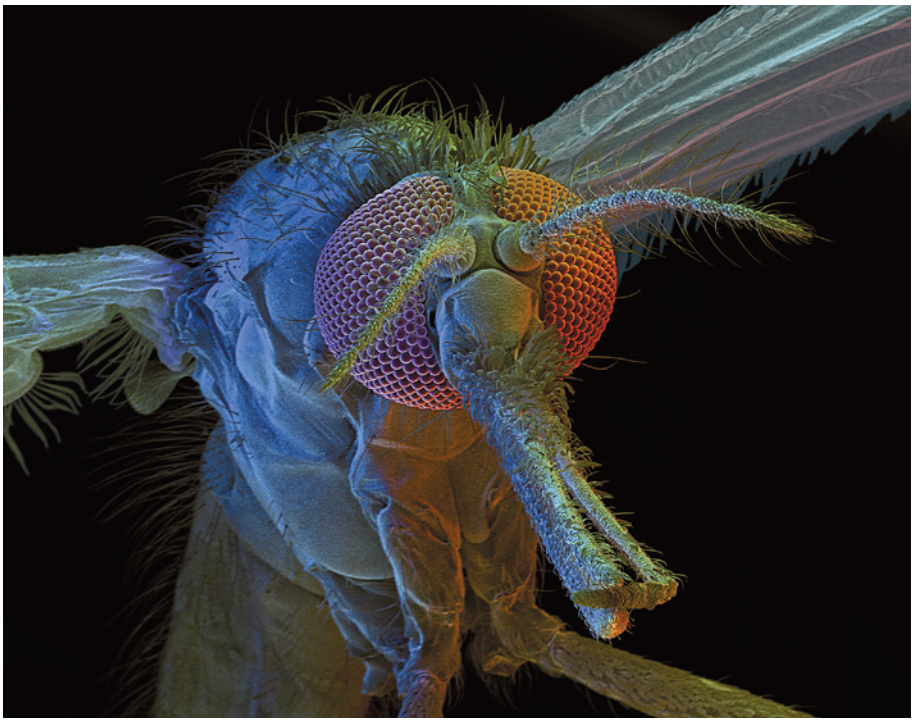

DAVID SCHARF/CORBIS

Malaria-carrying mosquitoes (*Anopheles gambiae*) are a prime target for gene-editing techniques.

BIOTECHNOLOGY

Caution urged over DNA editing in wild

Method for rapidly altering gene pools could harm ecosystems.

BY HEIDI LEDFORD

"Crap!" That was the first word out of Kevin Esvelt's mouth as he scanned a paper[1] published in *Science* last March. The work described the use of a gene-editing technique to insert a mutation into fruit flies that would be passed on to almost all of their offspring. Although intriguing, the report made Esvelt feel uneasy: if engineered flies escaped from a lab, the mutation could spread quickly through a wild population.

But that was exactly what exhilarated molecular biologist Anthony James at the University of California, Irvine. "Holy mackerel!" he wrote to the study's authors. "Can we use it in mosquitoes?"

On 30 July, the US National Academy of Sciences, Engineering, and Medicine (NAS) held the first in a series of meetings meant to find ways to balance the promise and perils of the technique, called 'gene drive'. The method can rapidly modify not just a single organism but a whole population, by inserting a desired genetic modification into an organism along with DNA that increases the rate at which the change is passed to the next generation. The technique could be used to render mosquitoes unable to carry malaria parasites or to wipe out harmful invasive species, but it could also have unanticipated environmental costs and might be impossible to reverse. "Once this is out there, you cannot call it back," says Walter Tabachnick, a population geneticist at the University of Florida in Vero Beach.

The idea of gene drive has been around for more than a decade[2]. But its practicality was given a huge boost around three years ago with the arrival of CRISPR, a gene-editing technique that allows precise changes to an organism's DNA[3].

"How do you test such a system, and how do you do it safely?"

The *Science* paper[1], by developmental biologist Ethan Bier and his student Valentino Gantz at the University of California, San Diego, used CRISPR to insert a modification into genes on both chromosomes in a pair, so that when the flies bred, they would pass the modification on to practically all of their offspring.

The work came out of a desire to develop a system that would make it easier to study genetic changes in organisms that are difficult to breed in the laboratory. Because CRISPR has been shown to work in a wide range of creatures, researchers hope one day to be able to engineer wild populations in much the same way.

CALL FOR CONCERN

Mindful of both the potential and the risks, Esvelt, a bioengineer at Harvard Medical School in Boston, Massachusetts, brought together a group of scientists to write a Comment in *Science*[4], published last week, laying out the need for multiple containment strategies for gene-drive research that is done in the laboratory. Meanwhile, the NAS meeting marks the start of a 15-month search for ways to minimize the risk in advance of field releases. Because no one is known to have made CRISPR work in mosquitoes — the mostly likely organism for the application of the technology — the committee has some time to do its work.

But there is still urgency, noted Todd Kuiken, who explores the interface of science and policy at the Wilson Center, a think tank in Washington DC. CRISPR gene-drive technology is developing at a breakneck pace, and has the potential to dramatically alter ecosystems in unexpected ways. At the meeting, Kuiken used the invasion of Asian carp into some US lakes as an example of how little is known about some wild ecosystems. "While this is an invasive species, it's also an established species," he says. "I don't think we have a good understanding of how we evaluate what happens when we remove a species from as large an ecosystem such as this."

Meanwhile, Esvelt and his colleagues are studying the CRISPR gene-drive system in the nematode *Caenorhabditis elegans* to learn more about what happens to a population as engineered DNA is passed down through generations, accumulating mutations as it goes. They are also testing ways to make sure that a gene drive can be countermanded once it has been set loose.

These issues need immediate attention, says geneticist Daniel Wattendorf at the US Defense Advanced Research Projects Agency (DARPA) in Arlington, Virginia. Security concerns may mean that DARPA needs to start working on the technology before guidelines are drawn up, he adds.

And Tabachnick remains concerned that these preparations may not suffice. "How do you test such a system, and how do you do it safely?" he asks. "I'm not convinced that any of this work could ever possibly provide the assurance of safety that one might demand." ■ SEE EDITORIAL P.5

1. Gantz, V. M. & Bier, E. *Science* **348,** 442–444 (2015).
2. Burt, A. *Proc. R. Soc. Lond. B* **270,** 921–928 (2003).
3. Jinek, M. *et al. Science* **337,** 816–821 (2012).
4. Akbari, O. S. *et al. Science* http://dx.doi.org/10.1126/science.aac7932 (2015).