(http://igtrcn.org/) Guidance Sought by Gene Drive Researchers

A letter to the editor (http://www.nature.com/nbt/journal/v35/n8/full/nbt.3926.html) of *Nature Biotechnology* authored by several individuals from some 20 organizations and including scientists, regulatory and policy experts make a case for the need to update existing research guidance documents related to research, development and testing of genetically engineered insects and arthropods.

"GENE DRIVE" ELEMENTS CAN RAPIDLY INCREASE IN FREQUENCY IN A POPULATION BECAUSE OF THEIR PREFERENTIAL INHERITANCE RESULTING FROM ANY NUMBER OF MECHANISMS. THIS RAPID FREQUENCY INCREASE IS OFTEN REFERRED TO AS 'SPREADING. The proximal drivers for this letter are the recent advances in so-called gene drive technologies – technologies that enable the assembly and introduction of transgenes into the germlines of sexually reproducing organisms so that when a transgenic individual is released into a natural population the

transgene's frequency will rapidly increase. These synthetic gene-introgression tools now enable the genetic modification of populations; in some cases leading to a reduction in size or elimination of the population. Consequently, they are being considered as potential solutions to nagging insect problems that have enormous impacts on human health and welfare – not the least of which are mosquitoes that transmit deadly human pathogens and parasites.

SYNTHETIC HOMING-BASED GENE DRIVE SYSTEM BASED ON SITE SPECIFIC DNA ENDONUCLEASES (HOMING ENDONUCLEASES, ZFN, TALENS, CAS9). TARGET SITES AND HOMOLOGY ARMS ARE CHOSEN SO THAT THE ENDONUCLEASE AND ASSOCIATED GENES (GRNA AND OTHER TRANSGENES) ARE COPIED INTO HOMOLOGOUS CHROMOSOMES. RNA-guided DNA endonucleases such as Cas9 and Cfp1 have made the assemble of homing-based gene drive technologies ie. systems that have the genetic characteristics of homing endonucleases, relatively straight forward.

Technologies for genetically manipulating natural populations, for all their potential to do good, are not without risks, controversies and opponents, even though the full potential and practicality of these technologies are far from being fully understood. The authors of the recent Nature Biotechnology correspondence are fully aware of this and this is the reason for their advocacy of additional guidance.

The authors provide a useful Table that captures the state of guidance documents for research on, and testing of, genetically engineered arthropods. Existing guidance are of two types – hard (obligatory) and soft (voluntary). The authors reference 15 different guidance documents.

The authors think that some of the existing guidance documents might be updated to account for the new insect genetic technology landscape and also acknowledge that new guidance documents might also be needed.

This is an interesting letter that reflects the considerable interest 'gene drive' technologies that has quickly evolved and the desire of those involved with it that the technology be explored in ways that enable its full potential to be assessed but in ways that are safe and acceptable.

This is worth reading.

Rules of the road for insect gene drive research and testing.

(http://www.nature.com/nbt/journal/v35/n8/full/nbt.3926.html)

Zach Adelman, Omar Akbari, John Bauer, Ethan Bier, Cinnamon Bloss, Sarah R Carter, Craig Callender, Adriana Costero-Saint Denis, Peter Cowhey, Brinda Dass, Jason Delborne, Mary Devereaux, Peter Ellsworth, Robert M Friedman, Valentino Gantz, Clark Gibson, Bruce A Hay, Mark Hoddle, Anthony A James, Stephanie James, Lyric Jorgenson, Michael Kalichman, John Marshall, William McGinnis, Jack Newman et al., Nature Biotechnology 35, 716–718 (2017) doi:10.1038/nbt.3926 Published online 08 August 2017 (http://www.nature.com/nbt/journal/v35/n8/full/nbt.3926.html)