**template for Peer Review comments**

**Technical series on synthetic biology**

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| **Comments on the Technical Series on Synthetic Biology** | | | |
| **Page #** | **Line #** | **Comment** | |
| 0 | 0 | **General Comment:**  Gene drives are consistently characterised as being in the advanced stages of research or on the cusp of commercialization throughout the text. It is unclear what exactly is meant by “advanced stages”, but gene drives are many years away from being deployed or placed on the market. The text should be revised to reflect the fact that no field trials of gene drives have yet taken place and any such test is likely years away, and that the most advanced gene drive applications currently under development are being developed by not-for-profit research consortiums, and will not be marketed on a commercial basis. | |
| 10 | 1 | It should be recognised that there is much ongoing work on non-profit applications of synthetic biology. They will not have market value per se but can support economic growth in other ways (e.g. through improved public health outcomes). | |
| 10 | 47 | Saying that “gene drives could reach the market in a few years” is potentially misleading, as the most advanced gene drive applications currently under development will not be sold or distributed on a commercial basis and are still far from being ‘ready for use. They are intended to complement public vector-control campaigns or public invasive alien species control campaigns. | |
| 14 | Table 1. | It may be premature to characterise “engineered gene drives in mosquitoes for control of vector-borne diseases” and “engineered gene drive for an agricultural pest” as in “advanced development” as both applications have not undergone field trials and are many years away from being ready for use. | |
| 19 | 33-34 | We welcome the recognition that “gene drive” refers to a broad array of approaches and applications and is best thought about in those terms rather than as a single technology. This should be stressed throughout the document. For more information on the different types of gene drives and how to refer to them, please see:   * Alphey LS, Crisanti A, Randazzo F, Akbari OS. *Opinion: Standardizing the definition of gene drive.* Proceedings of the National Academy of Sciences Dec 2020, 117 (49) 30864-30867; DOI: 10.1073/pnas.2020417117 <https://www.pnas.org/content/117/49/30864> | |
| 19 | 38 | Phenomena other than gene drives can also cause increases in the frequency of inheritance of a particular genetic element in a population (e.g. natural selection). | |
| 32 | 9-11 | This language is potentially misleading as it implies that Target Malaria’s work is not conducted in contained conditions. It should be rephrased to make clear that all of Target Malaria’s research to date involving organisms with engineered gene drives takes place in containment, and no field testing of a gene drive system has been undertaken or is planned for the near future.  (Target Malaria did perform a small-scale release of genetically modified mosquitoes in Burkina Faso in 2019, but they did not contain gene drives. For more information: <https://targetmalaria.org/results-from-months-of-monitoring-following-the-first-release-of-non-gene-drive-genetically-modified-mosquitoes-in-africa/> ) | |
| 32 | 5-19 | As mentioned elsewhere, neither “engineered gene drives in mosquito for potential control of vector-borne diseases” or “engineered gene drive for an agricultural pest” are considered to be in “advanced development”. | |
| 40 | 26-28 | As above, gene drives for disease vector control are not in the advanced stages of development. | |
| 43 | 22-23 | A “replacement drive” would not have the “ultimate goal” of “eradication of an invasive species or pest”, but rather to modify it so that it would no longer present a threat. | |
| 44 | 2-3 | A population replacement drive would not necessarily lead to lower numbers of a target species. | |
| 44 | 16-18 | Current research does not support the assertion that gene drives are “likely to be highly invasive”. Invasiveness of specific constructs and applications will be determined by their particular characteristics, and many applications will not be self-sustaining. | |
| 58 | 10-12 | Characterisation of the risk assessment challenges as “unprecedented” is unwarranted, as potential comparators exist, such as bio-control agents. In addition, the conclusion at the end of the paragraph that risks cannot be adequately assessed seems to be contradicted by the rest of the text in that paragraph, which notes that relevant principles and methodology for risk assessment of gene drives exist. It is also not consistent with the conclusions reached by the World Health Organisation, The European Food Safety Authority, and the report on the risk assessment of living modified organisms prepared by Perseus on behalf of the Secretariat of the Convention on Biological Diversity. | |
| 58 | 23-24 | References should be provided to support the assertion that existing risk assessment methodologies may be applicable to gene drive, recognizing that this is not a fringe position among regulatory experts and publications. | |
| 58 | 37-38 | Text should be added recognizing that modelling is a standard part of current risk assessments and not a novel practice unique to the assessment of gene drives. | |
| 62 | 21 | This section should also discuss multi-component and split drive approaches to biocontainment, which are distinct from the approaches intended to reverse a drive already included. | |
| 67 | 32-33 | The adequacy of existing guidance and methodologies for the risk assessment of gene drives should be included as another area in which concerns have been raised. | |
| 67 | 38 | It should be noted that the purpose of continued laboratory research is to improve understanding and knowledge of gene drives and their potential risks and benefits. | |
| 70 | 10 | This is potentially misleading, as gene drive researchers have collectively developed principles for responsible and safe gene drive research, for example:   * Emerson C, James S, Littler K, Randazzo F.  *Principles for gene drive research.* Science 358 (6367), 1135-1136 DOI:10.1126/science.aap9026. <https://science.sciencemag.org/content/358/6367/1135> * Akbari OS, Bellen HJ, Bier E, et al. *Safeguarding gene drive experiments in the laboratory*. Science. 2015;349(6251):927-929. doi:10.1126/science.aac7932. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4692367/> | |
| 73 | 13-18 | The reference to engineered gene drives should be removed, as they are nowhere near the point of commercial release. | |
| 96 | 4 | Section 9.2.1. omits WHO’s *Guidance framework for testing genetically modified mosquitoes* which is relevant to synthetic biology and should be referenced:  Guidance framework for testing genetically modified mosquitoes, second edition. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO. <https://www.who.int/publications/i/item/9789240025233> | |
| 132 | 7-9 | Gene drive research is mostly still at an early stage, so this technology may not represent the most “useful lens through which to evaluate overlaps and potential gaps in the governance of synthetic biology”. | |
| 133 | 8-10 | As mentioned earlier reference to engineered gene drives here is inaccurate, as they are not considered to be “in the advanced stages of development”. | |
| 134 | 3-4 | Citations for the “scientific research addressing community engagement in field trials, concerning for instance engineered gene drive organisms (i.e for malaria control)” should be included. | |

Please submit your comments to [secretariat@cbd.int](mailto:secretariat@cbd.int).