CAB is to bridge gaps in knowledge and to direct research and research-related practices consistent with participants' expectations and values.

Seek community authorization for field trials. Even after involving stakeholders and community members in developing ERAs, and seeking input from a CAB on site selection and other elements of the design of field trials, field trial sponsors ought to obtain community authorization before the release of GM insects. One reason that community authorization is ethically desirable is that informed consent is neither ethically required nor practically feasible[6]. There are, strictly speaking, no human subjects of field trials, so the regulations governing human subjects research, which require informed consent from every participant, do not apply. Thus, rather than go door-to-door to seek consent from every person who lives in a particular area, investigators and sponsors should seek community authorization for their field trials.

This suggestion is rooted in a commitment to democratic self-control. At the heart of democracy is the idea that citizens exercise control over policies or actions that could affect their activities or lifestyles—this includes actions that would release GM insects into their airspace. Deliberative democracy is distinct from other types of democratic decision-making procedures because the decision must issue from deliberating and reasoning with community members about how to move forward. Participants in deliberative democratic forums are exposed to the views of other people, encouraged to consider others' views, and invited to assess the collective best interest in addition to being afforded the opportunity to advance and explain their own subjective preferences[23].

There remain obstacles to operationalizing community authorization. Ways to delineate affected communities and to design and test methods of eliciting community authorization are still evolving. Still, requiring community authorization for field trials is a way of respecting persons and ceding some control to community members over what happens in their backyards, to their pets, and on their children's playgrounds.

Conclusions

None of the three suggestions in this paper is new or radical. Yet, all three are underused and have not been incorporated into decision-making procedures regarding field trials of GM insects. Taken together, they may seem like too much, like another case of ethics 'getting in the way'. But it is clear from the case studies that US Food and Drug Administration or EPA approval for a field trial of GM insects means nothing without community support. Field trials of GM insects ought not founder simply because communities have been left out of discussions. Trust and cooperation among community members, stakeholders, and the public more generally are essential to the success of field trials, and thus essential to science itself.

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Rules of the road for insect gene drive research and testing

To the Editor:

Approximately two years ago, two of us (E.B. and V.G.) demonstrated the first experimental application of CRISPR–Cas9 to 'drive' a desired trait throughout a population of fruit flies[1]. In November 2015, this same team at the University of California, San Diego, joined with A.A.J. and others at the University of California, Irvine, to develop a CRISPR-based gene drive for population modification of the malaria vector mosquito *Anopheles stephensi*[2]. A month later, a group in the United Kingdom applied a CRISPR-based gene drive to another malaria vector, *Anopheles gambiae*[3].

Many researchers around the world, including several additional authors of this Correspondence, are working to apply gene editing technologies, with the hope of safely and effectively engineering populations of insects and other pest arthropods in the wild, either to reduce diseases, such as malaria or dengue fever, or to control agricultural pests, such as those that transmit the bacterium that causes citrus greening disease. Important benefits could be realized if these research efforts are successful, but realizing these benefits requires sustained, open, and inclusive attention to potential environmental and social impacts, and regulatory and implementation challenges. Many of these challenges were outlined in the recent report by a committee convened by the US National Academy of Sciences, Engineering, and Medicine (NASEM) to review the science of gene drives and examine considerations for their responsible use[4].

In January 2016, the J. Craig Venter Institute (JCVI; La Jolla, CA, USA) and University of California, San Diego convened

a workshop to examine the governance challenges associated with the development and use of gene-drive-modified insects. The workshop brought together leading gene-drive researchers with federal officials, ecologists, ethicists, environmental policy analysts, and others.

The meeting not only identified and discussed key challenges that scientists and decision makers will face as researchers develop gene-drive insects (and other pest arthropods, such as ticks) intended for environmental release, but also identified a series of action items to help address these challenges. The resulting report[5], available online, outlines specific suggestions for researchers and research funders, US regulators and policymakers, and international organizations.

Here we focus on a subset of those action items, in particular the need for 'rules of the road', that is, guidance documents about best practices to be followed at each stage of development of the new technology. Assembling and sharing best practices among all involved is a vital component for fostering responsible development, testing, and application of rapidly advancing technologies such as gene drives.

Gene drives are a recent advance in a long line of genetic engineering techniques, thus much of the task is not the production of guidance documents *de novo*, but rather the update of the guidance prepared for earlier generations of genetically engineered insects and other pest arthropods. **Table 1** summarizes examples of important existing guidance documents, showing stage of product development (columns) and source of the guidance (rows). Boldface entries in **Table 1** anticipated gene drives, although only three[4,6,7] directly addressed the latest generation of CRISPR-based gene drives. Plain text entries were developed for earlier generations of genetically engineered arthropods. Many of us played key roles in the development of the listed documents; we understand firsthand the need for reviewing and updating guidance to take into consideration these very recent advances.

Governance of rapidly emerging technologies is often best achieved by a mix of self-governance, 'soft' governance, and enforceable ('hard') governance. Guidance by professional societies and *ad hoc* groups of scientists (the top row, **Table 1**) provides the most nimble approach, therefore, potentially the most responsive to a rapidly advancing technology, such as gene-drive-modified insects[4,6,8–11]. At the other end of the spectrum are various forms of legal or fiduciary governance, which range from guidances (which are recommendations) to regulations and statutes, which have the force of law[13–16]. Although government guidances represent the best thoughts of the agencies at the time of issuance, these forms of governance are typically more difficult to keep current. (**Table 1** includes guidance from US agencies only, although many other nations have similar documents.)

So-called 'soft governance' by regional and international organizations falls midway on this spectrum. These documents[7,17–20] provide guidance to countries—which use them as a basis for their own enforceable documents—and to product developers. Because many applications of gene-drive-modified insects are intended for use in both developed and developing nations, guidance from multi-national organizations plays a key role.

Given the current stage of scientific development, we believe the most pressing needs with regard to guidance are to update and develop guidance documents that could help the scientific community safely move insects and other pest arthropods containing gene drives from the laboratory to field trials (**Table 1**, middle column), starting with guidance on best practices for field trials in confined cages and then on best practices for small-scale open field tests.

Perhaps the strongest consensus to emerge during our workshop was the importance of incorporating community engagement before and during approved field testing of genetically engineered insects. Technical guidance is only part of the picture. There is a critical need for guidance on best practices for community engagement that consolidates and expands lessons learned from the case studies to date[10–12].

At the international level, the developers of these technologies strongly encouraged active engagement by the World Health Organization (WHO, Geneva). In particular, they urged the WHO to update its 2014 guidance framework document to their existing guidance document for testing of genetically modified mosquitoes[17]. The phased testing pathway first developed in that WHO report was extensively discussed both during our workshop and in the recent NASEM report. Although published only a few years ago, the WHO report does not directly address the latest generation of CRISPR-based gene drives. An updated WHO framework would also be a valuable resource for international and regional organizations that focus on insect and other arthropod pests of agriculture.

The potential benefits are clear if these ongoing research efforts are successful; however, the efficacy and risks must first be carefully evaluated. To do so, we need to develop societally acceptable rules.

Table 1 Guidance documents for research on, and testing of, genetically engineered insects and other pest arthropods

Type of governance	Confined laboratory studies	Field trials (confined and staged open field)	Application and post-implementation monitoring
Self-governance			
Guidance by professional societies or groups of scientists, for example	**Akbari *et al.* (2015)[6]** ASTMH (2003)[8]	**Benedict *et al.* (2008)[9]** **NASEM (2016)[4]** Brown *et al.* (2014)[10] Kolopak *et al.* (2015)[11] Lavery *et al.* (2010)[12]	n/a
Soft governance			
Guidance by regional and international organizations and bodies, for example	**WHO-TDR (2014)[17]** NAPPO (2007)[18]	**CBD (2016)[19]** **WHO-TDR (2014)[17]** **EFSA (2013)[20]** **WHO-VCAG (2017)[7]** NAPPO (2007)[18]	**CBD (2016)[19]** **WHO-TDR (2014)[17]** **EFSA (2013)[20]**
Federal governance			
Guidance by appropriate agencies in each country, shown for US only	APHIS Guidelines (2002)[13] NIH Guidelines (2016)[14]	APHIS (2012)[15] FDA (2017)[16]	APHIS (2012)[15] FDA (2017)[16]

Boldface, reports that explicitly mention gene drives. Plain text, reports that address earlier generations of genetic engineering. n/a, not available.

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