

Professor Allison A. Snow, Ph.D.
Department of Evolution, Ecology, and Organismal Biology
The Ohio State University, Columbus, OH 43214

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Topic: Risks of Environmental Releases of Synthetic GEOs

Good afternoon, and thank you for inviting me to speak to the Commission. I am a plant ecologist and I study gene flow via pollen and seeds, as well as hybridization between related species, and the ecological effects of transgenic crops. I have about 20 years of experience focusing on environmental biosafety issues related to transgenic crops. As an ecologist, I'm also interested understanding the ecological effects of *all* genetically engineered organisms (or GEOs), and I am the lead author of a 2005 position paper of the Ecological Society of America on this topic.

To set the stage for my comments today, I'd like to give you a brief look at what professional ecologists do. Ecologists include professors, graduate students, wildlife biologists, natural resource managers, and other researchers who investigate interactions among organisms and their environment. Our field is very interdisciplinary. We study all types of organisms, from microbes to plants and animals, in all types of habitats, all over the world. We often focus on one level of organization, such as individual organisms, populations, communities of species, or entire ecosystems. We also study many inter-related processes, including competition, predation, and mutualisms, as well as the cycling of energy, carbon, and nutrients in the environment. Some ecologists, like me, study rapid and ongoing evolutionary change. Much of the research that ecologists undertake relates to practical questions in agriculture, forestry, aquaculture, and even urban planning.

A common myth about the natural world is the idea that there is a balance of nature. Nature is not in a state of equilibrium, but rather a constant state of flux. Also, organisms are not perfectly adapted to their environment. This means that, in some cases, new traits of synthetic organisms could make a species much more successful than previously. Ecologists are very familiar with need for more sustainable sources of food, fiber, & fuel, and we hope that new approaches to these global problems can take advantage of the tools of synthetic biology.

My focus today

Next, I would like to focus on possible environmental risks of releasing synthetic and partially synthetic organisms into the environment, whether this is intentional or by accident. So far, there has been very little public discussion of such risks. I think environmental issues have largely been eclipsed by much greater concerns involving biosecurity and by the very heavy focus on potential benefits of synthetic biology.

In order to evaluate environmental risks, we need specific examples. Unfortunately, we don't have many of these yet. As with previous GEOs, there will be a great deal of variation among different applications in the potential for benefit or harm, and this requires a case by case approach. We shouldn't assume *a priori* that all synthetic organisms will be safe or that all will be dangerous.

So far, most applications of synthetic biology are still in the early R&D phase. Applications with completely contained synthetic organisms will be less worrisome to ecologists than environmental releases. However leakage of GEOs outside of contained facilities is likely to occur with large-scale operations, and we need to consider whether and when this might lead to problems. For applications that involve bacteria, it is important to emphasize that a bacterial cell is a living, self-replicating organism. Calling it just a cell or a machine or a chassis for a Bio-Bricks project can give lay people the idea that the cell is not going to be able to reproduce.

Applications that are mentioned most often for field releases involve microbes and algae, such as algae grown in acres and acres of outdoor ponds for biofuel. This is one of the few clear examples that is going forward quickly, and it is largely driven by industry. Unfortunately, though, it's very hard for the public or public researchers to know exactly what is under development due to private, proprietary concerns. For example, ExxonMobil is spending hundreds of millions of dollars to develop GE algae with Synthetic Genomics (founded by Craig Venter), but we don't know any details. I've been trying to find out more in preparation for this meeting, but I haven't been successful. Will they use fresh or salt water? What type of algae? Will the algae be contained in bioreactors or cultured in open ponds? Will the algae be engineered to have suicide genes? Answers to these simple questions are essential.

As a general framework for evaluating risks, it is helpful to examine what is different about synthetic biology and what preceded it. As many of you know, synthetic genes are not new, and there is no clear distinction between traditional genetic engineering and the newer era of synthetic biology. Both involve the transfer of genes that confer new traits in the recipient organism. This can involve one gene, several genes (as in the case of artemisinin), or a whole synthetic genome sometime in the future. For now, it seems that we are at this intermediate phase, involving one to several genes. Therefore, I view synthetic biology as a very advanced type of genetic engineering. A recent article in Scientific American (June 2010) calls it "genetic engineering on steroids," and this may be a good analogy.

Four simple guidelines from ecologists

Regardless of which new GEOs are proposed for outdoor settings, I'd like to review four simple ecological guidelines that should be taken into account. These four guidelines are discussed in detail in two position papers of the Ecological Society of America, and in many other reports.

Number 1 – The first guideline is that we need to be very careful whenever novel, self-replicating are let loose in the environment (intentionally or by accident).

Many will do no harm out in the environment, but important exceptions could occur, especially if the GEO can multiply and become more abundant. In some cases, the GEO might spread to new climate zones or new habitats, like other invasive species.

As a hypothetical example of a worst case scenario, a newly engineered type of high-yielding blue-green algae (cyanobacteria) could be grown in thousands of acres of outdoor ponds for biofuels. Algae grown in open ponds will be engineered to be very hardy and they could be more competitive than native strains. The new type of engineered algae might spread to natural habitats - to lakes, rivers, and estuaries, where it might flourish and displace other species. In some cases, this could result in algal blooms that suffocate fish and release toxic chemicals into the environment. So it would be a bad decision to go ahead with this kind of application. This is just hypothetical example, but it illustrates what we want to avoid.

Number 2 - A second general principle is that novel GEOs that seem innocuous or weak might evolve to become more successful when they start reproducing.

Even if they are highly domesticated, mutations or unexpected properties might allow them to multiply in some environments. Physical or biological confinement (which could be based on engineered suicide genes or chemical dependencies) may not work forever or in all cases because mutations, human error, or unexpected events might allow GEOs to escape and reproduce. It would take only a few survivors to propagate and spread if biological confinement breaks down.

The potential for rapid evolutionary change is especially high in microbes. Some will die out but others may thrive and evolve. GEOs that can exchange genes with related lineages or other species could evolve even faster – allowing synthetic genes to persist in hybrid descendants. So, we cannot assume that all domesticated or supposedly “suicidal” GEOs are unable to persist in the environment.

Number 3 - A third guideline is that once these organisms are released into the environment, novel GEOs cannot be taken back.

They cannot be cleaned up or degraded, like a chemical spill, because they reproduce. Obviously, reproducing organisms have the potential to occur in the environment indefinitely. There is simply no way to find and kill every last one, especially in the case of microbes, but also for plant and animal species. The dispersal of some GEOs could be rapid and widespread – as we have seen with unwanted species that are dispersing around the world due to globalization.

Number 4 – A fourth general guideline is that predicting which new organisms might cause irreversible harm can be extremely challenging.

This is much easier with a GE crop like Round-Up Ready soybean or insect-resistant corn, because these crops are completely dependent on humans, they have been well characterized,

and they don't have wild relatives in the United States. The baseline for comparing the environmental effects of a GE crop is the non-GE crop.

However, we have little or no experience with cultivating microalgae and bacteria outdoors, let alone new life forms that are entirely synthetic. This brings up the question of whether regulatory agencies will be able to evaluate or monitor all new types of synthetic or partially synthetic organisms that are proposed for release. I'm glad that Michael Rodemeyer will discuss the topic of regulations tomorrow – this is extremely important. In summary, then, the challenges of approving novel GEOs for environmental release are likely to become much, much greater in the next 5-10 years.

Recommendations

To begin to tackle these issues, the general public and public researchers need more information as soon as the first applications that involve releasing synthetic GEOs in the environment. In the case of microalgae, this information is needed now. Any technology could be beneficial or harmful, depending on how it is used, so I think the Commission really needs accurate and realistic information about how will this technology be used. Which species (existing or new) are under development for outdoor releases? Under what conditions? What are some possible risks? And which unwanted consequences would be irreversible?

Before regulatory agencies decide on whether an application for environmental release is acceptable, we need analyses of ecological risks and benefits. These analyses should not come just from industry. Ideally, results from independent research would be published in peer-reviewed journals and made available to the public, such as reports from the National Academy of Sciences.

For example, a good start for synthetic microalgae would be to publish professional monographs dealing with the biology and ecology of each species and its close relatives, including information about:

- Their ability to reproduce and spread under different conditions;
- Whether they could exchange genes with other strains or species;
- Their likelihood of dying out, persisting, or becoming very abundant.
- And whether they produce toxins or other unwanted side effects.

Ecologists can help with the development of synthetic GEOs that minimize risks, and ecologists will want to get involved as the technology moves forward. Most engineers and molecular biologists have little experience with ecological science, so it will be important to get input from experts in other fields of biology. The choice of organisms and traits should be discussed in light of possible ecological risks, and key knowledge gaps can be investigated. However, ecological research takes time and funding, which is why risk assessment research cannot be left to the last minute before a regulatory decision is needed. It is important for risk assessment research to proceed in tandem with R&D research.

When more is known about specific applications and their possible risks, open debate and discussion are needed to avoid bad decisions and allow safe uses of this technology to move forward. For example, scientific debates about which non-transgenic plants to use for biofuels already have been extremely useful, especially the “life cycle” approach to calculate the net amounts of land, water, fuel, fertilizer, and pesticides needed per the amount of biofuel produced, and anticipated effects on global carbon cycles. It would be great to have an added layer to these discussions that would include possible benefits and risks of using synthetic GEOs for biofuel production.

In closing, I’d like to read a quote from an editorial about Synthetic Biology in Nature magazine, May 27, 2010, titled “Challenges of our own making”. The editors mention the task ahead for Obama’s bioethics commission and they state that “. . . where there are concerns, they now need to be developed beyond the knee-jerk sound bite.” I couldn’t agree more, and I look forward to deeper discussions and debates on these issues.

Thank you.

Two position papers from the Ecological Society of America -

Snow, A. A., D. A. Andow, P. Gepts, E. M. Hallerman, A. Power, J. M. Tiedje, and L. L. Wolfenbarger. 2005. Genetically engineered organisms and the environment: current status and recommendations. *Ecological Applications* 15:377-404.

Tiedje, J. M., R. K. Colwell, Y. L. Grossman, R. E. Hodson, R. E. Lenski, R. N. Mack, and P. J. Regal. 1989. The planned introduction of genetically engineered organisms: ecological considerations and recommendations. *Ecology* 70:298–315.