Secretariat, Convention on Biological Diversity
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Submission: Risk Assessment and Risk Management of LMOS containing gene drives

The African Centre for Biodiversity (previously the African Centre for Biosafety) (ACB) is a South African non-governmental organisation committed to dismantling inequalities in the food and agriculture systems in Africa and our belief in people's right to healthy and culturally appropriate food, produced through ecologically sound and sustainable methods, and their right to define their own food and agricultural systems. The ACB has actively participated in various negotiations concerning biosafety and genetically modified organisms (GMOs) under the aegis of the Convention of Biological Diversity (CBD) and the Cartagena Protocol on Biosafety, as well as various regional and national biosafety processes over the past 15 years, in promoting biosafety best practice and the precautionary principle in regard to GMOs.

We thank the Secretariat of the CBD for inviting us to make submissions on Risk Assessment and Risk Management of Living Modified Organisms containing gene drives related to the topics dicussed below in regard to gene drives. We do not in this submission, deal with LM fish.

a) Experience in undertaking risk assessment of living modified organisms containing engineered gene drives and living modified fish (detailing how and for which cases); or else, lack of experience in doing so;

1. The advent of gene drive technologies is raising unprecedented challenges for legislators and regulators. Living modified organisms (LMOs) (using the parlance of the Biosafety Protocol) containing gene drives, though a continuation of evolving genetic modification technologies, have been described as "conceptually and biologically novel", displaying unique characteristics that distinguish them from genetically modified organisms developed to date (Simon et al., 2018). Such novelties present new and serious concerns for biological diversity conservation, with potential for negative effects on human health and socio-economic circumstances. These distinct features are not covered by current legislation here in South Africa particularly the Genetically Modified Organisms Act, 1997 (Act No. 15 of 19917) and its Regulations, or indeed elsewhere on the continent.

2. Most fundamentally, gene drive technologies are for the first time, allowing for the permanent genetic modification of wild populations. Previously in South Africa, all approved LMOs have thus far been restricted to cultivated species. Moving from the modification of cultivated species to wildlife,

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raises potential for major consequences on semi-natural and natural ecosystems that go beyond agroecosystems. A second and fundamental distinction between standard LMOs and those containing gene drives are that the latter are designed to persist and spread the modification throughout a population and even species. While for genetically modified organisms, the persistence and spread of transgenes has a high chance of eventually being diluted and lost in the population, with gene drive organisms, inheritance and spread is a prerequisite.

3. Another critical distinction is the inheritance of the genetic modification toolbox, such as CRISPR/Cas genome editing systems, by the gene drive organisms. This is essentially moving the genetic modification process from the confines of a laboratory, to the natural environment where the genetic modification of organisms occurs at each generation, in perpetuity.

4. South Africa and for that matter, Parties on the rest of the continent has/have no experience in performing risk assessments on gene drive organisms, and current national and international LMO protocols developed for the first generation LMOs are inadequate for addressing the above novelties raised by gene drive technologies.

5. We are strongly in favour of further guidance for conducting risk assessment and management on LMOs containing gene drives. Further, due to the potential grave effects they could exert on biological diversity, human health and socio-economic circumstances, any such risk assessment warrants adherence to the precautionary approach.

6. Furthermore, in the light of the potential grave effects, we further request that the AHTEG address issues relating to open, transparent consultations with stakeholders to elicit their views and participation in decision making, taking into account the relevant provisions of the Biosafety Protocol in this regard and especially the decisions taken by the Conference of the Parties (COP) at the COP in Sharm el Sheik in November 2019, in regard to free, prior informed consent that must be adhered to in this regard.

7. Issues arising from the potential negative impact on biodiversity from transboundary movements of gene drive organisms, particularly gene drive insects that may be released on the continent and indeed anywhere in the world, needs close attention and responses.

b) Challenges experienced or foreseen in undertaking risk assessment of living modified organisms containing engineered gene drives and living modified fish;

1. Gene drive technologies are in their infancy and scientific understanding of their potential impacts remains incomplete. Their novel features raise new risks and uncertainties and added complexities that we are yet to encounter when regulating genetically modified organisms in the country.

2. For the first time, we are dealing with genetic modification that is designed to spread and persist in the wild, aimed largely at modifying wild populations. This lack of controllability raises concerns over how to assess a gene drive organism whose potential ecological and health impacts cannot be adequately assessed without first deploying it. However, any deployment even as part of a field trial experiment, is effectively an open environmental release that is persistent and irreversible by design, with the capacity to spread beyond the initial area. Concerns over this lack of controllability has been raised by gene drive developers themselves, who have said that gene drives are likely to be "highly invasive" and spread to most interbreeding populations (Noble et al., 2018). The stepwise approach of risk assessment for LMOs thus cannot be performed as it includes field testing, which requires the release of gene drive organsisms into the environment which can turn into a full-scale release.

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Suggestions to perform field trials on islands are insufficient as a containment measure, as stated by the Ad Hoc Technical Expert Group on Synthetic Biology: 'Islands are not ecologically fully contained environments and should not be regarded as fulfilling the conditions in the definition of contained use as per Article 3 of the Cartagena Protocol unless it is so demonstrated' (AHTEG, 2017: Para 51 (b)).

3. The effects of modifying or eradicating entire populations or species on biological diversity and the wider ecosystems is impossible to predict, and potentially harder to reverse. Altering the course of evolution may have unforeseen circumstances for future generations. Yet, limited knowledge exists to be able to predict the ecological importance of removing/altering a species. There is potential for knock-on effects on the wider ecosystem affecting food webs such as pollinator, predator or pest numbers; niche replacement where a new species takes over the environment left behind by an eradicated species, including for example, another disease-carrying mosquito species; or unintentionally wiping out species that are culturally or economically important to particular regions of the world or to indigenous peoples and local communities.

4. Predicting potential impacts is further complicated by the fact that gene drives are effectively transforming natural ecosystems into laboratories. Standard genetic modification to date has focused on seed varieties that have been bred to behave uniformly. Gene drive releases target wild populations that are genetically diverse, making it difficult to predict how the gene drive will spread, and behave. Gene drives also have the capacity to erode genetic diversity as the gene drive organisms spread through a population.

5. At the molecular level, there are several risks associated with the gene drive technologies that could also introduce unintended effects on ecosystems and people. Gene drives developed with genome editing tools such as CRISPR/Cas systems can introduce heritable off-target changes to the genome of the gene drive organism (Hayes et al., 2018). Unwanted changes to DNA may go on to alter phenotypic characteristics of organisms such as enhancing capacity to transmit disease in the case of disease vector gene drive organisms such as mosquitoes, or altering toxicity to predators for example. Such off-target effects are difficult to predict and characterise before the release into the environment, particularly in genetically diverse wild populations.

6. There is also a risk the gene drive constructs could spread beyond the target species and thus permanently or for some time, eradicating non-target populations.

c) Specific needs (if any) to properly undertake risk assessment of living modified organisms containing engineered gene drives.

1. With respect, it is our submission that Africa and for that matter, the international biosafety regulatory community currently does not have sufficient experience and knowledge to handle this technology safely, reflective of the global situation that is grappling with a new technology that is in its infancy and still developing.

2. Huge gaps in knowledge remain globally within the scientific community that raise risks and uncertainties. For example, limited information exists regarding receiving environments, the species to be modified and their roles in ecosystems and the consequences of genetically altering or eliminating entire species.

3. With regard to public health applications of gene drives, their releases raise uncertainties and risks with regard to their potential to negatively affect disease epidemiologies. There is potential for niche-

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replacement of eradicated populations by other disease vectors, or for example, the occurrence of 'rebound effects' of diseases such as malaria if people lose acquired immunity to disease.

4. The issue of contained use also warrants special attention. Since the escape of a single LMO containing gene drives has the potential for widespread geographical diffusion, strict conditions need to be established. This also raises important questions regarding transboundary movement and the issue of free, prior, informed consent for potentially affected communities that may be at the receiving end of an unintended release.

5. Cost-benefits analysis of gene drive technologies are also critical for evaluating whether or not gene drive technologies are suitable for the South African context. Recent modelling papers suggest that limitations in efficacy may necessitate multiple and regular releases of LMOs containing gene drives (Eckhoff et al., 2017). Such analyses are necessary to be able to adequately assess their potential utility as a public health strategy against Malaria for example.

Kind regards

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