

The Principles for the Oversight of Synthetic Biology

The undersigned, a broad coalition of civil society groups, social movements, public interest, environmental, human rights, religious and labor organizations concerned about various aspects of synthetic biology's human health, environmental, social, economic, ethical and other impacts, offer the following declaration, The Principles for the Oversight of Synthetic Biology.

Executive Summary

Synthetic biology, an extreme form of genetic engineering, is developing rapidly with little oversight or regulation. A strict adherence to the Precautionary Principle is fundamental in guaranteeing the safe development of synthetic biology. A precautionary approach requires mandatory, synthetic biology-specific oversight mechanisms to account for the unique characteristics of synthetic organisms and products of synthetic biology. Within those mechanisms, ensuring public health, worker safety and ecosystem resilience requires a committed focus on critical risk research and immediate action to mitigate potential exposures until safety is demonstrated. Protection of the public includes a ban on using synthetic biology to manipulate the human genome in any form. Decisive action must also be taken to protect the environment and human health, and to avoid contributing to social and economic injustice. Developers and manufacturers must be responsible for the safety and effectiveness of their processes and products, and must retain liability for any adverse impacts. Throughout, oversight must be transparent and provide public access to information regarding decision-making processes, safety testing and products. Open, meaningful and full public participation at every level is essential and should include consideration of synthetic biology's wide-ranging effects, including ethical, social and economic.

This document outlines the following principles necessary for the effective assessment and oversight of the emerging field of synthetic biology:

- I. **Employ the Precautionary Principle**
- II. **Require mandatory synthetic biology-specific regulations**
- III. **Protect public health and worker safety**
- IV. **Promote environmental protection**
- V. **Guarantee the right-to-know and democratic participation**
- VI. **Require corporate accountability and manufacturer liability**
- VII. **Protect economic and environmental justice**

Governmental bodies, international organizations and relevant parties must immediately implement strong precautionary and comprehensive oversight mechanisms enacting, incorporating and internalizing these basic principles. Until that time, there must be a moratorium on the release and commercial use of synthetic organisms and their products to prevent direct or indirect harm to people and/or the environment.ⁱ

Introduction

"Synthetic biology" practitioners begin with computer-assisted biological engineering to design and attempt to construct new biological organisms or biological building blocks, or to redesign existing biological organisms. In building new life forms from scratch using published gene sequence information or by buying inexpensive, made-to-order DNA strands from so-called DNA foundries, synthetic biologists are not just reading and rearranging genetic code, but *writing* it. Synthetic biology is "extreme genetic

engineering” — re-engineering and designing genes and creating entire genomes that do not exist in nature.

Governments, universities, research institutes and corporations around the world are now racing to develop and commercialize products using synthetic biology. Synthetic biologists have already synthesized working viruses, including the 1918 influenza virus and the poliovirus. In May 2010, the J. Craig Venter Institute announced that its lab had built the first synthetic, self-replicating bacterial cell — that is, researchers inserted an entirely synthetic genome, which did not match the DNA sequence of any natural genome, into a working cell; the cell accepted the synthetic genome and reproduced. This technical feat is a wake-up call to governments around the world.

Despite industry claims that these technologies are safe, this new technological frontier poses significant health, safety and environmental hazards, as well as profound social, economic and ethical challenges.

The technical ability to synthesize DNA and create synthetic organisms far outpaces our understanding of how these novel products may work. Even engineering supposedly simple organisms could have major ecological and health effects. This unpredictability makes the task of precautionary risk assessment that much more difficult, but also even more necessary. Research on the effects of these new technologies and synthetic biology-specific regulations must keep pace with the technologies’ development. Commercializing synthetic biology at this stage is premature.

The risks of releasing synthetic organisms into the environment — intentionally or unintentionally — have barely begun to be defined, and the urgently needed ethical, legal and regulatory oversight mechanisms have yet to be developed. Without proper safeguards, we risk letting synthetic organisms out of the laboratory with unknown potential to disrupt ecosystems, threaten human health and undermine social, economic and cultural rights.

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The Principles

I. Employ the Precautionary Principle

The Precautionary Principle must be applied to synthetic biology because the risks of the technology are inherently unpredictable with potentially far-reaching and irreversible impacts. The Precautionary Principle, integrated into many international conventionsⁱⁱ and national laws, is aptly described in the Wingspread Consensus Statement on the Precautionary Principle:

“When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. In this context the proponent of an activity, rather than the public, should bear the burden of proof. The process of applying the Precautionary Principle must be open, informed and democratic and must include potentially affected parties. It must also involve an examination of the full range of alternatives, including no action.”ⁱⁱⁱ

Applying the Precautionary Principle to the field of synthetic biology necessitates a **moratorium on the release and commercial use of synthetic organisms, cells, or genomes** until:

- Governmental bodies, with full participation of the public, have conducted proper risk assessments.
- The health, environmental and socio-economic risks of synthetic biology are fully known and strategies for mitigating those risks are in place.
- National and international oversight and security mechanisms equipped to keep pace with the risks are in place.

The Cartagena Protocol on Biosafety provides guidelines for the safe handling, transport and use of any living modified organism.^{iv} The 193 nations that are Parties to the UN Convention on Biological Diversity agreed at their 10th Conference that the release of synthetic biology’s products requires precaution. The agreement from the 10th Conference of the Parties reads:

“Parties and other Governments [are] to apply the precautionary approach in accordance with the Preamble to the Convention, and the Cartagena Protocol, to the introduction and use of living modified organisms for the production of biofuels as well as to the field release of synthetic life, cell, or genome into the environment, acknowledging the entitlement of Parties, in accordance with domestic legislation, to suspend the release of synthetic life, cell, or genome into the environment.”^v

Additionally, the CBD agreed to study further the risks this technology poses to the environment, biodiversity, livelihoods and human health.

II. Require mandatory synthetic biology-specific regulations

Implementing enforceable and prosecutable synthetic biology-specific regulations must be a prior condition for future developments in synthetic biology. Such regulations should complement and **strengthen**, not replace, any other applicable regulations, such as worker protections, environmental regulations, drug laws and restrictions on pathogens, among others.

Voluntary, self-regulation by practitioners is not a substitute for synthetic biology-specific regulations enacted by governments and international treaties. Self-regulation does not allow for oversight or public participation, diminishes transparency and does not provide recourse in the event of worker/public health accidents, environmental disruption or economic harms.

Different methods and techniques of synthetic biology will need different forms and levels of oversight. Therefore risk assessments and regulations must be tailored to fit specific applications, uses and

products. Furthermore, assessments should include full comparative consideration of alternative approaches.

Regulations should specify civil and criminal penalties for violations. Penalties should be imposed for failure to obtain proper licenses, failure to adhere to laboratory standards, unauthorized release of synthetic DNA, RNA, or synthetic organisms, failure to train and equip workers, exposing workers to harm and failure to report adverse incidents to government authorities.

The absence of mandatory synthetic biology-specific regulations necessitates a moratorium on release and commercialization of synthetic organisms, cells or genomes.

III. Protect worker safety and public health

Adequate and effective synthetic biology oversight requires an immediate emphasis on preventing known and potential human exposures to synthetic organisms not proven safe.

Workers in synthetic biology laboratories will likely be the first to be exposed to any potential hazards. Existing workplace safety procedures and laws must be augmented to take into account the unique risks and challenges to human health posed by organisms created through synthetic biology. Many of the organisms engineered through synthetic biology (e.g., algae) are easily aerosolized and can easily be inhaled and escape confinement. Because these products are imperceptible, workers could unknowingly carry them out of the workplace and into the broader community. Protocols must be in place and strictly adhered to in order to ensure that synthetic organisms and their products are adequately contained.

The public must be informed if such work is being conducted in their community. Workers and the public must be informed of the risks involved with synthetic biology and those working with synthetic organisms must generate clear and reliable means to track, disable and/or destroy strains as a prerequisite to carrying out experiments with them.

Additionally, workers should be allowed to refuse work without fear of retaliation or termination if they report safety concerns regarding the use of synthetic biology products and associated technologies. Workers must have access to qualified safety representatives with whom health and environmental safety concerns can be disclosed and subsequently assessed.

Occupational medical and exposure records must be available to workers and their representatives immediately upon request and disclosure of such records cannot be withheld as confidential business or trade secret information.

All employees must be notified at the time synthetic biological products are being used within their immediate vicinity or anywhere within their laboratory or workplace.

All containment failures, worker injuries and illnesses, and human exposures must be documented and reported to the proper workplace safety authorities and details must be available upon request. The public must have prompt access to full and complete accident reports on government web sites, including specific locations of accidents and synthetic constructs or organisms involved, with the sole exemption being personal medical information.

The environmental and health risks of synthetic organisms and their products must be assessed and disclosed prior to any release or commercial use. Continued systematic disclosure of health and safety information throughout the lifecycle of the organism and its products is necessary to help people protect themselves, improve oversight of government and industry decisions, and encourage development of safer alternatives.

The use of synthetic biology to change the human genetic makeup — including the human genome, epigenome and human microbiome — must be prohibited.

The convergence of synthetic biology with other technologies such as gene transfer through viral, nanomaterial or stem cell vectors make the possibility of altering the human genome even more troubling. Any alterations to the human genome through synthetic biology — particularly inheritable genetic changes — are too risky and ethically fraught with concerns.

IV. Protect the environment

Synthetic biology requires the strictest levels of physical, biological and geographic containment as well as independent environmental risk assessment for each proposed activity or product.

Synthetic biology's environmental risks are unknown. In order to identify potential environmental risks and regulatory gaps, governments must require that pre-market environmental impact and lifecycle risk assessments are conducted for each distinct synthetic organism, each synthetic construct and the products derived from synthetic organisms and constructs.

The capacity of each synthetic organism to survive in the environment and reproduce must be known before any such organisms leave the laboratory. Unlike most other environmental contaminants that become more diffuse over time, synthetic organisms are designed to reproduce and will evolve. Once released into the environment, these organisms may be impossible to recall or eliminate.

When synthetic organisms are released into the environment, either intentionally or unintentionally, they could find an ecological niche and become a new invasive species that disrupts ecosystems. Moreover, the ability of many microorganisms to take up DNA from living and even dead organisms means that synthetic DNA can be spread in the environment even after the synthetic organism dies.

Confinement strategies for preventing the release of synthetic organisms into the biosphere must include:

- 1) Means to prevent the whole organism, and its components, from entering and surviving in a receiving environment.
- 2) Means to prevent gene contamination from the synthetic organism to 'wild' or naturally occurring organisms.

Adequate containment must include:

- 1) Physical containment to keep the synthetic organism from entering the environment.
- 2) Geographical containment that only allows growing an organism in a location where it cannot survive in the surrounding environment if it escapes. This also includes locating facilities outside

earthquake fault zones, coastal zones where tsunamis or strong storms could damage the facility, or in flood plains.

- 3) Biological containment to inhibit the movement of the synthesized organisms, to inhibit the ability of the organism to reproduce outside a contained system, to prevent reproduction once it enters the environment, and to prevent expression of synthesized genetic constructs in other wild-type organisms in the environment.

Some proponents have suggested relying on methods of biological containment originally designed for genetically engineered plants and animals, such as so-called “suicide genes” and other types of self-destruction technologies. These methods are no substitute for physical, geographical and biological containment designed to prevent the release of synthetic organisms. Scientists who have studied “terminator technologies” in seeds have concluded that they are not failsafe. Frequently occurring mutations allow organisms to overcome the intended sterilization thereby allowing those organisms to remain viable. Specifically, “suicide genes” and other genetic use restriction technologies represent an evolutionary disadvantage; selective pressures will lead organisms to overcome intended biological constraints.^{vi} Attempts to develop alternative genetic systems (such as xenobiology¹, mirror biology² or novel amino acids³) are not well enough understood to claim they provide safety. They should not be tested outside the laboratory.

Importantly, the UN Convention on Biological Diversity has mandated an international moratorium on the use of “terminator technologies” such as “suicide genes,” and other genetic use restriction technologies, which has been in place for the past decade. Reliance on an unproven technology that has been deemed unacceptable by 193 nations as a principal method to “contain” synthetic organisms is irresponsible and legally dubious.

Additionally, the intentional release of synthetic organisms into the environment for such things as bioremediation or other applications must be prohibited.

The failure to prioritize (e.g., properly fund) environmental impact research allocated for risk-relevant research^{vii} necessitates a moratorium on the release and commercial use of synthetic organisms, cells or genomes into the environment.

V. Guarantee the right-to-know and democratic participation

Full and comprehensive public and worker participation should be provided throughout the decision-making processes involving synthetic biology.

¹ Xenobiologists explore the possibility that life might be created without relying on carbon or water or using the 20 usual amino acids found in life on Earth.

² Mirror biology is a biology based on the mirror image of amino acids. Mirror image molecules were not at first thought to be a problem. That is why the 1960s controversy over the anti-nausea drug thalidomide was such a surprise—the right-handed version calmed morning sickness in pregnant women, but the left-handed version caused birth defects.

³ Chemists long have been aware of literally hundreds of amino acids in addition to the normal 20 that make up all protein molecules coded by DNA in biology.

Information about human health and environmental effects must be communicated throughout the complete stream of commerce so that all users of products of synthetic biology know the hazards of the organisms and products they use.

Researchers and companies seeking approval for development and commercialization of any products derived from synthetic biology must provide government agencies with the necessary testing to detect synthetic organisms in the case of unintended release or exposure. In addition to requiring synthetic biology researchers to report their activities in detail to the communities in which they work, to their national governments, and publicly on the Internet, researchers must also develop protocols for destroying the organisms when the research is completed and report the results to their communities and nations.

All accidental releases into air, water or soil should be reported to the local community and national authorities promptly and contact information for such reporting must be prominently posted in all laboratories and facilities. Safety data should be available for public inspection on websites and reported to public bodies.

All containers holding synthetic organisms should be clearly labeled. Mandatory labeling will help governments track these synthetic organisms. Products, including medicines, vaccines, biofuels and other industrial materials created through synthetic biology should be labeled at all phases — in the lab, while in transport and, if commercialized, on the physical products. Marketing materials and advertisements for these products must state that they are products of synthetic biology.

Closely linked with the right-to-know is our essential right-to-participate in decisions about environmental and societal hazards that affect our lives.

The public must have the legally enforceable right to halt dangerous applications, not just comment after decisions have been made. Governments must provide meaningful involvement for the public and workers throughout the decision-making process related to the development of synthetic biology and the products of synthetic biology. This includes making sure that communities have access to independent scientific and legal opinions on the proposed projects. Opportunities for participation in decisions on synthetic biology should not be narrowed to only scientific input. Other forms of knowledge including traditional knowledge as well as analysis of cultural, legal, social and economic considerations should also carry weight in decision-making processes.

These processes must be open, facilitating equal input from all interested and affected parties around the globe including and especially:

- 1) Communities that could be impacted — especially poor communities where many of the first commercial facilities using synthetic organisms will be located.⁴
- 2) Labor unions and workplace safety groups concerned about exposure.
- 3) Communities concerned about feedstock procurement, land use and other social, economic and cultural implications (See Principle VII below).

⁴ For example, Amyris Biotechnologies is currently raising synthetic yeast for the production of biofuels and cosmetics in Brazil. This is to have access to large amounts of cheap sugarcane to feed their yeast.

The use of synthetic biology techniques to develop drugs and vaccines is already underway. Data on any health effects from these techniques cannot be considered “confidential business information” by companies and researchers. Additionally, long-term, follow-up studies of patients taking synthetic biology-derived medicines or therapies must be mandatory and there must be full disclosure of all the material facts from these studies.

VI. Require corporate accountability and manufacturer liability for all products of synthetic biology

Those using synthetic biology must be financially and legally accountable for any harm to public, worker health or the environment.

For a product produced through synthetic biology to be placed on and remain in the market, manufacturers must provide all available safety information about the synthetic organism and its products. The information must be sufficient to permit a reasonable evaluation of the safety of the synthetic organism for human health and the environment, including hazard, use and exposure information. This means that if there are no data, the product should not be on the market. Prior to regulatory approval of the products of synthetic biology, developers must demonstrate that they are able to accept the financial and legal liability that could come from manufacture, use and disposal of their products.

Developers of synthetic biology and their funders must establish financial mechanisms, even at the research stage, to assure that adequate funds are available to mitigate and compensate for health, worker or environmental damages. If commercial insurers are unwilling to provide insurance for this purpose, governments should not insure the developers of synthetic biology. If the risk is too great for private investors, it is too great for the public.

Synthetic biology companies should bear the cost of producing accurate environmental and health safety information. This information must be a precondition for products intended for marketing and before significant quantities of a product are manufactured to assist in protection of workers. Industry should produce data on the earliest phases of the research and development of its products, but full assessments on health and safety should be generated and conducted by governments or independent laboratories at industry expense to ensure the information is publically available and reliable. Strict standards that prohibit conflicts of interest should be maintained in the oversight of synthetic biology research, including but not limited to prohibiting persons with financial interests in synthetic biology research, development and commercialization from roles in its health and safety oversight.

VII. Protect economic and environmental justice

It is necessary to ensure that the development of synthetic biology does not deepen economic and social injustices.

The impacts that synthetic biology could have on ecosystems and communities in the global South are of special concern. At present, most commercial interest in synthetic biology is focused on enabling a new “biomass-based” economy in which any type of plant matter can be used as feedstock for tailored synthetic microbes to transform into high value commercial products — anything from fuels to plastics or industrial chemicals. As major industries shift to biomass-derived feed stocks, larger and larger

quantities of plant material will be required. Biomass to feed synthetic microbes will be extracted from or cultivated mostly in the global South, disrupting fragile ecosystems and exacerbating environmental damage from industrial crop production. Further pressure will be placed on land and water resources, already in short supply for food production. There is simply not enough land (or plant matter) for all the uses that are being contemplated. Furthermore, a number of current applications of synthetic biology propose to replace botanical production of natural plant-based commodities (e.g., rubber, plant oils, artemisinin) with vat-based production systems with synthetic microbes or to move production to genetically engineered plants. In time these substitutions could have devastating economic impacts on farming, fishing and forest communities who depend on natural compounds for their livelihoods. These impacts and the impacts of biomass extraction and associated land grabbing must be considered in any assessment of risk and these assessments must include the full and active participation of those communities that will be impacted.

Corporations have already applied for extremely broadly worded patents on synthetic biology techniques. If granted, they could give a small number of companies virtual *de facto* monopoly control over entire economic sectors, affecting the rights of small producers, patients (in the case of pharmaceutical patents) and the public at large. Patents on synthetic biology processes, synthetic organisms or products derived from synthetic biology could further the privatization and control of natural occurring products and processes. Companies and researchers must not be permitted to patent synthetic versions of natural organisms. These patents could open up new avenues for bio-piracy and ways to circumvent access and benefit-sharing agreements. Transparency, public safety and environmental protection must take legal precedence over any patent or intellectual property protections.

Until the above principles are incorporated into international, federal and local law as well as research and industry practices, there must be a moratorium on the release and commercial use of synthetic organisms.

Conclusion

Synthetic biologists predict that new and extreme genetic engineering will usher in dramatic changes in all areas of human life. While some have argued that synthetic biology can be a research tool to better understand biology, it poses significant and unprecedented hazards. Synthetic biology must, therefore, be accompanied by precautionary mechanisms in order to safeguard the health of workers and local communities, to preserve the biodiversity of the planet, to ensure public participation, to provide for democratically decided social goals, and to restore public trust in scientific researchers and government regulators. The undersigned organizations call for the governments of the world to incorporate these principles into local, national and international frameworks to provide oversight to this extreme form of biological engineering.

Endorsing Organizations

Center for Food Safety

ETC Group

Friends of the Earth U.S.

Food & Water Watch

International Center for Technology Assessment

Please e-mail Eric Hoffman of Friends of the Earth U.S. at ehoffman@foe.org if your organization wishes to endorse the Principles or if you have any questions.

ⁱ This declaration in no manner limits or binds the signatories from any other relevant actions or statements, including unilateral or joint superseding statements on synthetic biology policy. Each organization continues to fulfill their respective mission statements in accordance with their own fundamental guiding principles. This joint declaration supplements our organizations' work in this and related areas. This declaration is not intended to be a comprehensive statement of all possible oversight principles or to encompass all subsequent steps needed for their implementation; rather, it is a starting point from which future implementations of oversight policy can build.

ⁱⁱ See, e.g., RIO DECLARATION ON ENVIRONMENT AND DEVELOPMENT, June 14, 1992, 31 I.L.M. 874, 879 (*"Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation."*); CARTAGENA PROTOCOL ON BIOSAFETY, Jan. 29, 2000, 39 I.L.M. 1027 Art. 10(6) (*"Lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Part of import, taking also into account risks to human health, shall not prevent that party from taking a decision, as appropriate, with regard to the import of the living modified organism in question . . . in order to avoid or minimize such potential adverse effects."*); U.N. FRAMEWORK CONVENTION ON CLIMATE CHANGE, May 9, 1992, 21 I.L.M. 849, (*"The Parties should take precautionary measures to anticipate, prevent or minimize the cause of climate change and mitigate its adverse effects. Where there are threats of serious or irreversible damage, lack of full scientific certainty should not be used as a reason for postponing such measures."*); THE WORLD CHARTER ON NATURE, G.A. Res. 37/7, ¶ 11, U.N. Doc. A/RES/37/7 (Oct. 28, 1982) (*"Activities which might have an impact on nature shall be controlled, and the best available technologies that minimize significant risks to nature or other adverse effects shall be used."*); THE LONDON CONVENTION ON THE PREVENTION OF MARINE POLLUTION BY DUMPING WASTES AND OTHER MATTER, 1996 Protocol to the Prevention of Marine Pollution by Dumping of Wastes and Other Matter, Mar. 24, 2006, art. 3, para. 1 (*"Appropriate preventative measures are[to be] taken when there is reason to believe that wastes or other matter introduced into the marine environment are likely to cause harm even when there is no conclusive evidence to provide a causal relation between inputs and their effects."*); AGREEMENT FOR THE IMPLEMENTATION OF THE PROVISIONS OF THE UNITED NATIONS CONVENTION ON THE LAW OF THE SEA OF 10 DECEMBER 1982 RELATING TO THE CONSERVATION AND MANAGEMENT OF STRADDLING FISH STOCKS AND HIGHLY MIGRATORY FISH STOCKS, G. A. 164/37, art. 6, U.N. Doc. A/CONF164/37 (*"States shall apply the precautionary approach widely to conservation...."*).

ⁱⁱⁱ "The Wingspread Consensus Statement on the Precautionary Principle." Science & Environmental Health Network, 26 Jan. 1998. <<http://www.sehn.org/wing.html>>.

^{iv} Text from the Cartagena Protocol to the Convention on Biological Diversity can be viewed here: <http://bch.cbd.int/protocol/text/>

^v "COP 10 Decision X/37." *Biofuels and Biodiversity*. UN Convention on Biological Diversity, Oct. 2011. <<http://www.cbd.int/decision/cop/?id=12303>>.

^{vi} Steinbrecher, Ricarda A. *V-GURTs (Terminator) as a Biological Containment Tool?* Rep. EcoNexus, June 2005. <http://www.econexus.info/sites/econexus/files/ENx_V-GURTs_brief_2005.pdf>.

^{vii} One study of U.S. and European government funding into synthetic biology research conducted by the Wilson Center's Synthetic Biology Project found that while the U.S. government has spent around \$430 million between 2005 and 2010, only 4% of this money went to examine the ethical, legal and social implications of synthetic biology. When researchers searched for projects looking into risk assessment related to potential accidental release of synthetic organisms from a lab or confinement, or risks from intentional release of synthetic organisms they found no such projects. See: "Trends in Synthetic Biology Research Funding in the United States and Europe." *Synthetic Biology Project*. Woodrow Wilson International Center for Scholars, June 2010. Web. <http://www.synbioproject.org/process/assets/files/6420/final_synbio_funding_web2.pdf?>.