Published in final edited form as:

Am J Bioeth. 2017 September ; 17(9): 24–26. doi:10.1080/15265161.2017.1353170.

Field Trials of Genetically Modified Mosquitoes and Public Health Ethics

David B. Resnik

National Institutes of Health

Lisa Lee's (2017) target article "A bridge back to the future: public health ethics, bioethics, and environmental ethics" presents a compelling case for using a public health ethics framework for reconnecting biomedical ethics and environmental ethics. She describes how biomedical ethics and environmental ethics have drifted apart since Van Rensselaer Potter characterized bioethics as global discipline in the 1970s that addresses ethical dilemmas in medicine, public health, and the environment. She argues that public health ethics can serve as a bridge back to Potter's vision of an inclusive bioethics because it deals with health at individual, community, and environmental levels.

Elsewhere (e.g. Resnik 2009, 2012) I have argued for basically the same thesis that Lee defends in her article. Accordingly, my goal in this commentary is not to criticize Lee's viewpoint but to provide additional evidence for it by discussing an example that illustrates the need for a bioethical perspective that addresses individual, community, and environmental concerns. The example I have in mind is the use of genetically modified (GM) mosquitoes to control mosquito-borne diseases, such as malaria, dengue fever, and the Zika infection (Resnik 2014, Forthcoming).

Mosquito-borne illnesses are a serious public health problem, especially in developing countries. Malaria kills over 400,000 people per year, mostly children living in Africa, and 20,000 people die annually from the hemorrhagic fever caused by the dengue virus (World Health Organization 2014). In 2015, millions of people in Central and South America contacted the Zika virus. Although most adults only develop a mild fever, rash, and headache from a Zika infection, the virus poses a significant threat to fetuses and can increase this risk of birth defects, including microcephaly (Resnik 2012, Forthcoming).

Since the beginning of this century, researchers have been developing genetically modified mosquitoes to help prevent the spread of mosquito-borne diseases. One of the reasons why researchers have undertaken this task is that other methods of controlling mosquito populations have significant disadvantages (Macer 2005, World Health Organization 2014). Pesticides, for example, can pose risks to human health and to non-human species (such as some species of birds, insects, and fish). Also, some species of mosquitoes are becoming resistant to pesticides. Eliminating mosquito breeding grounds (such as wetlands and ponds) can disrupt the ecosystem and threaten biodiversity (Resnik 2012).

The two approaches to producing GM mosquitoes that have gained the most attention are 1) modifying male mosquitoes so that they cannot produce viable offspring, and 2) modifying male and female mosquitoes so that they resist certain diseases or are incapable of transmitting them (World Health Organization 2014, Servick 2016). Scientists working for the biotechnology company Oxitec have tested the first approach in field trials involving the release of thousands of mosquitoes into the wild; the second approach has only been tested in laboratory settings (Resnik Forthcoming). Oxitec's genetically modified *Anopheles aegypti*¹ male mosquitoes have a mutation that causes larva to die unless they are exposed to the antibiotic tetracycline. The GM males mate with the females in the wild but do not produce viable offspring. Because the GM mosquitoes are not viable, researchers must periodically reintroduce GM males to keep the population in check. Oxitec has tested this approach in parts of Brazil, the Cayman Islands, and Malaysia. The Food and Drug Administration and the Monroe County, Florida, Mosquito Control District have approved field trials of Oxitec's mosquitoes, which have not taken place as of the writing of this commentary (Resnik Forthcoming). Field trials of Oxitec's mosquitoes have reduced *Anopheles aegypti* mosquito populations 80-95% and dengue fever cases by as much as 91% (Carvalho et al 2015, Oxitec 2016).

Both approaches can produce different benefits and risks for individuals, communities, and the environment. A benefit of the first approach for individuals and communities is that it can reduce the prevalence of mosquito-borne diseases by controlling mosquito populations with introducing pesticides into the environment. Since male mosquitoes do not bite, this approach poses no risk of infection from a GM mosquito bite. A potential environmental risk of this approach is that it could disrupt the food web by drastically reducing or eliminating the local population of *Anopheles aegypti* mosquitoes, which are important source of food for amphibians, bats, birds, fish, insects, and reptiles. However, it is possible that these species could adjust to loss of this food source and that other mosquito species would fill the ecological niche vacated by *Anopheles aegypti* (Macer 2005, World Health Organization 2014).

A benefit of the second approach for individuals and communities is that it could reduce the prevalence of mosquito-borne diseases by making mosquitoes resistant to those diseases or incapable of transmitting them. A potential risk for individuals and communities is that the genetic modification might not work as intended and could theoretically increase the prevalence of some types of mosquito-borne diseases. For example, a genetic modification might promote malaria resistance but increase yellow fever susceptibility. A potential environmental risk is that the gene drive² mechanism used to increase the prevalence of targeted genes in the population might be transmitted to other species by viruses, with unpredictable effects on human health and the environment (World Health Organization 2014, National Academy of Sciences 2016).

¹This mosquito species can carry dengue, malaria, Zika, and yellow fever.

²A gene drive mutation distorts Mendelian inheritance so that it increases in prevalence in the population irrespective of the effects of natural selection or random drift (National Academy of Sciences 2016). Genes linked to these mutations will also increase in prevalence.

Both approaches raise significant ethical issues at the level of the individual, community, and environment, such as (Macer 2005, Resnik 2012, Forthcoming, World Health Organization 2014):

- Individual consent: Should individuals have the right to decide whether they will be exposed to GM mosquitoes? How should such a right be balanced against the community's interests in promoting public health? Should individual consent be required only for people who will be subjects of research studies related to a field trial?
- Community consent: Should the affected community have the right to approve or disapprove a field trial of GM mosquitoes? How should researchers or public health officials engage the local community? Should outside groups (such as organizations opposed to genetically modified organisms) be allowed to prevent the community from implementing a strategy to promote the health of its members?
- Public health benefits and risks: What are the public health benefits and risks of field trials of GM mosquitoes? How should benefits and risks be compared?
- Environmental risks: What are the potential environmental impacts of a field trial of GM mosquitoes? How should these impacts be evaluated? Should public health be promoted at the expense of the environment? Does introducing GM mosquitoes into the wild set a dangerous precedent for environmental policy?

As one can see from this list of questions, the issues raised by field trials of GM mosquitoes affect individuals, communities, and the environment and cannot be addressed by a decision-making method which focuses solely on clinical, research, or environmental ethics. To adequately address these issues, one must employ a more comprehensive framework, such as public health ethics or environmental health ethics, which encompasses these different ways of thinking about ethical dilemmas related to human health and environment. I applaud Dr. Lee for her efforts to move bioethics in this direction.

Acknowledgments

This research was supported, in part, by the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH). It does not represent the views of the NIEHS, NIH, or US federal government.

References

- Carvalho DO, McKemey AR, Garziera L, Lacroix R, Donnelly CA, Alphey L, Malavasi A, Capurro ML. Suppression of a field population of *Aedes aegypti* in Brazil by sustained release of transgenic male mosquitoes. *PLoS Neglected Tropical Diseases*. 2015; 9(7):e0003864. [PubMed: 26135160]
- Lee LM. A bridge back to the future: public health Ethics, bioethics, and environmental ethics. *American Journal of Bioethics*. 2017
- Macer D. Ethical, legal and social issues of genetically modifying insect vectors for public health. *Insect Biochemistry and Molecular Biology*. 2005; 35(7):649–660. [PubMed: 15894183]
- National Academy of Sciences. *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values*. Washington, DC: National Academies Press; 2016.

- Oxitec. Press release, 14 July 2016: Dengue fever cases drop 91% in neighbourhood of Piracicaba, Brazil, where Oxitec's Friendly™ Aedes were released. 2016. Available at: <http://www.oxitec.com/dengue-fever-cases-drop-91-percent-neighbourhood-piracicaba-brazil-oxitecs-friendly-aedes-released/>. Accessed: April 28, 2017
- Resnik DB. Human health and the environment: in harmony or in conflict? *Health Care Analysis*. 2009; 17(3):261–276. [PubMed: 19130245]
- Resnik DB. *Environmental Health Ethics*. Cambridge, UK: Cambridge University Press; 2012.
- Resnik DB. Ethical issues in field trials of genetically modified disease-resistant mosquitoes. *Developing World Bioethics*. 2014; 14(1):37–46. [PubMed: 23279283]
- Resnik DB. Ethics of community engagement in field trials of genetically modified mosquitoes. *Developing World Bioethics*. Forthcoming.
- Servick K. Winged warriors. *Science*. 2016; 354(6309):164–167. [PubMed: 27738153]
- World Health Organization. *Guidance Framework for Testing of Genetically Modified Mosquitoes*. Geneva, Switzerland: World Health Organization; 2014.