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# Two unresolved issues in community engagement for field trials of genetically modified mosquitoes

David B. Resnik

National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, USA

**ABSTRACT**

There is an emerging consensus among scientists, ethicists, and public health officials that substantive and effective engagement with communities and the wider public is required prior to releasing genetically modified mosquitoes into the environment. While there is little disagreement about the need for community and public engagement prior to releasing genetically modified mosquitoes into the environment, two important issues have not been resolved, namely: defining the community and dealing with potential conflicts between the community and the wider public. This commentary addresses these unresolved issues.

**KEYWORDS**

Field trials; genetically modified mosquitoes; community engagement; ethics

## 1. Introduction

There is an emerging consensus among scientists, ethicists, and public health officials that substantive and effective public and community engagement is required prior to releasing genetically modified (GM) mosquitoes into the environment [1–15]. Public and community engagement helps to promote deliberative democracy and support from local populations and the wider public [1–7]. Public and community engagement is also often required by local or national laws [10–14]. While there is little disagreement about the need for public and community engagement prior to releasing GM mosquitoes into the environment, two important issues[1] have not been resolved, namely: defining the community and dealing with potential conflicts between the community and the public. In this commentary, I will address these unresolved issues.

## 2. Genetically modified mosquitoes: background

Mosquito-borne diseases pose a serious threat to public health [2]. Malaria is caused by microorganisms from the *Plasmodium* group, which are transmitted to humans by female mosquitoes from the *Anopheles* genus. In 2017, 219 million people worldwide contracted malaria and 435,000, mostly young children in African nations, died from the disease [16]. Dengue fever is caused by several types of dengue viruses, which are carried by *Aedes aegypti* and *Aedes albopictus* female mosquitoes. Each year, between 50 and 100 million people are infected with the dengue virus and about 22,000 die from dengue fever [17]. Prevention of mosquito-borne illnesses is preferable to treatment or vaccination, given the limited availability of health-care resources in some countries and the burden of these diseases [2]. However, many widely used methods of prevention, such as wearing protective clothing, spraying pesticides, or eliminating mosquito breeding grounds, have practical limitations and adverse effects on human health and the environment [2].

In the last decade or so, scientists have developed methods for genetically modifying mosquitoes as a means of preventing mosquito-borne diseases, but only one has been tested in the field [2–6,13,15]. One of these methods suppresses mosquito populations. Scientists working for Oxitec have genetically modified *Aedes aegypti* male mosquitoes to carry a lethal gene that causes 95% of offspring to die prematurely unless they are exposed to the antibiotic tetracycline. When the male mosquitoes are released into the wild, they mate with the females, which can suppress the population. Oxitec has conducted field trials of its GM mosquitoes in the Cayman Islands, Malaysia, and Brazil [6]. Field trials of Oxitec's mosquitoes in Brazil have reduced *Aedes aegypti* populations from 80% to 95% and dengue fever cases by more than 90% [18,19].

Oxitec has submitted applications to the Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) to conduct field trials of its GM mosquitoes in the US, but none have taken place thus far. In August 2016, the FDA published an environmental assessment of Oxitec's proposed investigational

**CONTACT** David B. Resnik resnikd@niehs.nih.gov National Institute of Environmental Health Sciences, National Institutes of Health, 111 Alexander Drive, Box 12233, Mail Drop E1-06, Research Triangle Park, NC 27709, USA

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[1]Some other important issues have also not been resolved, such as how to engage the community effectively [16–18] and how to incorporate community engagement into existing laws and policies [11–14], but my commentary will not focus on these issues.

use of its mosquitoes in a field trial in Key Haven Florida, located in Monroe County [20]. The FDA concluded that investigational use of the mosquitoes in Key Haven would be unlikely to produce adverse effects on human health or the environment. In elections held on November 2016, Florida voters endorsed a proposal to allow field trials of Oxitec's GM mosquitoes to take place in the state, and Monroe County voters also endorsed the field trials, but Key Haven residents voted against them [21]. However, the Florida Keys Mosquito Control District and several other communities in Monroe County approved the field trials [21]. The EPA is currently assessing the environmental and public health risks of Oxitec's mosquitoes and is accepting public comments on proposed field trials in Monroe County Florida and Harris County, Texas [22].

Another method prevents mosquitoes from transmitting diseases. Several different research groups have used CRISPR-Cas9 gene editing tools to insert genes into *Anopheles* female mosquitoes that code for proteins which kill or disable the malaria parasite [3,23]. Researchers have also used CRISPR-Cas9 gene editing tools to incorporate malaria-resistance genes in gene drive systems to enable them to spread rapidly through the population [3,24].[2] In theory, a gene incorporated into a gene drive system could become highly prevalent in a mosquito population after multiple generations [3]. Gene drive systems for malaria resistance have been developed in the laboratory but not tested in the field [23].

Both methods have limitations and potential environmental and public health risks. A risk that both methods have in common is that the GM mosquitoes might migrate out of the release site [1–3]. However, this risk can be minimized with proper site selection and containment measures [1–3]. The most significant risk of the method that suppresses the targeted mosquito population is that it could have adverse effects on the food web, because some species of bats, birds, amphibians, insects, and fish eat mosquitoes in adult or larval forms. However, it is likely that impacted predator species would find substitute food sources, so the food web would adjust [1–3,13,20]. Another potential adverse outcome that the lethal gene could have harmful impacts on non-target species if it is transferred to non-target species by horizontal gene transfer and is expressed.[3] However, the FDA has determined that the probability of this type of adverse outcome is very low because horizontal gene transfer is a rare event [20]. While some citizens and health-care professionals have been concerned that the GM mosquitoes could transfer the lethal gene to human beings, this risk is negligible because male mosquitoes do not bite [20]. The main limitation of this method is that it would need to be re-implemented periodically to keep targeted mosquito populations in check [3,13,20].

The method that alters the mosquito populations has several potential risks and limitations. First, the targeted species might evolve resistance to the gene drive. This problem would need to be overcome before the method could induce permanent changes in the population [3,23]. Second, the method might not work as intended. It might, for example, immunize the mosquito population against malaria but equip it to carry another disease [2,3]. Third, pathogens might evolve in response to changes in the targeted mosquito population [3]. For example, the malaria parasite might develop resistance to lethal proteins introduced into the *Anopheles* populations. Fourth, the gene drive could become linked to other, not-targeted genes in the mosquito population, with unpredictable effects [3]. Fifth, the gene drive could have adverse impacts on non-target species if it infects these species by means of horizontal gene transfer and attaches to genes that are expressed in harmful ways. However, as noted above, the probability that this type of event would happen is very low, due to the rarity of horizontal gene transfer [20]. In sum, the ecological and evolutionary consequences of using gene drives to alter mosquito populations to enable them to resist diseases are not well-understood at present and require further study [3,12].

Field trials are a necessary, precautionary step prior to extensive releases of GM mosquitoes, because they allow scientists and public health officials to study the genetic, evolutionary, ecological, and human health impacts of introducing these organisms in the environment, and to develop strategies for minimizing or mitigating risks [1–3,12]. Field trials should occur in geographically isolated areas that face a significant burden of mosquito-borne illnesses [2]. Geographic isolation is important to contain GM mosquitoes and minimize adverse impacts [3]. For example, Oxitec's first field trials occurred in 2009 and 2010 in isolated parts of the Cayman Islands. [6]

## 3. The rationale for engaging the public and the community

There is a widespread consensus among ethicists, researchers, and public health officials that substantive and effective public and community engagement is a moral prerequisite for approving and conducting field trials of GM mosquitoes [1–7]. The National Academy of Sciences, Engineering, and Medicine (NASEM) report *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public*

[2]Gene drives are naturally occurring genetic sequences that bias Mendelian inheritance in favor of those sequences.
[3]Horizontal gene transfer is a process in which DNA moves between organisms other than by sexual reproduction. Viruses can transfer DNA to numerous species, including humans. Horizontal gene transfer can transfer DNA across species [3].

*Values* defines engagement as, 'seeking and facilitating the sharing and exchange of knowledge, perspectives, and preferences between or among groups who often have differences in expertise, power, and values [3, p.131].' Engagement, according to this definition, involves much more than sharing information or soliciting opinion: it is an active dialog among members of different groups who have a stake in a decision.

Though some scientists and industry leaders may view engagement as important only as a means of obtaining public support for new technologies, engagement has value for its own sake because it facilitates deliberative democracy [6,7,12]. Deliberative democracy is a form of public decision-making that demonstrates respect for human dignity by directly involving citizens in decision-making [7,25–29]. Deliberative democracy also promotes procedural justice[4] because it helps to ensure that disadvantaged and underrepresented populations are included in policy debates, and it helps it minimize the impact of powerful corporations and interest groups on decision-making [7,25–29]. Engagement supports deliberative democracy because it gives citizens from diverse perspectives and backgrounds the opportunity to have meaningful input into government actions (such as legislation and regulatory decisions) that affect their interests [6–8]. Citizens can express their opinions and concerns in a variety of ways, such as by participating in public meetings, voting on referenda related to specific issues, voting or campaigning for elected officials, writing letters to and lobbying elected representatives and government agencies, and submitting public comments on proposed actions [27].

While it is important for all citizens to have the opportunity for meaningful input into government actions that affect their interests, those who are likely to be most directly affected deserve special attention and consideration in the engagement process, because they have more at stake than other members of society [3,7]. For example, if a government is considering relocating a solid waste disposal facility to a new location, those who live near the proposed site (i.e. members of the local community) deserve special consideration in the engagement process because their health and the environment will be directly impacted by the decision. People who live further away from the proposed site have less of a stake in the decision than those who live nearby, and their interests can be addressed during the public engagement process. Thus, governments should make special efforts to engage communities that will be directly impacted by policy decisions and include them in the deliberative process, so that their interests will be adequately considered [3]. Community engagement should be conducted separately from public engagement to ensure that communities receive substantive and effective consultation [3].

## 4. Community engagement

Community engagement is an ongoing process that should take place through multiple forms of communication and interaction. It should build relationships between researchers, public health officials, and the community and should empower community members [3,6,7]. Community engagement should promote honest, transparent, respectful, and inclusive dialog among researchers, public health officials, local government leaders, and community members [3,6,7]. It should not only provide communities with information related to the benefits and risks of proposed experiments or interventions but should also allow them to have a meaningful and impactful role in decision-making [3,6,7,30–32]. The World Health Organization (WHO) [2], the NASEM [3], and numerous authors have proposed some principles and strategies for effective community engagement related to public and environmental health [6,7,30–33].

Lavery and colleagues have developed the following points to consider for community engagement for public health research [30]:

(i) Rigorous site-selection procedures
(ii) Early initiation of community engagement activities
(iii) Characterize and build knowledge of the community, its diversity, and its changing needs
(iv) Ensure the purpose and goals of the research are clear to the community
(v) Provide information
(vi) Establish relationships and commitments to build trust with relevant authorities in the community: formal, informal and traditional
(vii) Understand community perceptions and attitudes about the proposed research
(viii) Identify, mobilize, and develop relevant community assets and capacity
(ix) Maximize opportunities for stewardship, ownership, and shared control by the community
(x) Ensure adequate opportunities and respect for dissenting opinions
(xi) Secure permission/authorization from the community
(xii) Review, evaluate and if necessary, modify engagement strategies [30]

When Oxitec initiated its first field trial of GM mosquitoes in the Cayman Islands in 2009, its community engagement efforts were neither substantive nor effective. While the company had received approval from the

[4]Procedural justice refers to fairness in a decision-making process; substantive justice refers to fairness related to the outcome of the process [28,29,42].

Cayman Islands Mosquito Research and Control Unit, it had not consulted with members of affected community or obtained their approval prior to releasing its mosquitoes. Although Oxitec did engage the affected community prior to its second release in 2010, critics argued that the engagement still was not substantive or effective [6]. Oxitec learned from its mistakes in the Cayman Islands and made more substantial efforts to engage the affected community prior to conducting field trials in Brazil in 2011. In 2010, Oxitec obtained approval from the Brazilian National Biosafety Technical Commission and local public health authorities and community leaders to conduct field trials. Oxitec employees made announcements of the proposed field trials in the media, distributed fliers and leaflets, held meetings with community members, made presentations at schools, and visited the homes of residents to answer questions and learn more about their opinions and concerns. Community members expressed strong support for the field trials and were optimistic that GM mosquitoes could help control dengue fever, which they recognized as a significant public health problem [6]. Community engagement was more successful in Brazil than the Cayman Islands not only because it was more extensive but also because it exemplified the engagement values mentioned above, such as transparency, respectfulness, and inclusiveness [6,7].

## 5. Unresolved issues in community engagement

### 5.1. Defining the community

The first unresolved issue is how to define the community. A community can be defined in different ways, depending on the purpose of the definition [6,30]. For example, some communities include people who live in the same area, while others include people who share common racial, ethnic, cultural, ideological, religious, or other characteristics [6,30]. For community engagement to play a distinct role in the engagement process related to field trials of GM organisms, the definition of 'community' should include people whose interests will be directly impacted by the release [3,6,7]. Numerous groups people may have interests that could be directly impacted, such as:

- People living in the immediate area of the release;
- People living in neighboring areas that may be impacted by the release;
- People living in areas that may be targets for subsequent releases;
- People working for or managing companies that are developing GM mosquitoes;
- Investors in those companies;
- People belonging to industry groups;
- Scientists who are developing GM mosquitoes;
- Citizens who are philosophically opposed to GM organisms or have other environmental concerns;
- Health-care professionals who treat patients with mosquito-borne diseases;
- Public health professionals.

As one can see from this list, there are many people who have interests that may be directly impacted by field trials of GM mosquitoes. Although all of these people need to be included in the engagement process, one could argue that community engagement for field trials of GM mosquitoes should focus on a smaller subset of people who have interests related to their own health or their environment to ensure that their opinions are represented adequately [2,3,6]. People who have interests not directly related to their own health or their environment should be included in public but not community engagement. In the Key Haven case, for example, people living outside of the proposed release site significantly influenced the vote pertaining to the proposed field trials. An online petition collected 170,000 signatures in opposition to the field trials but only 32,000 people live in Key Haven [6].

While specifying that the relevant interests at stake should relate to one's own health or environment helps to narrow the definition of the community, there is some disagreement in the literature about how to delineate this smaller subset of the public. The WHO's *Guidance Framework for Testing of Genetically Modified Mosquitoes* emphasizes the importance of community engagement prior to conducting field trials of GM mosquitoes but does not explicitly define the 'community.' [2] Since the guidance document refers to engagement with 'those living near a research project,' 'local populations,' and people within 'geographical proximity to the site of research,' it is reasonable to assume that it uses an implicit definition of a community as people living near the research site. [2,pp.72–73]

The NASEM's report on gene drives distinguishes between communities, stakeholders, and publics and equates a community with people living in a geographic area: 'In the context of this report, we define *communities* as groups of people who live near enough to a potential field trial or release site that they have a tangible and immediate interest in the project.' [3,p.121] Stakeholders include people with personal or professional interests who may be impacted by the field trial but do not live near the release site. Stakeholders might include, for example, scientists who are developing GM mosquitoes and environmental activists. Publics are larger groups of people who have an interest in the field trials but are not impacted by them [3]. The public could include everyone living in the nation or state where a release is proposed, or even a group of neighboring nations or states.

Clearly, people who live near the proposed release site have a morally legitimate interest in participating in community engagement concerning the field trial, because the GM mosquitoes may directly impact their health or their environment [6,7]. While the NASEM definition of community seems to be clear and operationalizable, it may be too narrow, because people living outside of the release site, who are not mere stakeholders, may be significantly impacted by the field trial. For example, mosquitoes released in one location might migrate to neighboring areas (despite efforts to contain them) or approving a release in one location might set an ethical and regulatory precedent for release in similar, nearby locations. According to Kofler and colleagues:

> Characterizing what defines an affected "local" community will be an important part of this process and will depend on the nature of the technology and how it is predicted to interact with the environment. For example, if a self-propagating gene drive is under deliberation to counter malaria transmission, then representatives from much of sub-Saharan Africa would deserve a voice. [11,p.528]

Recognizing that people who live outside of the release site may also have a morally legitimate interest in being consulted about a proposed public health research project, Lavery and colleagues define the community as 'those individuals who share identified risks associated with the proposed research.' [31, p.210] This definition would include people who live near the release site as well as people in neighboring areas that may be impacted by the release or included in subsequent releases.

This definition may be too broad, however, since people who live anywhere in the world might claim that they share identified risks with those who live in the release site, because a successful field trial might enhance public acceptance of using GM organisms (GMOs) to prevent disease, which could build political momentum for additional releases of mosquitoes or other organisms around the globe. If the community is defined too broadly, then community engagement may become unworkable, and the local community's voice could be drowned out by people living outside the release area.

Developing a workable and morally sound definition of the community is essential for community engagement for field trials of GM mosquitoes. The definition should be narrow enough that it focuses on people who are likely to be directly and immediately impacted by the release, but it should not be so broad that community engagement is tantamount to stakeholder or public engagement, so that community engagement will be given the attention it deserves.

To resolve these definitional issues, I propose that for the purposes of community engagement for field trials of GM mosquitoes, the community should be defined as 'people who live near enough to the proposed field trial site that their health or environment is likely to be directly and immediately impacted by the release.' This definition would include people living in the area near the field trial site and possibly people living in neighboring areas, depending on how well the release can be contained. It would not include people who live in areas that may be included in subsequent releases. These groups could be engaged initially as part of public engagement and then later as part of community engagement, if they live near subsequent, proposed releases.

### 5.2. Conflicts between the community and the public

The second unresolved issue is how to deal with potential conflicts between the community and the public, which sometimes occur in matters relating to health and the environment. Conflicts between the local community and the greater public often occur, for example, when governments select sites for disposing municipal, hazardous, or radioactive waste [28,34]. Proper waste disposal is essential for protecting the health of the population as a whole, but people who live near the waste site are likely to face greater health and environmental risks than other members of the population. The environmental justice movement in the US emerged when members of socioeconomically disadvantaged and minority groups objected that waste disposal sites had been located near them without their input or consent [28,33]. The concept of environmental justice has been extended to a variety of issues, including pollution control, urban planning, and climate change [34,35]. The Environmental Protection Agency defines environmental justice as: 'fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income, with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies.' [36]

An environmental justice issue could arise if an affected community vetoes a proposed field trail of GM mosquitoes, but the government determines that the field trial should take place nevertheless. As mentioned earlier, Oxitec received approval to conduct field trials of its GM from the state of Florida and Monroe County Voters, but since the community where the mosquitoes would be released, Key Haven, voted against a proposed field trial, its wishes were respected. While few people disagreed with allowing Key Haven residents to prevent the field trials from taking place where they live, the situation could have played out differently. Suppose that dengue fever had posed a significant threat to public health in various parts of Florida and the state was considering conducting field trials Oxitec's mosquitoes in anticipation of widespread release of these

organisms to prevent disease. Suppose, also, that scientists and public health officials had determined that Key Haven was the optimal site to launch a field trial before releasing GM mosquitoes in other parts of the state. In this hypothetical scenario, the community's and public's interests would conflict and issues of justice and fairness would be paramount.

To gain some insight into these issues, it is worth noting that most commentators agree that field trials should not take place without the consent of the affected community [6,7,9,30]. One could argue that the community's right to autonomy implies that communities should be able to approve or disapprove of actions (or policies) that significantly impact their health or their environment, such as releasing GM mosquitoes in their vicinity [2,3,6,7]. Although we normally think of the right to autonomy as applying to individuals, one could argue that it also applies to communities insofar as they are self-governing groups of individuals with values and interests that should be respected [2,6,7].

While viewing the issue from the perspective of honoring community autonomy helps to frame the discussion of environmental justice relating to field trials of GM mosquitoes, it does not entirely resolve the moral conflict between the community and the public. The right to autonomy, as recognized in individuals or communities, is not absolute, and can be restricted to prevent harm to others or to promote compelling social goals, such as public health [34,37–39]. For example, many countries and states mandate that children receive an array of vaccines for childhood diseases [40]. Although parents have a moral and legal right to make decisions for their children, many would argue that this right can be restricted to protect the public from infectious diseases. The US Supreme Court has ruled, for example, that states can require people to be vaccinated to protect public health [41].

If one accepts the idea the governments are morally justified in overriding individual autonomy to promote public health under appropriate circumstances, then it follows that they may be morally justified overriding community autonomy for the same reason. Working from the analogy with individual autonomy, the strength of the public health argument for overriding community autonomy would depend on several factors, including the benefits to the public, the risks to the community, and the availability of suitable, alternative options for benefitting the public [37]. One might argue that the history of unjust treatment of the community is another important factor to consider, since it would be particularly unfair to continue to override the wishes of a community, such as an indigenous population in an African or South American nation, which has historically been victimized by oppression or exploitation.

Taking these four factors into account, we could say that it would be ethically acceptable to override community autonomy only when the benefits to the public substantially outweigh the risks to the community, there is no significant history of unjust treatment of the community, and there are no suitable, alternative options available. In the Key Haven case, the argument for overriding the community's autonomy was weak, since that benefits to the public did not substantially outweigh the risks to the community, given that threat posed by diseases carried by the targeted mosquito was significant, and there were suitable, alternative locations for conducting the field trials.

Ideally, a community's decision concerning a proposed field trial should be respected. If a community decides against a proposed field trial, then another suitable site should be sought. However, justice often involves difficult trade-offs between the interests of groups or individuals and those of society [29,34,37], and since situations may arise in which a community rejects a proposed field trial and suitable alternative sites are not available, it is wise to anticipate such conflicts in advance and be prepared to deal with them in a fair and reasonable way.[5] Engaging the community in an honest, transparent, respectful, and inclusive dialog about the benefits and risks of a proposed field trial allows the community's voice to be heard, even if the interests of society ultimately prevail in some situations.[6] Also, compensating the community for harms related to the field trial, such as by providing the community with medical care or financial remuneration, would be an appropriate way of offsetting actual or perceived injustice.

## 6. Conclusion

Community engagement is an integral part of field trials of GM mosquitoes. While considerable progress has been made in the last decade concerning concepts, methods, and procedures of community engagement, some important issues have not been resolved. In this commentary, I have addressed two of these issues: defining the community and dealing with conflicts between the community and the public. I have argued that the community should be defined as 'people who live near enough to the proposed field trial site that their health or environment is likely to be directly and immediately impacted by the release,' and that the

[5]In theory, the opposite type of conflict could argue, i.e. the community might seek access to GM mosquitoes that have been not approved by the public. However, given the structure of biotechnology regulation in most countries, this issue is not likely to arise because approval at the national level is required before community approval is sought [9,13].

[6]It is likely that cases involving conflicts between the community and the public will end up in the courts, which will have to weigh the interests of the community in relation to the interests of society.

community's rejection of a proposed field trial can be overridden only when the benefits to the public substantially outweigh the risks to the community, there is no significant history of unjust treatment of the community, and there are no suitable, alternative options available. Additional research, scholarship, and debate are needed to advance our understanding of principles and best practices of community engagement.

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