Ethics of Biotechnology Research

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Ethics, scientific controversies, and risk management

Genetically modified organisms (GMOs) have been hotly debated by scientists since they first appeared, and many of their questions remain unresolved. Since the initial genetic manipulations were performed in the 1970s, questions have swirled around the possible risks these new organisms might pose to human and animal health. An appeal by Paul Berg in *Nature* in 1973 ignited the debate.[1] He and the others who signed the article led the first DNA manipulations in the United States, but later recommended a moratorium on genetic manipulations such as those that introduced antibiotic-resistant genes into bacteria like *Escherichia coli*. This appeal was at the origin of the 1975 Asilomar Conference, an example of ethical reflection by the scientists of the time, who questioned whether they had the right to continue research if they did not fully understand the associated risks. Perceptions of the risks and uncertainties of biotechnology have evolved quite a bit in the years since that conference. Issues have ranged from the impact of GMOs on human and animal health to broader environmental concerns (e.g., reduced biodiversity, transgene flow to related wild relatives, and the development of herbicide resistance in plants).

More recently, studies of the socioeconomic impact of GMOs on agriculture and innovation systems (the coexistence of GMO and non-GMO crops, “organic” labeling, concentration of seed industries, appropriation of genetic resources, etc.) have further expanded the field of GMO risk analysis. Each of these issues has been the subject of scientific controversy. Researchers will therefore increasingly need to consider the ethical implications of the uncertainties associated with biotechnology to guide them in their work.

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1. Berg, P., Baltimore, D., Boyer, H. W., Cohen, S. N., Davis, R. W., Hogness, D. S., ... Zinder, N. D. (1974). Potential biohazards of recombinant DNA molecules. *Science, 185*, 303.

Biotechnology through the lens of the ethics of conviction, responsibility, and values

Ethicists contrast three types of ethics: conviction, responsibility, and values. How can these principles help us address the issues raised by the emerging biotechnologies in the countries in the Mekong region?

The ethic of conviction takes an absolute stand on an action, regardless of the context. The answer can only be “yes” or “no,” as in the question “is it ethical to eat meat?” The ethic of responsibility shifts the focus from the action itself to its consequences: can someone continue to eat industrial poultry knowing how the animals are treated? The values approach questions the motivations that underlie behavior. Not eating meat may in fact simply be a matter of taste and not involve ethics at all.

The ethic of conviction, as it pertains to biotechnology, asks if it is ethical to modify a living organism. Differing beliefs may clash: “life is sacred and should not be modified”; “life is a biochemical process devoid of any sacred meaning”; “genetic modifications are a drop in the ocean of evolution”; “modifying microorganisms is acceptable but not complex organisms”; “modifying plants is acceptable but not animals”; “modifying animals is acceptable but not humans”; and so on. Other arguments may include “long live augmented humans!” or even the Orwellian “why not diminished humans who we can control?”

Questions about the consequences of our choices can also be debated: “What are the effects on health? On biodiversity? On ecosystems?”; “GMOs represent the privatization of living organisms for the benefit of multinationals”; “Biotechnologies aren’t only GM plants; they also represent important tools for healthcare, like gene replacement therapy”; and so on.

Let’s look at a case study to better understand these ethical principles.

Is it ethical to genetically modify mosquitos?

Case no. 1: GM mosquitos for the prevention of dengue

The Vietnamese Ministry of Health released a genetically modified (GM) mosquito to combat dengue outbreaks. The *Aedes aegypti* (AA) mosquito is the conventional transmission vector to humans. The GM version contains Wolbachia bacteria, which inhibits the insect’s ability to transmit dengue, and also happens to shorten its lifespan. This mosquito has been tested in Vietnam by the National Institute of Hygiene and Epidemiology since October 2012. It was released in April 2014 on the island of Tri Nguyen, within the city of Nha Trang, and in the province of Khanh Hoa (southern Vietnam). Studies conducted in May 2015 indicated that 95% of the AA mosquitos carried Wolbachia. No cases of dengue have been reported on the island since mid-2014. The Institute is preparing to release the mosquito throughout the entire city of Nha Trang.

This issue has been extensively discussed among medical doctors. In 2015, 40,000 people were diagnosed with dengue in Vietnam, 25 of whom died. Mortality for this disease is increasing by 72% per year. Modifying the *Aedes aegypti* mosquito may seem ethical to any reasonable person; in fact, it would appear unethical not to!

Yet there are other ways of looking at the situation, including from an ethic of nature perspective. The term “biocentrism” refers to the practice of ascribing every living organism with intrinsic value (such as in Jainism in India). “Ecocentrism” takes a more pragmatic approach, assigning intrinsic value to biotic communities or ecosystems as a whole. The ethic of nature may also be anthropocentric, or utilitarian, if it holds that humans have a self-serving interest in taking care of nature. In this view, man is the proud “master and owner of nature,” who should be cautious when using biotechnology to alter the natural balance.

Thus the genetic modification of a mosquito poses a series of ethical problems, from the intrinsic value of maintaining a species (biocentrism), to the consequences of a species disappearing from the food chain (other species that feed on *Aedes aegypti* mosquitos could themselves disappear (ecocentrism)), to the more utilitarian: humanity may grant itself the right to disrupt ecosystems to our advantage as long as we do not compromise the resilience of these systems. In ecology, the Rivet Hypothesis[2] postulates that the loss of one species is not necessarily dangerous for an ecosystem (just as the failure of one rivet on an airplane wing is not necessarily devastating for the flight), but the N+1 subsequent extinction may result in a general disruption to the equilibrium in unpredictable ways.

Note that there is no way to counter the position against the genetic modification of mosquitos if it comes from an ethic of conviction (belief in the animal “cause”), because it is sealed against any other considerations, or to counter the more responsible pro-biotechnology position that judges consequences more than actions. Both positions are based on personal convictions and a sense of responsibility, but they do not focus their attention on the same consequences and the same legal entities (do humans alone have rights or does nature have rights as well?):

1. The ethical position defending genetic modification is anthropocentric because it only considers the positive consequences for humanity or societies; and

2. The challenge to genetic modification is based on a different ethic, one that extends to non-humans at least some of the moral principles that societies generally bestow on human beings and acknowledges that every element of nature has intrinsic value.

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2. Ehrlich, P., & Ehrlich, A. (1981). Extinction: the causes and consequences of the disappearance of species. New York: Random House.

We should also consider the values that drive the actors. What motivated the research on genetically modifying *Aedes aegypti* mosquitos? Why, for example, did the Bill and Melinda Gates Foundation finance this research in Vietnam? Are similar tests being conducted in the United States? Why are experiments being conducted in Vietnam and other developing countries? Are the precautionary principles too demanding (and restrictive) in rich countries? Is civil society there more watchful? Is technical democracy more vibrant? The list of questions goes on, each deserving of in-depth research to better understand the values that inspire the various actors involved as partners in the Mekong region programs. Doubtless most are motivated by true altruism, but it is a good bet that others have less lofty intentions.

What can we learn from this first case study? First of all, the genetic modification of a mosquito, even for the best of reasons (saving human lives), poses ethical questions. Second, a well-constructed ethical argument should be cross-pollinated by a variety of beliefs and concepts of responsibility and should examine both the explicit and implicit values of the actors. Third, an ethical opinion must be rooted in reality and when possible based on scientific evidence.[3] This last point leads to a central question in research ethics: how do we act ethically in a context of scientific controversy and uncertainty?

Let's look at a second case study.

Do GMOs provide a definite benefit by decreasing pesticide consumption across the world?

Case no. 2: GMOs and pesticides

Decrease…

"GM crops (...) have been rapidly adopted. By 2012, GM crops were grown on more than 170 million [hectares], and for the first time, more than half of this land was located in developing countries. The economic benefits GM crops can now be fully described (...) For example, (...) the calibrated yield effect of GM cotton for Argentina is 33% [and] pesticide reduction [is] 46%… For the United States, the increased yield effect is 11% [and] pesticide reduction [is] 30%. GM crops, especially GM insect-resistant cotton, have contributed to a large reduction in insecticide use globally, whereas there are contradictory estimates of the effect of GM herbicide-treated crops on herbicide use."[4]

3. In France, for example, the use of GM mosquitos was evaluated by the Haut Conseil des Biotechnologies. HCB (2017). Avis du conseil scientifique du HCB concernant l'utilisation de moustiques génétiquement modifiés dans le cadre de la lutte anti-vectorielle. Retrieved from: http://www.hautconseildesbiotechnologies.fr/sites/www.hautconseildesbiotechnologies.fr/files/file_fields/2017/06/06/aviscshcbmoustiques170607.pdf
4. Bennett, A. B., Chi-Ham, C., Barrows, G., Sexton, S., & Zilberman, D. (2013). Agricultural biotechnology: Economics, environment, ethics, and the future.

... or increase?

"Herbicide-resistant crop technology has led to a 239 million kilogram increase in herbicide use in the United States between 1996 and 2011, while *Bt* crops [which produce insecticides] have reduced insecticide applications by 56 million kilograms. Overall, pesticide use increased by an estimated 183 million kg, or about 7%. Contrary to often-repeated claims that today's genetically-engineered crops have, and are reducing pesticide use, the spread of glyphosate-resistant weeds (...) has brought about substantial increases in the number and volume of herbicides applied. If new (...) forms of corn and soybeans tolerant of 2,4-D are approved, the volume of 2,4-D sprayed could drive herbicide usage upward by another approximate 50%."[5]

The issue of whether GMOs have led to a decrease or increase in pesticide consumption across the world is a debate that the scientific data do not appear to resolve.

In an article published in *The Annual Review of Environment and Resources* in 2013, the authors state that GM cotton has led to a 46% reduction in pesticide consumption in Argentina and a 30% reduction in the United States. They conclude that GMOs have contributed to a massive global reduction in the use of insecticides, and therefore represent significant progress both for the environment and for farmers' health. Reading this article, which was published in a scientific journal with a peer-review committee, one concludes that GMOs provide indisputable benefits for the health of farmers and the environment.

A second article, by Benbrook and published in 2012 in *Environmental Sciences Europe*, comes to precisely the opposite conclusion. The use of herbicide-resistant GM plants led to a 239-million kg increase in the use of herbicides in the United States between 1996 and 2011, while *Bt* crops (which produce their own insecticides) reduced the application of insecticides by 56 million kg. The overall use of pesticides (herbicides + pesticides) increased by 183 million kg, or nearly 7%. The Benbrook article also sounds the alarm for the dual problem of insects and weeds that become resistant to herbicides through the use of GMOs. Studies in the U.S. on the emergence of glyphosate-resistant (GR) weeds show that there are currently 22 GR species, which sources say may affect between 6 and 40 million hectares. This last figure comes from a study by the Dow Chemical Company to convince American authorities to allow 2,4 D to be sold in order

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The Annual Review of Environment and Resources, 38:19.1 19.31, DOI 10.1146/annurev-environ-050912-124612

5. Benbrook. C. M. (2012). Impacts of genetically engineered crops on pesticide use in the U.S.—the first sixteen years. *Environmental Sciences Europe*, *24*, 24.

to launch its new 2,4 D-resistant strain of corn. In other words, Dow Chemical, a multinational agrochemical company and major global producer of GMOs, makes scientific use of GMO failures to obtain more relaxed rules on the sale of long-banned pesticides in order to market new GMOs. For multinational firms like this, scientific data have become political and economic weapons.

How do you arrive at an ethical stance in such controversial contexts? You must examine the quality of the data, consider the honesty of the authors, gather additional information... in short, conduct research to reduce the uncertainty to a level where a consensus can be reached. This is the hurdle faced when crafting an expert consensus or conference consensus, which strive to come up with at least temporary solutions. There is often some residual scientific uncertainty, but the decision to authorize or ban a product or procedure cannot be delayed. Fortunately today we have several institutional mechanisms to help manage this uncertainty when making such decisions:

1. The Precautionary Principle, based on the idea that we do not have to wait for absolute, definitive scientific certainty before taking measures to limit the potential risks of research or technological innovation. This principle was behind the de facto moratorium on GMOs in European markets until 2005. The Precautionary Principle can be understood in different ways, from strong to weak. The concept of “known risk” assumes there must be a certain probability of the risk occurring before cautionary measures are applied.

2. Common rules for assessing the risks of disseminating GMOs have been established at the international level. The international reference text is the Cartagena Protocol, which defines biosafety standards, i.e., protocols for assessing the environmental and health risks of GMOs.

3. Many national biosecurity standards have been established on the basis of this international legal framework. Some countries use the principle of “substantial equivalence” i.e., they consider GMOs to be identical to other products so no particular marketing regulations are needed. However most countries have defined rules for tracking and labeling GMOs. Regardless of one’s position on the issue, administrative mechanisms create an essential basis for moral and legal responsibility for research and industry in case of any problems.

4. One other important institutional mechanism for managing risks should be mentioned: public debate, citizen forums, and consensus conferences. Ideally, political decisions are based on scientific truths, but in reality uncertainty is an integral part of science in action. The solution to this conundrum is to create mechanisms through which scientists, citizens, and political decision-makers can deliberate. Jürgen Habermas and Bruno Latour talk of “dialogical frameworks,” or theoretical mechanisms to facilitate dialogue between

various actors who may have access to unequal levels of information. The goal is to construct a consensus for controversial issues to better inform the public and allow citizens to take responsibility for supporting or opposing one technology or another, or finding yet another path.

Conclusion

Like elsewhere in the world, there is no blanket solution to the wide variety of ethical issues raised by the spread of biotechnology in developing countries. The only reasonable recommendation is to analyze each situation on a case-by-case basis. Unlike wealthy countries, resource-limited countries face a deficit of information and independent experts, leaving them vulnerable to the full force of industrial lobbies as they seek to direct their scientific choices.

Scientific cooperation between public research institutions should play a key role here. It is an area of development aid that should be strengthened at all levels of scientific cooperation. Most emerging countries have the scientific expertise necessary to formulate their scientific guidelines but generally lack the political and administrative culture to implement mechanisms to manage the types of scientific controversy that we have described.

Europe and the United States have been engaged in furious diplomatic battles over rules to frame the use of GMOs, and developing countries have been inexorably drawn into this conflict. The U.S. considers a ban on GMOs on the Precautionary Principle to be an infraction of World Trade Organization (WTO) free trade rules[6] (non-tariff barriers) and has brought the issue before the dispute settlement body of the WTO. We therefore find ourselves caught between the strong opposition of two sides: “science-based decision-making” on the American side, which states that any risk must be demonstrated scientifically, and the “Precautionary Principle” on the other, which was invented precisely to face the issues of scientific uncertainty. At this time the U.S. is clearly winning this battle, imposing the Sanitary and PhytoSanitary (SPS) standards of the FAO’s Codex Alimentarius as the sole basis for discussion to determine whether or not GMOs are dangerous to our health.[7]

Technical democracy still has a long road to travel in resource-limited countries. It is both a great challenge and a great opportunity: ethical debates on technical issues are fertile ground for the practice of democracy and with intervention from civil society could lay the groundwork for political democracy.

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