

Experiments performed before constructing a competent drive

Evaluate candidate target sequences for cutting efficiency and specificity
Evaluate candidate guide RNAs vs equivalent sequences in related species
Measure the fitness effects of expressing Cas9 + guide RNAs on the organism
Build a 'dependent' cassette with guide RNAs targeting a unique sequence and no Cas9
Calculate homing efficiency in Cas9-expressing organisms with the unique sequence added
Determine whether the guide RNAs to be used can cut the relevant loci of related species
Generate organisms bearing the proposed genomic alterations without the drive
Measure the fitness effects of the genomic alterations in the laboratory
Evaluate the stability of non-drive cassettes and genomic alterations in the laboratory
Model gene drive spread and population-level effects using laboratory non-drive data
Run contained field trials to measure fitness of non-drive alterations in the wild
Run contained field trials to measure ecological impact of non-drive alterations in the wild
Model gene drive spread and population-level effects using field non-drive data

Relative Ecological Risk

Negligible
Negligible
Negligible
Negligible
Negligible
Negligible
Negligible
Negligible
None
Minor
Minor
None

Experiments performed after drive construction

Build and test the drive in a laboratory whose location affords ecological containment
Measure the rate of drive spread through laboratory populations
Test the rate of spread and effectiveness of reversal drives in the laboratory
Test the rate of spread and effectiveness of immunizing drives in the laboratory
Evaluate drive stability during the spreading process in the laboratory
Evaluate drive stability after reaching fixation in the laboratory
Determine whether the drive can spread into the loci of related species in the laboratory
Model gene drive spread and population-level effects using laboratory drive data
Run contained field trials to evaluate all the characteristics listed above
Run contained field trials of an autonomously spreading population suppression drive
Model gene drive spread and population-level effects using available drive data

Negligible
Moderate
Moderate
Moderate
Moderate
Moderate
Moderate
None
Moderate-High
High
None

Experiments releasing a “neutral” drive that makes no other changes

Determine whether the drive mechanism itself has any ecological impact
Measure gene flow in the target wild population
Determine whether two successive drives can recode all members of the population

Moderate
Moderate
Moderate