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California Residents' Perceptions of Gene Drive Systems to Control Mosquito-Borne Disease

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1 **California residents' perceptions of gene drive systems to control mosquito-borne disease**

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41

42 **California residents' perceptions of gene drive systems to control mosquito-borne disease**

43 **Abstract**

44 Scientists developing gene drive mosquitoes for vector control must understand how residents of
45 affected areas regard both the problem of mosquito-borne disease and the potential solutions
46 offered by gene drive. This study represents an experiment in public engagement at an early
47 stage of technology development, intended to inform lab scientists about public attitudes toward
48 their research and inspire consideration and conversation about the social ramifications of
49 creating mosquitoes with gene drive. Online focus groups with California residents explored
50 views on mosquito-borne disease risk, current mosquito control methods, and the proposed
51 development and use of different classes of gene drives to control *Ae. aegypti*. Rather than a
52 dogmatic rejection of genetic engineering or gene drive, many participants expressed pragmatic
53 concerns with cost, control, the ability to narrowly target specific species, and the challenges of
54 mistrust and institutional cooperation. Work like this is required to better align and balance
55 professional and community priorities.

56

57

58 1. Introduction

59 Mosquito vectors of disease represent one of the greatest worldwide threats to human health. Of
60 particular concern is the *Aedes aegypti* (*Ae. aegypti*) mosquito, which can transmit diseases such
61 as Zika, dengue, yellow fever, and chikungunya. This mosquito thrives in urban environments,
62 can live out an entire life cycle indoors, and can lay eggs in very small amounts of water – for
63 example in the tray under a house plant. Because the eggs may dry out and stay viable for over a
64 year, the eggs can hitchhike on objects that once hosted small amounts of dew or rainwater
65 (shipping containers, for example). Due to climate change and global trade, *Ae. aegypti* has
66 appeared in new regions over the past decade, including in California where it was first identified
67 in 2013 (Gloria-Soria, Brown et al. , Metzger, Hardstone Yoshimizu et al.).

68 *Ae. aegypti* is particularly worrisome to vector control professionals because traditional methods,
69 such as draining standing water, treating large bodies of water with larvicides and mosquito fish,
70 or using repellants and pesticides, are not effective controls. Therefore, there is a need for new
71 approaches to controlling this disease vector. In response, geneticists are developing novel
72 methods for vector control based on new CRISPR-based gene editing techniques, including the
73 use of gene drive to introduce new genetic traits with preferential inheritance into a wild population
74 (National Academies of Sciences Engineering and Medicine). However, genetically engineered
75 (GE) organisms are controversial, and public support for research on the development of such
76 strategies, particularly in the United States (U.S.), is not well understood.

77 In 2017 the U.S. Defense Advanced Research Projects Agency (DARPA) created the Safe Genes
78 program, with stated aims of gaining a fundamental understanding of how CRISPR-based gene
79 editing technologies function; devising means to harness them safely, responsibly, and predictably
80 for beneficial ends; and addressing potential health and security concerns related to their accidental
81 or intentional misuse. Team California Safe Gene Drives (hereafter, Team California) was one of
82 the projects funded by this program and aims to safely engineer various classes of gene drive to
83 control the *Ae. aegypti* disease vector. Team California also includes social scientists tasked with
84 investigating the Legal, Ethical, Environmental, Dual-use and Responsible Innovation (LEEDR)
85 dimensions of the technical aims. The technical research is being conducted in public Californian
86 universities and targets a vector present in many parts of the state; therefore, as part of the LEEDR
87 work, we engaged California residents in online focus groups to learn how they responded to the
88 idea of controlling *Ae. aegypti* with gene drive. Here, we report on how these participants discussed
89 the threat of *Ae. aegypti* as well as benefits and concerns associated with proposed GE-based
90 systems with and without gene drive.

91 This study contributes to the growing literature on public attitudes toward novel forms of vector
92 control and the uses of gene drive. Since the identification of CRISPR systems and their early
93 applications to gene editing, a community of scientists and other stakeholders has rallied to
94 establish paths toward the responsible and safe development of these tools (Oye, Esvelt et al.
95 2014, Akbari, Bellen et al. 2015, National Academies of Sciences Engineering and Medicine
96 2016, Adelman, Akbari et al. 2017, Doudna and Sternberg 2017, Esvelt 2017, Kuzma, Gould et

97 al. 2018, Long, Alphey et al. 2020). Community and Stakeholder Engagement (CSE) is a
98 cornerstone of these calls for responsible innovation. In addition to facilitating field trials and
99 informing science communication strategies, CSE can help scientists and developers to gain and
100 maintain awareness of the needs and desires of those who will likely be affected by their
101 products. Each of these goals may require different approaches to CSE (Schairer, Taitingfong et
102 al.). Broad public engagement is only one form of CSE and requires specialized social science
103 methods appropriate for collecting perspectives from a large and diverse set of people. To this
104 end, public engagement often takes the form of surveys and public opinion polls conducted to
105 establish political will and influence policy debates, as well as inform more democratic scientific
106 processes. (Pew Initiative on Food Biotechnology , Marshall, Touré et al. , Ernst, Haenchen et al.
107 , Glenza , Hudson, Mead et al. , Jones, Delborne et al. , MacDonald, Balanovic et al. 2020,
108 MacDonald, Edwards et al. 2020, MacDonald, Neff et al. 2021, Schairer, Najera et al. 2021)

109 The LEEDR activities conducted by Team California represent an experiment in public
110 engagement at an early stage of technology development, intended to inform lab scientists about
111 public attitudes toward their research and inspire consideration and conversation about the social
112 ramifications of creating mosquitoes with gene drive. We aimed to collect information from
113 California residents about a) the perceived acceptability of the gene drive systems being
114 developed by Team California and b) whether there are specific experiments or design criteria
115 that could be added to the Team California research plan that would address any concerns
116 expressed by Californians. To do so, we held a series of online chat-based focus groups that
117 allowed us to collect responses from a larger and more geographically diverse group of people
118 than would typically attend traditional community meetings or public lectures. The focus group
119 format also allowed us to encourage and center the candid responses of participants in a way that
120 is not possible in other public fora.

121 Here we present a qualitative analysis of the data collected from these focus groups, comparing
122 the benefits of and concerns about GE and gene drive mosquitoes discussed by participants.

123 **2. Methods**

124 **2.1 Participants**

125 This project was designed as a program evaluation of the experimental gene drive systems being
126 developed at the University of California, with the goal to provide scientists with feedback from
127 the public. The protocol was reviewed by the institutional review board at the University of
128 California, San Diego (project #170944) and was determined to meet the criteria for program
129 evaluation and was therefore not considered human subjects research. In program evaluation,
130 data collected are about the program rather than the participants, and therefore individual
131 informed consent is considered unnecessary.

132 To reach a cross section of Californians, we contracted with Ipsos (formerly GfK Custom
133 Research) to recruit focus group participants from their national probability-based online panel
134 (GfK KnowledgePanel). We asked Ipsos to recruit English-speaking participants based on
135 education level (with or without a Bachelor's degree) and proximity to counties in which *Ae.*
136 *aegypti* are known to be present. English-speakers from zip codes with a population density over

137 45 people/square mile were invited to focus groups according to their level of education and the
138 presence or absence of *Ae. aegypti* in their county. Spanish-speakers were invited from all
139 California zip codes. Presence of *Ae. aegypti* was determined based on reports from the
140 California Department of Public Health (California Department of Public Health). We planned 3
141 focus groups for each cohort but added groups to supplement for low enrollment. Overall, we
142 conducted a total of 18 groups (Table 1).

143 Dividing the focus group participants according to education or language preference was
144 intended to create some degree of affinity among participants per best practices in focus group
145 design (Barbour 2007). We clustered participants based on presence or absence of *Ae. aegypti* to
146 be sure that we heard from people who might be directly affected by novel vector control
147 technologies and those who would be more indirectly affected. Because of the large Spanish-
148 speaking population in California, we felt it was especially important to include this group. As
149 this was conducted as a program evaluation, we did not collect individual-level demographics.

150 2.2 Focus Group Format

151 We elected to conduct our online focus groups using text-chat instead of video to maintain a high
152 level of privacy for respondents. We used the online platform, FocusVision, made available
153 through a partnership with Ipsos. The interface allowed us to simultaneously present videos or
154 images, ask fixed-choice polling questions, and facilitate a group chat (see Figure 1).

155 Traditionally, in-person focus groups have been convened to record talk and interactions among
156 a group of people over a topic already familiar to them (Barbour , Macnaghten 2017). However,
157 we sought to use online focus groups as an “anticipatory method” (Macnaghten 2017) to
158 investigate public responses to novel emerging technologies. While GE for vector control has
159 received some media attention, reports have not been frequent enough nor of sufficient general
160 interest to be considered common knowledge. Therefore, a primary challenge in collecting public
161 responses to these techniques was presenting accessible and reasonably unbiased information
162 about a rapidly emerging technology in a new field where there is still disagreement among
163 experts (Yeo and Brossard 2017, Brossard, Belluck et al. 2019).

164 We devoted considerable time to creating informational narrated slideshows through a close
165 collaboration between members of the Bloss and Akbari labs, that is described in detail
166 elsewhere (Schairer, Triplett et al.). The focus group protocol was organized around four
167 narrated slideshow videos covering 1) mosquitoes in California and basic mosquito facts; 2) a
168 comparison of the GE based sterile insect technique (GE-SIT) and GE mosquitoes with gene
169 drive; 3) a comparison of gene drive mosquitoes designed to suppress populations versus gene
170 drive mosquitoes designed to modify populations; and 4) a comparison of different types of
171 control strategies for gene drive mosquitoes (self-limiting, threshold-dependent, and self-
172 sustaining with callback measure). The topics, total number of slides, duration of each video, and
173 the number of forced choice polling questions included in each section are presented in Table 2.

174 The GE sterile male system discussed in the slideshow was based on precision guided sterile
175 insect technique (pgSIT) proposed by Kandul and colleagues (Kandul, Liu et al.). Similar to
176 traditional sterile insect technique (SIT) where radiation is used to produce sterile insects, pgSIT
177 introduces sterile males to the environment to mate with wild mosquitoes resulting in non-viable

178 eggs and reducing the overall population. Unlike traditional SIT, however, pgSIT uses GE to
179 produce mosquito eggs that, when hydrated, will only hatch sterile male and intersex mosquitoes.
180 The gene drive systems presented in the slideshows were based on proposals to introduce lethal
181 genes that could theoretically eliminate an entire wild population over time (Kyrou, Hammond et
182 al. 2018).

183 Between each video, the moderator presented participants with a combination of polling
184 questions and open-ended questions in a chat box. The polling questions had fixed response
185 options and were designed to start conversations and contextualize the open-ended answers.
186 Slideshow videos and a listing of the polling and discussion questions are posted and published
187 (Cheung, Gamez et al. , Schairer, Triplett et al.). [Supplemental Material provided for blind
188 review.]

189 **2.3 Analysis**

190 The videos and polling questions created a standard structure across all 18 focus groups that we
191 exploited in the analysis as a way to systematically break up the transcripts and compare
192 responses across all focus groups. We categorized text chat answers following Slideshow 1
193 according to a set of common themes about the threat of mosquitoes, and the text chat following
194 Slideshows 2 through 4 according to a set of common themes about mosquito control strategies
195 using GE and gene drive. Themes included types of information that participants noted as
196 interesting or surprising (e.g., that male mosquitoes do not bite); noted features of GE
197 mosquitoes (e.g., their ability to target one species); and common concerns (e.g., impact on local
198 ecosystems). For ease of reading, we have edited quotes for spelling, punctuation, and
199 capitalization, including accents and specials characters for Spanish quotes. Any grammar
200 changes or additional words added for clarity appear in brackets.

201

202 **3. Results**

203 One-hundred-thirty-six (136) individuals participated in 18 focus groups. All recruited
204 participants lived in different zip codes. Table 1 presents the number of focus groups held for
205 each cohort and the number of participants in each group.

206 **3.1 Considerations of GE and Gene Drive Mosquitoes**

207 After both GE and gene drive methods to control mosquitoes were presented to these groups, the
208 focus of comments moved freely between genetic engineering generally (including gene drive as
209 a subset of GE) and direct comparisons of GE-SIT with gene drive mosquitoes. Participants
210 noted appealing features and concerns that apply to all GE systems and some that apply
211 differently to GE-SIT and gene drive systems. Table 3 summarizes these features and concerns.

212 **3.1.1 Appealing Features**

213 Participants pointed to two features of GE systems as particularly appealing: that they work
214 without the use of pesticides and that, unlike pesticides, they target only specific species. For
215 example, after viewing Slideshow 2, one participant commented, “Finally! A solution that

216 doesn't require spraying dangerous pesticides all over the city. Can't wait for them to do this"
217 (204BA-/Aa+). Another said, "*Sería mejor que lo que hicieron en los 80s que traían avionetas*
218 *fumigando y danando nuestra salud*" ([Gene drive] would be better than what they did in the 80s
219 when they brought in planes fumigating and damaging our health.)(912S). The preference over
220 pesticides continued to be expressed after Slideshows 3 and 4, culminating in the answers to a
221 poll at the end of the sessions where 125 respondents (92%) indicated that genetic engineering
222 would be "better" than pesticides while only 7 indicated that it would be "worse." We also saw
223 many discussions about the ability of genetic engineering approaches to target single species.
224 Some participants wanted to clarify that this would be the case, often asking questions about
225 breeding behavior among mosquitoes. For example, one participant asked, "can they leave all
226 other kinds alone?" (775BA-/Aa-) and another asked, "*¿Como reaccionarán los mosquitos*
227 *hembras con estos mosquitos modificados? ¿Se aparearan de la misma manera?*" (How do
228 female mosquitoes react to the modified mosquitoes? Do they still mate the same way?)(738S).

229 As participants made sense of the differences between the GE-SIT system and the various gene
230 drive systems presented throughout the session, many participants were particularly interested in
231 the relative cost of the methods. For example, one participant commented, "Both seem like
232 viable solutions. My deciding factor would be the price point" (559BA+/Aa-). Some focused on
233 the fact that, because gene drive could potentially work after only one release, this method would
234 be more cost effective, asking versions of the question, "Is it [GE-SIT] economically feasible?"
235 (788BA-/Aa-).

236 Control was also top of mind for many when comparing the methods that were presented. For
237 example, a participant commented, "I'd say I'm more ok with GE sterile [GE-SIT] because
238 there's more opportunities to stop it if something bad were to happen with the gene editing"
239 (201BA-/Aa+). A similar concern was geographical control, or confinement of gene drive
240 systems that might, in theory, lead to the eradication of a population after only one release.
241 Regarding gene drive, one participant asked, "*¿Cómo se controla la población en un área?*
242 *Estos vuelan de zona a zona, estado a estado,*" (How do you control the population in an area?
243 These [mosquitoes] fly from area to area, state to state)(2036S). With respect to control and
244 confinement, the GE-SIT system had the attractive feature of a clear way to stop.

245 When considering the different control strategies for gene drive systems presented in Slideshow
246 4, the importance of confinement was again discussed. While some were in favor of more
247 controlled methods, 43% of participants selected self-sustaining gene drive (the least controlled
248 option) as the "most acceptable to use" in their communities in response to a poll. At the same
249 time there were some discussions of how the use of gene drive might be coordinated across city,
250 county, state, or international borders. In two groups, such responses were accompanied by
251 comments that the decision to use a self-sustaining system would require federal action because
252 individual states or counties would not be able to make the decision on their own.

253 **3.1.2 Common Concerns and Questions**

254 Most of the concerns raised by participants were applicable to both GE and gene drive systems.
255 While the potential efficacy, cost-efficiency, and control of these systems were appealing,

256 participants also voiced concerns and asked critical questions about whether and how these
257 features will be achieved. These technical concerns included whether the GE systems would be
258 effective in reducing the mosquito population; if the systems would be prohibitively expensive to
259 use; or if they will be developed in time to address vector-borne disease before an outbreak.
260 Some such comments called for more information or research. For example, one participant
261 wondered about how many mosquitoes would be necessary: “My suspicion about gene drive is
262 that research would be required to determine the mating rate and reproductive rate to determine
263 if a huge cloud of GE males would need to be released in order to be effective.” (734BA-/Aa-)
264 Another participant expressed a desire to see “proof that these methods are making a difference
265 without much altering [of] other problems.” (784BA-/Aa-) Other participants wanted more
266 information about the state of the science: “¿y cuál fue el récord? Dos años es muy corto el
267 plazo para ver verdaderamente las consecuencias.” (How has this been working out so far? Two
268 years is a very short time to truly see the consequences) (2056S). In these discussions,
269 participants often expressed conditional approval, for example, “If the data provides that it is safe
270 within margins and is double checked by other agencies then fine use it.” (109BA+/Aa+)

271 Many comments about unwanted outcomes revolved around possible adverse effects on the local
272 ecosystem should *Ae. aegypti* be successfully eliminated. Though the slideshows presented *Ae.*
273 *aegypti* as non-native to California, participants wondered, “Does AA [*sic*] have any function in
274 our ecosystem or can we get along without it?” (529BA+/Aa-), “Would this have a negative
275 effect on other insects?” (739BA-/Aa-), and “I assume the bugs that eat mosquitoes are just as
276 willing to eat sterile/gene modified ones as not?” (110BA+/Aa+). Some worried about possible
277 dangers related to being bitten by modified mosquitoes and the possibility of either the
278 mosquitoes or the pathogen developing resistance to a genetic intervention. For example, “I am
279 more concerned about what's in the bite than the bite [itself]” (785BA-/Aa-) and, “What if the
280 diseases evolved to become better at infecting the mosquitos?” (522BA+/Aa-).

281 Some participants raised concerns about the social context of these technologies. Participants
282 across groups addressed the importance and cost of public education for both acceptance and
283 cooperation. For example, “Before funding the research, [unspecified subject] should let
284 everyone know. And educate them” (760BA-/Aa-). Some worried that the public will not accept
285 these technologies without enough education or that they could undermine the intervention by,
286 for example, killing the GE mosquitoes. As one participant put it, “Una duda que tengo es si se
287 alertaría a la población para no rociar insecticidas sobre los mosquitos machos.” (Will the
288 public be instructed not to spray pesticides to combat the male mosquitoes?) (804S)

289 Other social concerns revolved around who will decide what research to fund or when to use GE
290 mosquitoes. Such discussions often included expressions of mistrust of the government or for-
291 profit companies. For example, “As long as no company can somehow claim any copyright [of]
292 this method or the like.” (109BA+Aa+) One participant voiced questions about the transparency
293 of the focus group itself: “No es debata, es información, para acudir opinión del público para
294 entonces utilizar como sea adecuada. Quién pagó a [moderator] para ser este proceso?” (This
295 isn't a debate, it's information, in order to get public opinion which will then be used however
296 they see fit. Who paid [moderator] to do this?) (2036S). Another participant felt that educated
297 citizens should be consulted: “Citizen oversight can be a good thing, but the citizens should

298 understand a little about science and the scientific method, and not be employed by the
299 companies providing chemical or modified mosquitoes” (522BA+/Aa-). Another raised
300 questions about how voters may respond to these methods: “I keep asking how many years and
301 voters will complain about cost. Some in big cities may not have the problem but they do vote!”
302 (539BA+/Aa-).

303 Finally, some participants voiced general discomfort with using GE, and a few expressed
304 outright rejection of GE or questioned the assumption that GE mosquitoes would be better than
305 pesticide use. For example, “Why are we replacing spraying them? Is that worse than changing
306 their DNA?” (539BA+/Aa-). Many others worried about unforeseen consequences connected to
307 gene drive in particular and the possibility of a slippery slope toward other types of gene drive
308 organisms. For example, participants commented, “I don't have a problem with it if it was only
309 used to control mosquitoes. I have a problem if it starts with mosquitoes and leads to other
310 things” (619BA-/Aa+), and “I am not sure of the risks associated with Gene Driving. It might be
311 a solution... or it might also create another problem” (724BA-/Aa-). Some of the participants
312 who voiced these concerns gravitated toward the GE-SIT method. For example, after viewing
313 slideshow 3, comparing gene drive for population reduction vs. gene drive for modification, one
314 participant stated, “Interesting concepts but I always wonder about any unanticipated side
315 effects; I like the GE model” (134BA+/Aa+).

316 Some focus groups clearly weighed or debated these concerns and questions with reference to
317 the threat of human disease and alternative solutions, such as pesticides or vaccines. As two
318 participants put it, “the fact [that GE mosquitoes are] not hazardous to humans is a plus but not
319 doing anything is the hazard” (703BA-/Aa-), and “Well, hypothetically, any gene modification
320 could have unintended consequences. That doesn't change the fact there is a threat that needs to
321 be addressed.” (501BA+/Aa-) Another group had an extended exchange about the possibility of
322 pursuing a vaccine for these diseases. One participant contributed, “Well a vaccination sounds
323 good but why put that on humans = there is already the immunization vaccines having issues
324 with parents vs doctors vs schools, if we can eliminate humans getting the disease another way I
325 think that is the better option” (703BA-/Aa-).

326 **4. Discussion**

327 In these focus groups, California residents engaged in a nuanced consideration of GE and gene
328 drive for mosquito control. Along with positive comments and willingness to consider these
329 technologies came many questions and clarifications that would be critical to address had we
330 been asking participants to make a commitment to any of these methods. Just as participants saw
331 reasons for optimism, they also raised many reasons for caution. The same participants who
332 expressed openness to GE for vector control also often voiced worry and discomfort with the
333 unknowns, possible adverse outcomes, and complexity associated with these methods. When
334 participants discussed possible adverse consequences, they weighed them with their perception
335 of the disease threat and the risks of alternative possible solutions. These comments reflect the
336 how California residents consider a broad set of priorities that may differ from the more focused
337 professional priorities of scientists and vector control specialists.

338 The merits and concerns raised by these California residents are quite similar to those found in
339 other survey, interview, and focus group studies. Other studies of communities or publics
340 consistently discuss hopes that GE and gene drive will provide effective, safe, and economical
341 solutions to the threat of vector-borne diseases (Marshall, Touré et al. , Hudson, Mead et al. ,
342 Jones, Delborne et al. , Hartley, Smith et al. , MacDonald, Neff et al.). Likewise, these studies
343 have recorded common concerns related to environmental impact, off-target impacts, human
344 health risks, and general wariness of GE technologies. Concerns about governance (Hudson,
345 Mead et al. 2019, Jones, Delborne et al. 2019, Hartley, Smith et al.) and socio-political impact
346 (Marshall, Touré et al. , Hudson, Mead et al. , Hartley, Smith et al.) have featured in only some
347 of these prior studies. We note that cost appeared to be more central to our participants’
348 considerations than is suggested by the documentation of other studies.

349 These findings suggest that gene drive systems for mosquito control could find support in
350 California, especially if experts are able to adequately address concerns about the impact of
351 eliminating the target species, cost, and efficacy. Additionally, support of gene drive for
352 mosquito control will likely hinge on awareness of the threat of mosquito-borne disease in
353 California and how addressing this threat ranks among competing priorities. These findings
354 suggest that establishing the threat of these diseases may be enough to engender openness to, if
355 not support for, gene drive systems.

356 Given the controversy surrounding Oxitec’s trials of GE mosquitoes in Florida (Bloss, Stoler et
357 al. 2017, Schairer, Najera et al.), it is reasonable to wonder if Californians would support the use
358 of gene drive mosquitoes without the presence of endemic mosquito-borne disease. We note that
359 in this study, Slideshow 1 appears to have convinced many participants of this threat in the
360 course of a 5-minute narrated slideshow. It is not clear, however, that such a presentation would
361 be equally convincing in other venues, such as mass media campaigns or community forums.
362 Community leaders and public health officials should not assume that citizens are aware of the
363 threat of mosquito-borne disease in California, nor should they assume citizens will dismiss this
364 threat in the absence of endemic cases.

365 **4.1 Limitations**

366 While our sample size would be small for a survey study, our 18 focus groups make this a large
367 qualitative study that captured the geographic diversity within California through the use online
368 focus groups. As a qualitative study, it was designed to study the presence rather than the
369 prevalence of the opinions and themes we observed. The findings from this study could inform
370 the collection of more generalizable data through a survey of a larger sample.

371 An important consideration for this study was the content of the narrated slideshows used as
372 stimulus materials for these focus groups. Because the slideshows were prerecorded, they
373 allowed for a uniformity in both content and structure across the groups. However, this also
374 made it more difficult for participants to ask clarifying questions and gave the moderator less
375 flexibility in leading the conversation. Though we worked hard to produce accurate and
376 reasonably neutral content, we acknowledge the possibility of bias in such materials. To address
377 and mitigate this, we have made our slideshows publicly available (Bloss 2018, Bloss 2018,

378 Bloss 2018, Bloss 2018) and extensively documented the process of development (Schairer,
379 Triplett et al.).

380 The chat-based format for these focus groups also created challenges for moderating. Though
381 this format allowed for complete anonymity of the participants, it precluded our ability to use
382 non-verbal cues when interacting with the group. The text-chat allowed for everyone to type at
383 once, which helped us collect many opinions but likely hindered discussion between participants.
384 Some groups seemed to address most of their comments to the moderator, while others did
385 generate conversations and some debate, especially in the second half of the sessions. Some
386 guides on conducting online focus groups suggest asking participants to take turns and mind the
387 interface's signal that another is typing (Lobe 2017). Such a practice may have fostered even
388 more discussion, but also would have afforded less time for everyone to contribute.

389 **4.2 Implications and Future Directions**

390 Efforts to create more democratic science, inclusive public debate, and community and
391 stakeholder engagement surrounding the use of gene drive rely on diverse groups of people
392 listening to each other and an openness to learn from the experiences of others. This focus group
393 project was one approach to collecting reflections of California residents to share with the
394 scientists who work in public state universities. The hope is that projects like this one will help to
395 build a bridge between scientists and members of the lay public who might not otherwise be able
396 to hear one another. Rather than create a public meeting that centers expert presentations, this
397 focus group approach provided space for participants to ask questions and discuss the presented
398 technology without the potential inhibitions some feel in the presence of experts or in large
399 groups. This approach also allowed us to reach a more geographically diverse group of people.

400 The findings can inform the work of scientists and gene drive developers by providing insight
401 into how uninitiated California residents respond to the problem of *Ae. aegypti* control and
402 potential solutions being explored in current research. These findings are a reminder that most
403 Californians are unaware of the special challenges related to controlling *Ae. aegypti* that motivate
404 the research of Team California. The study also illustrates the many competing priorities
405 California residents will consider when faced with GE and gene drive solutions. In this case,
406 most participants agreed that the problem was worrisome, despite little prior knowledge, and
407 many were receptive to novel approaches to vector control. However, understanding the problem
408 did not lead to unquestioned acceptance of the proposed possible solutions; participants sought to
409 balance priorities and risks and desired more information and assurances of transparency before
410 supporting any given solution. In addition, participants expressed more concerns about GE
411 mosquitoes in general rather than gene drive specifically. This suggests that resistance to GE
412 technologies as a general category may be more of a barrier than resistance specific to gene
413 drive.

414 We note that findings from this work have inspired the outline of a set of core commitments for
415 field trials of gene drive organisms (Long, Alphey et al. 2020). Prior to any gene drive field
416 release, these commitments include fair partnership and transparency, testing of product efficacy
417 and safety, regulatory evaluation and risk/benefit analysis, and developing monitoring and

418 mitigation strategies. Additionally, given the apparent fear of non-confineable gene drive
419 technologies observed in this study, the Akbari lab is prioritizing research on confineable
420 technologies for controlling populations such as self-limiting drives (Li, Yang et al. 2020) and
421 GE-SIT systems (Li, Yang et al. 2021).

422 This study underscores the crucial and on-going work of identifying and aligning the priorities of
423 citizens and professionals in public health efforts. As the research on gene drive mosquitoes
424 progresses, developers and their partners in public health agencies must remember to state the
425 problem they are trying to address and listen to how community members and other stakeholders
426 may weigh the problem in the context of broader considerations. Maintaining awareness of this
427 will help developers to create solutions that are both acceptable and usable for the communities
428 they wish to serve.

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430 5. References

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551 Table 1. Number of focus groups and participants in recruitment cohorts.

	<i>Ae. aegypti</i> Not Reported		<i>Ae. aegypti</i> Reported		Total	
	Focus Groups	Participants	Focus Groups	Participants	Focus Groups	Participants
Less than a Bachelor's degree	3	29	4	25	7	54
More than a Bachelor's degree	3	33	3	20	6	53
Spanish Speakers	-	-	-	-	5	29
Total	6	62	7	45	18	136

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553 Table 2. Structure of Chat-Based Focus Group Sessions

Sequence	Title / Theme	Slideshow Duration	Number of Slides	Forced Choice Polling Questions	Open Discussion Prompts
Opening	Initial Perceptions of the Problem	-	1	2	3
Slide Show 1	"Mosquitoes in California"	5:10 min	10	3	2
Slide Show 2	"Genetic Engineering for Mosquito Control"	5:50 min	8	4	2
Slide Show 3	"Modifying Mosquitoes with Gene Drive"	2:49 min	5	2	1
Slide Show 4	"Controlling Gene Drives"	5:49 min	8	4	2
Closing	Review and Discussion	-	-	4	3

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Table 3. Comparison of appealing features and concerns across presented technologies.

System	Appealing Features	Concerns
Any GE	<ul style="list-style-type: none">• Not pesticides• Targeted	<ul style="list-style-type: none">• Skepticism about functioning as intended• General discomfort with GE• Unwanted environmental outcomes• Social resistance• Distrust of government and industry
GE-SIT	<ul style="list-style-type: none">• Control and confinement clear and intuitive• Local decision to use	<ul style="list-style-type: none">• Expense (many releases)
Gene Drive	<ul style="list-style-type: none">• Cost effective (fewer releases)	<ul style="list-style-type: none">• Requires geo-political cooperation• Not timely (will not be ready in time)

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