthetic biology and encourage companies to comply with EPA safety standards. Subpart C will delineate FDA rule modifications that would require explicit plans for containment and control of all synthetic biology development. If followed, this set of modifications would

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<sup>205</sup> See Edward Korwek, *The NIH Guidelines for rDNA Research and the authority of the FDA to require compliance with the guidelines*, 21 JURIMETRICS J. 264, 266 (1981).

<sup>206</sup> See 21 U.S.C. § 331 (2006).

adequately fill U.S. regulatory gaps and should assuage concerns regarding the risks posed by synthetic biology development.

#### A. *NIH Modification*

The NIH's guidelines are not sufficient for addressing all synthetic biology concerns. However, creative options could be employed for effective use of the agency's enforcement tools for bioconfinement. Gene manufacturers and organism retailers could be given the option to register with NIH, and the agency could offer an incentive such as a label of "NIH Certification" to be more attractive to consumers. A corresponding licensing procedure could be implemented that made orders for particularly dangerous organisms, gene fragments, and gene combinations available only to institutions funded by the NIH and approved for particular experiments. The NIH could then refuse to fund genetic research that uses gene products purchased from unregistered manufacturers. Additionally, to address private research the NIH could issue strong recommendations that the biobrick registry and other public databases of genetic information should transition to limited access with sliding scale licensing. The general public would then have access to a basic set of gene codes and researchers could be required to have a security clearance or license to access gene information with increasing danger and complexity.

#### B. *EPA and TSCA Modification*

Simple language addition to the "intergeneric microorganisms" definition in the 1997 rules could cover the gap through which synthetic cells have slipped. Language like "Microorganisms that are formed in whole or in part by laboratory synthesized DNA" would be sufficient to require the tracking and screening of synthetic microbial "chemicals" in laboratory research and development, and in commercial production.

The EPA exempts research that is required to comply with the NIH guidelines or that operates under functionally equivalent biosafety conditions,<sup>207</sup> which provokes two concerns for lab

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<sup>207</sup> See 40 C.F.R. § 725.232 (2011).

confinement regulations. The first was already expressed in the shortcoming of the NIH guidelines; that regulation can be circumvented if companies use outside funding. The second is the incentive created by allowing “functionally equivalent” biosafety procedures. If the EPA’s intent is to streamline authority by covering mostly commercial and/or environmental trial chemical substances and assign laboratory regulations predominantly to the NIH, then it should not leave room for research labs to operate outside of the latter’s framework without providing more specific standards. If the intent is to allow genetic engineering research to occur outside of NIH funding, then the activities of garage biohackers must be considered legal. This may be intentional to encourage innovation, but the EPA cannot put its money where its rules are. Without the ability to track the use of gene fragment combinations and synthetic biology lab equipment, it would be difficult for any organization to adequately monitor private synthetic biology activity, let alone perform “functional equivalence” analysis for every science garage operated by a molecular biology undergrad with a centrifuge and a credit card. Thus, it should not build this kind of safe-space into its rules.

To compensate for the EPA’s inability to monitor the chemical producers for which it is responsible, either one or both of the following modification options should be pursued. The first is to dedicate more resources to the EPA for careful monitoring of companies engaging in synthetic biology production methods. A dedicated staff of data collectors should be able to seek out companies doing synthetic biology production and return information on production methods to an internal EPA review committee. The threat of research audits would encourage companies to submit TERAs and MCANs. The second option is to create financial incentives for companies to willingly provide the EPA with research information. One example might be carbon-offset subsidies in proportion to the potential “greening effect” of safe synthetic cell-based chemical production.<sup>208</sup> If the

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<sup>208</sup> To address the concerns specified in this Article, these standards for “safe” synthetic biology practices would include proof of organism mutation control,



new method demonstrates cleaner and less resource-intensive production in comparison to conventional methods, the EPA can issue certificates that provide tax breaks or direct subsidies. Companies that willingly come forward in this way will allow the EPA to verify the safety of the practice and, thus, reward those companies for transparency and environmental friendliness. Both options should be pursued, but because of financial constraints, the latter should receive greater attention.

### C. *FDA and FDCA Modification*

Because of the FDA's gatekeeper position, it should take a lead role in the establishment of standards for synthetic biology production practices. The secretary of the FDA should promulgate two primary rules. The first should require manufacturers to establish containment capability for the proposed synthetic organism beyond a reasonable doubt in the development of foods, drugs, biologics, and medical devices. This will require demonstration of: (1) designed controls internal to the organism; and (2) laboratory confinement measures. Internally designed controls may include "kill switches," hyper-specific resource requirements preventing cell survival outside of the lab, or natural reproduction-cessation or reproduction-incapacity. Laboratory confinement measures should include standards for sterilization, quarantining, research access limitations during development, and emergency shutdown and termination procedures. The second primary rule should require synthetic biology producers to show that their organisms will perform the desired function, whether as process or as product, with reasonable certainty, without losing substantial efficacy or developing unforeseeable pathogenic attributes. These changes would be a result of mutation, which is very difficult to control.<sup>209</sup> The sections of the FDCA to which

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protection of agricultural community resources, and proof of efficacy greater than reasonable alternatives. These standards should be shared between NIH, EPA, and FDA.

<sup>209</sup> See Edward Cox, *Bacterial Mutator Genes and the Control of Spontaneous Mutation*, 10 ANN. REV. GENET. 135, 135-56 (1976), available at <http://www.annualreviews.org/doi/pdf/10.1146/annurev.ge.10.120176.001031>.

these amendment rules can apply includes § 355-1(f)(1), which allows the Secretary of Health and Human Services to “require that the risk evaluation and mitigation strategy for a drug include such elements as are necessary to assure safe use of the drug, because of its inherent toxicity or potential harmfulness.”<sup>210</sup> These amendments can be supplemented by the FDA’s continued support of the NIH’s guidelines for rDNA, including recognition of uncertainty generated by unprecedented combinations of genes and potentially synergistic effect of even those genes that are considered well-understood.

### VIII. CONCLUSION

Microorganisms controlled by laboratory synthesized DNA are substantially similar to the cell products of gene splicing, but there is a greater need for regulation because of increased uncertainty. Although many transgenic organisms exhibit phenotypes mostly consistent with their non-modified natural counterparts, organisms controlled by synthetic genomes have not been observed over time. As researchers move further away from the natural toward the synthetic, they incur increasing responsibility for understanding genetic expression and gene-environment interaction. The development of synthetic cells as “living factories” must remain behind scientific confidence in genetic understanding. This will require dedicated oversight to ensure that profit motives do not drive the industry prematurely into production, which could compromise health and equal access.

While it is too optimistic to hope for new legislation specific to the concerns produced by synthetic biology, it is not unreasonable to require modifications of existing rDNA regulation. A basic coordinated effort between three appropriate regulatory entities would prevent a serious accident or malicious use of synthetic biology. Each of the three agencies discussed should hone their focus on one aspect of synthetic biology regulation: the NIH on lab confinement and access to information, the EPA on environmental release and commercial production, and the FDA on

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<sup>210</sup> See 21 U.S.C. § 355-1(f)(1) (2006).

human and other animal application products. Each should define the boundaries of their roles by (1) adopting each other's standards where appropriate and (2) delegating oversight tasks just outside of their scope to the most appropriate counterpart without allowing room for ambiguous "functional equivalence." Finally, the United States should adopt an international presence of concern for synthetic biology hazards by joining the Convention on Biological Diversity and supporting the regulation of Living Modified Organisms. These measures, if employed consistently and thoroughly, will promote safe and advantageous development of synthetic biology.

