

Some call synthetic biology an epochal development—the start of a new industrial revolution, the moment humans learned to be gods. Others think it is an incremental advance with an iffy payoff. In these essays, the chair of the Presidential Commission for the Study of Bioethical Issues and participants from a recent Hastings project examine the social challenge it presents.

The Ethics of Synthetic Biology: Guiding Principles for Emerging Technologies

BY AMY GUTMANN

The Presidential Commission for the Study of Bioethical Issues released its first report, *New Directions: The Ethics of Synthetic Biology and Emerging Technologies*, on December 16, 2010.¹ President Barack Obama had requested this report following the announcement last year that the J. Craig Venter Institute had created the world's first self-replicating bacterial cell with a completely synthetic genome. The Venter group's announcement marked a significant scientific milestone in synthetic biology, an emerging field of research that aims to combine the knowledge and methods of biology, engineering, and related disciplines in the design of chemically synthesized DNA to create organisms with novel or enhanced characteristics or traits. Intense media coverage followed. Within hours, proponents and critics made striking claims about the discovery—ranging from “Frankencell” to the idea of humans “creating life”—often invoking the kind of eye-catching terms that heighten interest, and anxiety, about risks and benefits.

The commission had a unique opportunity to contribute proactively to a field of scientific inquiry that is relatively young. While the synthetic genome is a significant

technical achievement, synthetic biology as a field is still in its early stages. Its most promising potential benefits and most worrisome risks are not yet upon us, allowing time for efforts to publicly consider and recommend safe development of this field for the good of all.

The president gave the commission six months to review this emerging science and produce recommendations “to ensure that America reaps the benefits of this developing field of science while identifying appropriate ethical boundaries and minimizing identified risks.”² This task fit the commission's mandate to identify and promote “policies and practices that ensure scientific research, healthcare delivery, and technological innovation are conducted in an ethically responsible manner.”³ It also offered the opportunity for the commission to convene in an open and public forum to encourage reasoned deliberation and consideration of public issues, including the impact of new technologies on our collective human well-being and our responsibilities to the environment.

The commission considered the potential risks and benefits of the field, reviewed the technology in the context of essential conceptions of human agency and life, as well as the human relationship to nature, and unanimously concluded that the field of synthetic biology does not require new regulation, oversight bodies, or a moratorium on advancing research *at this time*. But these concerns, along with uncertainties about how the field may develop in the future, were central to the commission's unanimous conclusion that responsible stewardship requires that existing federal agencies conduct an ongoing and coordinated review of the field's risks, benefits, and moral objections as it matures.

The commission calls this strategy “prudent vigilance.” Some commentators mistook these conclusions as a pass on any restraint of this emerging science.⁴ Rather, the commission called not only for more coordinated agency oversight and monitoring of risks and benefits, but also for experts and policy-makers to actively and openly engage in public dialogue as the science evolves, so that all concerned citizens can understand and offer their own perspectives on what lies ahead. The commission worked to model such public outreach in its

Amy Gutmann, “The Ethics of Synthetic Biology: Guiding Principles for Emerging Technologies,” *Hastings Center Report* 41, no. 4 (2011): 17-22.

deliberations, and in its conclusions underlined the responsibility of experts, policy-makers, and federal agencies to carry forward this critical work of public feedback, education, and outreach.

The Commission's Deliberations

The commission held meetings in Washington, D.C., Philadelphia, and Atlanta that provided opportunities for its members to deliberate publicly and to hear from nearly three dozen invited experts on scientific, ethical, and policy aspects of synthetic biology and its applications. At each meeting, time was set aside for public comments, and the commission heard a range of perspectives on the future of synthetic biology. Several dozen additional public comments were received in writing following published requests for comment from the commission.

The guests who spoke at our meetings and the public comments that we received highlighted the remarkable potential benefits that synthetic biology may yield for human health, energy, agriculture, and other areas. They also discussed the range of risks associated with research and commercial development of these advances and the significant uncertainty regarding both the likelihood and magnitude of those risks and benefits.

Most previous and ongoing analysis of synthetic biology has examined specific policy and ethical issues, focusing, for example, on the evaluation of risks and benefits and strategies to optimize that balance.⁵ Some other work has looked at the field more broadly and begun analyzing the fundamental concerns that it may raise by considering the work in the context of essential conceptions of human agency and life; its overall impact on biodiversity, ecosystems, or food and energy supplies; and its impact on the balance between humans and nature.⁶ Some of this research extends beyond issues unique to synthetic biology to concerns common among emerging technologies or for biotechnology overall.

Since much of this broader analysis is still in its infancy, President Obama's request gave the commission an exceptional opportunity to look forward instead of to merely react, and to lead a proactive review of this emerging field. The commission aimed to learn from the collective insights of the ongoing research in the science and ethics of synthetic biology and to consider how best to translate these at times conflicting perspectives into actionable recommendations for the federal government. In light of the parallels between the ethical issues raised by synthetic biology and those of emerging technologies generally, the commission developed a set of basic principles that may be applicable to the ethical analysis of all emerging technologies, including those already present and others that develop in the future.

Principles for Assessing Emerging Technologies

The commission found many efforts to shape policy, governance, and regulation related to synthetic biology, but

few examples of a broad-based ethical framework upon which to base such proposals. We identified five ethical principles relevant to the social implications of synthetic biology and other emerging technologies and used these to guide our evaluation of the current state of synthetic biology and its potential risks and benefits, as well as our policy recommendations.

The guiding principles are: (1) public beneficence, (2) responsible stewardship, (3) intellectual freedom and responsibility, (4) democratic deliberation, and (5) justice and fairness. These principles are intended to serve as provisional guideposts subject to refinement, revision, and comment.

Public beneficence. The ideal of public beneficence is to act to maximize public benefits and minimize public harm. This principle encompasses the duty of a society and its government to promote individual activities and institutional practices, including scientific and biomedical research, that have great potential to improve the public's well-being. In the case of emerging technologies, this improvement may be by means of providing improved or more widely available forms of medical and health care, food, shelter, transportation, clothing, and eco-friendly fuel, along with other means of improving people's lives. Scientific and technological discoveries often have the added potential of increasing economic opportunities, which also redound to the public good.

The principle of beneficence should be applied beyond the individual level—the focus of beneficence in the *Belmont Report*—to the institutional, community, and public levels, while not overlooking possible harms and benefits to individuals.⁷ Policy-makers should adopt a societal perspective when deciding whether to pursue particular benefits of emerging technologies in the face of risks and uncertainty. If considering whether to restrict these pursuits, a similar examination of community interests and potential positive and negative impacts is essential. When seeking the benefits of synthetic biology and other emerging technologies, public beneficence requires the public and its representatives to be vigilant about harms and prepared to revise policies that pursue potential benefits with insufficient attention to risks.

Responsible stewardship. Among living beings, humans are in a unique position to be responsible stewards of nature, the earth's bounty, and the world's safety. Responsible stewardship recognizes the need for citizens and their representatives to think and act collectively for the betterment of all, especially those who cannot represent themselves. Benefits and risks extend to current and future human generations, nonhuman species, and the environment, each with unique needs and vulnerabilities. Emerging technologies present particularly profound challenges for responsible stewardship because our understanding of the potential benefits and risks is incomplete, preliminary, and uncertain. The possibility of intentional misuse by malicious actors further complicates efforts to respond adequately to benefits and risks.

Responsible stewardship addresses these varied challenges by calling for actions that embrace potential benefits while simultaneously mitigating risks over time and across populations. It calls for broader risk-benefit discussions than

would typically be required based on a concern for public beneficence alone. The principle of responsible stewardship rejects two extreme approaches: an extreme action-oriented approach that pursues technological progress without limits or due regard for public or environmental safety, and an extreme precautionary approach that blocks technological progress until all possible risks are known and neutralized. While the action-oriented approach is irresponsibly brazen, the precautionary approach is overly wary. Both fail to carefully assess the most likely and significant benefits against the most likely and significant harms. Through the development of agile, measured oversight mechanisms, responsible stewardship rejects positions that forsake potential benefits in deference to absolute caution and positions that ignore reasonably foreseeable risks to allow unfettered scientific exploration.

This principle is applied to emerging technologies through open decision-making processes informed by the best available science. Responsible stewardship calls for “prudent vigilance”: establishing processes for assessing likely benefits along with safety and security risks both before and after projects are undertaken. A responsible process will continue to evaluate safety and security as technologies develop and diffuse into public and private sectors, and will also include mechanisms for limiting their use when indicated.

Prudent vigilance does not demand extreme aversion to all risks. Not all safety and security questions can be definitively answered before projects begin, but prudent vigilance does call for ongoing evaluation of risks along with benefits. The iterative nature of this review is a key feature of responsible stewardship. It recognizes that future developments demand that decisions be revisited and amended as warranted by additional information about risks and potential benefits.

Intellectual freedom and responsibility. Democracies depend on intellectual freedom, coupled with the responsibility of individuals and institutions to use their creative potential in morally responsible ways. Sustained and dedicated creative intellectual exploration is critical for expanding the boundaries of human knowledge and achievement, developing innovative technologies that can compete in the global marketplace, and fostering collaborations among industry, academia, and government that yield useful products, tools, and policies. While some potentially beneficial emerging technologies could also be put to malevolent “dual use,” these risks alone are generally insufficient to justify limits on intellectual

freedom. Public policy must promote the creative spirit of scientists and unambiguously protect their intellectual freedom because creative and complex intellectual explorations, sustained over time, promote scientific and technological progress.

At the same time, the history of science is sadly full of examples of intellectual freedom exercised without responsibility, resulting in appalling affronts to vulnerable populations, the environment, and the ideals of science itself. Scientists who act irresponsibly are capable of harming not only themselves and other individuals, but also their communities, their nations, and international relations.

As a corollary to the principle of intellectual freedom and responsibility, the commission endorsed a principle of *regulatory parsimony*, recommending only as much oversight as is truly necessary to ensure justice, fairness, security, and safety while pursuing the public good. Regulatory parsimony is especially important in emerging technologies—still in formation by their very definition—where the temptation to stifle innovation on the basis of uncertainty and fear of the unknown is particularly great. The blunt instruments of statutory and regulatory restraint may not only inhibit the distribution of new ben-

efits, but can be counterproductive to security and safety by preventing researchers from developing effective safeguards. With sufficient freedom to operate, tomorrow’s achievements may render moot the risks of today.

Democratic deliberation. The principle of democratic deliberation reflects an approach to collaborative decision-making that embraces respectful debate of opposing views and active participation by citizens. It calls for individuals and their representatives to work toward agreement whenever possible and to maintain mutual respect when it is not. At the core of democratic deliberation is an ongoing, public exchange of ideas, particularly regarding the many topics—in science and elsewhere—in which competing views are advocated, often passionately. A process of active deliberation and justification promotes an atmosphere for debate and decision-making that looks for common ground wherever possible and seeks to cultivate mutual respect where irreconcilable differences remain. It encourages participants to adopt a societal perspective over individual interests.

Importantly, democratic deliberation recognizes that while decisions must eventually be reached, those decisions need not (and often should not) be permanently binding,

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particularly when subsequent developments warrant additional examination. An ongoing and dynamic deliberative process recognizes the importance of challenging previously reached conclusions in light of new information and is by its very nature able to correct the inevitable mistakes that arise in collective decision-making.

The principle of democratic deliberation is particularly well suited to the assessment of emerging technologies. These fields offer the promise of remarkable potential benefits to science and society, yet they also raise risks regarding unintended consequences or possible malicious use. Each of these areas is clouded by uncertainty and incomplete information, complicating efforts to promote innovation while minimizing the likelihood of harm. Finding this balance demands careful ongoing review of the science and its applications. It presents an ideal opportunity for broad engagement and dialogue among the scientific community, policy-makers, and the citizenry, both by fostering conversation and debate among scientific and policy experts and by spurring meaningful outreach and education for the lay public.

Justice and fairness. The principle of justice and fairness relates to the distribution of benefits and burdens across society. Emerging technologies like synthetic biology affect all persons, for good or ill. Society as a whole has a claim toward reasonable efforts on the part of both individuals and institutions to avoid unjust distributions of the benefits, burdens, and risks that such technologies bring. This same claim extends internationally to all those who may be affected—positively or negatively—by synthetic biology and its applications. A fundamental principle of fairness suggests that society should seek to ensure that the benefits and burdens of new technologies are shared as much as possible.

A commitment to justice and fairness is a commitment to ensuring that individuals and groups share in the benefits of new technologies and that the unavoidable burdens of technological advances do not fall disproportionately on any particular individual or group. Technological innovation benefits from public investment and from societal contribution toward safe and supportive research environments, and so it is reasonable that society expects a return on that investment.

Justice and fairness extend not only from individual societies to their constituents but also from individual societies to the international community overall. Emerging technologies can and likely will have global impacts. For that reason, every nation has a responsibility to champion fair and just systems to promote the widest availability of information, the broadest distribution of beneficial technologies, and the most expansive culture of responsibility for biosafety and biosecurity.

Applying These Principles to Synthetic Biology

The commission's development of an ethical framework concurrently with its specific policy recommendations differs from the approach of earlier bioethics advisory bod-

ies, which formulated principles and conclusions only after several years of study and debate. By taking this approach, the commission encouraged constructive public debate by making explicit the values underlying particular policy recommendations.

The extraordinary promise of synthetic biology to create new products for clean energy, pollution control, and medicine; to revolutionize chemical production and manufacturing; and to create new economic opportunities comes with a concurrent duty to attend carefully to potential risks, be responsible stewards, and consider thoughtfully the implications for humans, other species, nature, and the environment. While future developments may raise further objections, the commission unanimously recommended that no additional federal regulations or a moratorium on work in this field be enacted at this time. Instead, the commission urged ongoing government monitoring and dialogue between the private and public sectors.

The commission's eighteen recommendations are organized according to the five ethical principles outlined earlier. While many of the recommendations are directed to the federal government, our report also highlights the role of citizens and experts, including the absolutely critical role of the scientific community in promoting an environment that allows emerging biotechnologies to flourish yet remains sensitive to known and anticipated risks.

Among the recommendations arising from the principle of public beneficence are a coordinated review of public funding for synthetic biology research (including research on ethical and social issues) and an examination to ensure that research licensing and sharing policies are sufficient to promote innovation.

Working from the principle of responsible stewardship, the commission endorsed neither a moratorium on synthetic biology until all risks are identified and mitigated, nor unfettered freedom for scientific exploration. Instead, the commission embraced a middle ground—an ongoing process of prudent vigilance that carefully monitors, identifies, and mitigates potential and realized harms over time. To promote clarity, coordination, and accountability across the government, the commission recommended that the Executive Office of the President lead an interagency process to evaluate existing oversight authorities and ensure that the government remains informed of developments, risks, and opportunities as this field grows. In light of the interdisciplinary character of synthetic biology, ethics education similar or superior to the training required today in the medical and clinical research communities should be developed and required for all researchers and student-investigators outside the medical setting, including in engineering and materials science.

The commission recommended revisiting the moral objections to synthetic biology as the field advances, but we were not persuaded that synthetic biology currently fails to respect the proper relationship between humans and nature. The commission believes that opposition to synthetic

biology on such grounds alone does not adequately reflect the relationship of the technology to previous scientific activities and the current limited capabilities of the field.

The question relevant to the commission's review of synthetic biology was whether this field brings unique concerns that are so novel or serious that special restrictions are warranted at this time. Based on our deliberations, the commission concluded that special restrictions are not needed, but that prudent vigilance can and should be exercised. As our ability to engineer higher-order genomes using synthetic biology grows, other deliberative bodies ought to revisit this conclusion.

Recommendations based on the principle of intellectual freedom and responsibility direct the government to support a continued culture of responsibility among individual researchers and research institutions, coupled with institutional monitoring, enhanced watchfulness, and the expanded application of relevant regulations, if necessary. Also recommended are periodic assessments of safety and security risks and the applicability of current oversight practices.

The importance of ongoing dialogue is central to the commission's recommendations related to democratic deliberation. These recommendations endorse continued exchanges among scientific, religious, and civil society groups as synthetic biology develops, and they call on all individuals and groups to describe the capabilities and limitations of the field accurately and clearly. To further promote public education and discourse, we support the creation of a privately managed online tool to check the veracity of public claims regarding advances in synthetic biology. These activities would be enhanced by comprehensive programs to improve scientific and ethical literacy among all age groups, regarding both synthetic biology and science generally.

From the principle of justice and fairness, the commission recommends an evaluation of current requirements and alternative models to ensure that the risks of research in synthetic biology—including for human subjects and other affected parties—are not unfairly or unnecessarily distributed. A companion recommendation encourages manufacturers and others seeking commercial applications for synthetic biology to manage risks and potential benefits to communities and the environment so that the most serious risks, including long-term impacts, are not unfairly or unnecessarily borne by certain individuals, subgroups, or populations. These groups

should strive to make available the important advances that may result from this research to those individuals and populations who could most benefit from them.

Bioethics Commissions and Public Dialogue

Only with an ongoing, open, and well-informed discourse can our society realistically hope to reap the benefits of scientific progress with due regard for the serious concerns that new biotechnologies always raise. Without an open and well-informed dialogue, we risk grave harm, not least to the public support upon which the scientific enterprise is built.

While by no means a substitute for robust, ongoing exchanges among citizens, the scientific community, and policy-makers, the commission's deliberations on this matter sought to provide an inclusive forum for discussion. Our hope is that the commission's recommendations will be a catalyst for future deliberations among other groups interested in synthetic biology.

To that end, the commission was pleased by the interest in and reactions to our report following its release in December 2010. Stakeholder individuals and groups—including university-based scientists, biotechnology firms,

bioethicists, religious organizations, and others—responded largely favorably to the commission's assessment and recommendations. Early reactions to the principle of prudent vigilance as an appropriate approach to the ongoing assessment of the risks and benefits of synthetic biology were similarly positive overall, coming from individuals and groups representing a range of perspectives regarding biotechnology and its regulation.

A coalition of civil society organizations was more skeptical of the merits of prudent vigilance. In comments to the media and in an open letter to the commission and government officials, these groups argued that the precautionary principle ought to guide the regulation of synthetic biology.⁸ Based on certain conceptions of the precautionary principle, these groups advocate “a moratorium on the release and commercial use of synthetic organisms until a thorough study of all the environmental and socio-economic impacts of this emerging technology has taken place.”

Throughout its work, the commission was particularly sensitive to ensuring that the government remains attentive to the risks related to synthetic biology, including risks that may emerge as the field matures. It concluded that an

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approach characterized by prudent vigilance allows policymakers to continue assessing safety and security as technologies develop, and to include mechanisms for limiting their practical applications and use when necessary. Prudent vigilance shares with the precautionary principle a concern for identifying and mitigating risks. However, it advocates continued progress in the pursuit of potential benefits in tandem with that ongoing sensitivity to risks and the development of appropriate responses. The commission believes that prudent vigilance will prove to be a valuable approach to the assessment of risks related to synthetic biology and other emerging technologies. We welcome ongoing debate and discourse in light of existing literature on the precautionary principle and conventional risk analysis practices.

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2. Letter from President Barack Obama to Dr. Amy Gutmann, Chair, Presidential Commission for the Study of Bioethical Issues, May 20, 2010, <http://bioethics.gov/documents/Letter-from-President-Obama-05.20.10.pdf>.

3. Executive Order no. 13521, "Establishing the Presidential Commission for the Study of Bioethical Issues," *Federal Register* 74, no. 228 (November 30, 2009), <http://www.bioethics.gov/documents/Executive-Order-Establishing-the-Bioethics-Commission-11.24.09.pdf>.

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Staying Sober about Science

BY ROB CARLSON

Biology, we are frequently told, is the science of the twenty-first century. Authority informs us that moving genes from one organism to another will provide new drugs, extend both the quantity and quality of life, and feed and fuel the world while reducing water consumption and greenhouse gas emissions. Authority also informs that novel genes will escape from genetically modified crops, thereby leading to herbicide-resistant weeds; that genetically modified crops are an evil privatization of the gene pool that will with certainty lead to the economic ruin of small farmers around the world; and that economic growth derived from biological technologies will cause more harm than good. In other words, we are told that biological technologies will provide benefits and will come with costs—with tales of both costs and benefits occasionally inflated—like every other technology humans have developed and deployed over all of recorded history.

Rob Carlson, "Staying Sober about Science," *Hastings Center Report* 41, no. 4 (2011): 22-25.