**SA comments on draft study applying annex I of decision CP-9/13 to living modified organisms containing engineered gene drives**

|  |  |  |  |
| --- | --- | --- | --- |
| **Page Number** | **Line in text** | **Section** | **Comments and Rationale** |
| **18**  | **1** | **BACKGROUND** |
| 19 | 25 | Status of application of LMO with engineered gene drives | **Comment:*** This space should be monitored for further developments that may have implications for the Protocol. Risk Assessment pertaining to LMOs with gene drives should take a precautionary approach that takes into account the worst possible case scenario when assessing potential risks to the environment, humans and animals.
* Risk assessment for research phase of LMOs with gene drives in contained use should be greatly anchored on prevention of adverse effects to the environment by enforcing measures to prevent the release of any LMOs with gene drives into the environment.
* In the step-wise approach, more thought would need to go into the risk assessment for the field releases, the conditions under which this would be released if accepted and the risk management measures including monitoring.
* More research is needed in this area.
* Experience from regulatory approvals and field release of Wolbachia-infected species would be useful for LMOs with engineered gene drives.

**Rationale:**Engineered gene drives have a potential for exploitation in various sectors of the economy including supporting health program targeted at controlling disease vectors of public health importance, fight against invasive species and other emerging agricultural pests.South Africa is considering regulatory approval for pilot trials to assess the sterile insect technique for malaria mosquitoes as part of South Africa malaria control programme. The mosquitoes are not genetically modified and do not contain gene drives, however, as with the Zheng et al (2019) example, this anticipated approval process and the subsequent release if accepted will be good experience for the GMO regulatory system when considering applications for LMOs with engineered gene drives.  |
| **24** | **1** | **CONSIDERATIONS FOR RISK ASSESSMENT** |
| **24**  | **9** | **Applications** |
| 24 | 15-19 | Broad diversity | **Comment:** South Africa supports the case-by-case approach given the broad diversity of applications of gene drives, the range of host organisms, the target species and the potential receiving environments. **Rationale:** South Africa considers LMO applications on a case-by-case and considers this to be appropriate for gene drive LMOs as well.  |
| 24 | 25 | Introducing a modification tool rather than a finished product | **Comment:** This is a different approach to the current GMOs which get release as finished products. The fact that gene drives will modify organisms in the field requires some thought in terms of what the risk assessment will entail and what information will be accepted to support the risk assessment. The use of models to help predict ecological effects and estimate certain risks should be considered to support risk assessment. |
| 24 | 40-41 | Targeting non-domesticated species | **Comment:** In terms of choice of comparator, considerations could be given to cases such as the Wolbachia-infected species if it’s same species as the gene drive LMO. This will however depend on availability of information and experience with the release of these species. |
| 25 | 4-6 | Targeting non-managed environments | **Comment:**The release of gene drive LMOs into unmanaged environments will require that an Environmental Impact Assessment (EIA) be conducted to evaluate the likely environmental impacts of the intended release. **Rationale:**South Africa’s environmental legislation makes provision for an EIA to be conducted for LMOs intended for release into the environment which may pose a threat to any indigenous species or the environment. In this regard, the environmental risk assessment framework provides a list of possible triggers of an EIA, which includes LMOs with the potential to become invasive, those with a potential to negatively impact on threatened or protected organisms, if the release involves indigenous LMOs, LMOs that have wild indigenous relatives, those with cultural or geopolitical significance, or that could have potentially negative socio economic impact. Gene drive LMOs could trigger an EIA.  |
| 25 | 7 | Managing a step-wise approach | **Comment:**The stepwise pathway to deployment supports generation of data for risk assessment. However, given the difference in risk profiles to the current LMOs, further consideration is need in terms of what would be acceptable under the regulatory system.  |
| **25** | **18** | **Effects on the gene drive-bearing organism** |
| 25 | 24 | Stability of the gene drive system | **Comment:** The stability of the gene drive system is considered in the risk assessment. There would be a need for post-market monitoring to demonstrate that the gene drive system with the payload gene are stable in the host organism.  |
| 25 | 28 | Modified susceptibility | **Comment:**The risks of the vector organism having modified competency for pathogen transmission and becoming a more susceptible host to other viruses should be weighed against the benefits. |
| **25** | **33** | **Consideration for biodiversity** |
| 26 | 4 | Target organism | **Comment:**Consideration should be given to what is the ecological role of the target organism and the host organism and what are the implications of extinction. |
| 26 | 9 | Non-target organisms | **Comment:**The risk assessment should consider the presence of indigenous related species and potential impacts. It should also consider impact on other important species, taking into consideration appropriate assessment endpoints. Post-release monitoring plans should be developed for continued monitoring on non-target organisms. |
| 26 | 28 | Alternative protection mechanisms and herd immunity | **Comment:**This is a socio-economic considerations issue where parties would weigh the risks and benefits based on national circumstances.  |
| 26 | 33 | Relating to resistance development | **Comment:** Development of resistance is considered in the risk assessment including how this would happen, the likelihood and the consequences. A resistance management plan would be needed. |
| 27 | 23 | Effects beyond the target area | **Comment:**Regional cooperation and integrated approaches to risk assessment assessing gene drive applications and decision making are necessary given that gene drive LMOs may spread outside the intended geographical area including across national borders.**Rationale:** South Africa’s participation in the NEPAD Agency gene drives workshops held in SADC in 2017 and 2019 highlighted the need for such regional co-operation. |
| 28 | 1 | Perspectives of indigenous peoples and local communities | **Comment:** IPLCs are consulted as part of the public consultation processes under the regulatory system. **Rationale:** South Africa’s regulatory system has a process for the public to submit comments on applications lodged under the GMO Act. All interested and affected parties have an opportunity to submit comments. These comments are considered in decision making.  |
| **29** | **1** | **INFORMING THE APPLICATION OF ANNEX I OF DECISION CP-9/13** |
| 29 | 11 | Priorities identified by Parties | **Comment:**South Africa also considers gene drive LMOs as a priority topic requiring further guidance on how to evaluate certain aspects related to gene drive LMOs.**Rationale:**South Africa has not yet reviewed or undertaken a risk assessment on an actual application of gene drive LMOs. While a risk assessment framework for LMOs is in place which would be appropriate for gene drive LMOs, their distinguishing features could potentially impact on biodiversity. They would therefore require that risk assessment guidance is developed on specific elements, especially the problem formulation including defining assessment and measurement endpoints.  |
| 29 | 31 | Scope and objective of the Cartagena Protocol | **Comment:** A coordinated approach should be maintained between the AHTEG on Synthetic Biology and the AHTEG on Risk Assessment during the development of guidance on risk assessment of gene drive LMOs given the linkages with the synthetic biology discussions under the CBD. |
| 30 | 5 | Challenges to existing risk assessment frameworks | **Comment:*** South Africa supports the views that current environmental risk assessments guidance can be used as a framework for risk assessment of gene drive applications. It also our view that additional guidance is required on specific aspects of risk assessment based on the features that distinguish gene drive LMOs from current LMOs that could increase the overall complexity of the assessment that may require different approaches in certain aspects.
* The lack of information to support risk assessment is a concern and more research is need. Whilst risks and consequences pertaining to the release of LMOs with gene drives may not be fully known or understood, it might be necessary to incorporate other tools such as modelling to support RA as a requirement. Modeling could be used to predict the ecological effects of removing species or altering complex ecological networks in a certain ecosystem, estimate the risk of introgression of drive systems into non-intended populations.
* There is a need for further capacity building on basic scientific knowledge and understanding of gene drive for the purpose of assisting parties to be competent in undertaking risk assessment and reviewing gene drive applications and decision-making. Such could also benefit from the expertise of experts in the work involving gene drives that are not LMOs (such as the case of Wolbachia system where organisms based on this system have been released into the environment).

**Rationale:*** South Africa has a risk assessment framework for LMOs in place and is currently in the process of defining assessment and measurement endpoints for current GMOs. The availability of additional guidance of specific elements of risk assessment for gene drives could be incorporated into this process taking into account national circumstances.
* SA participated in two AU-NEPAD Agency gene drive mosquito capacity building workshops for the SADC region in 2017 and 2019 respectively. These workshops did not only provide scientific knowledge and understanding on the topic and the risk assessment process, but were also a good platform to build relationship to foster regional cooperation on development of frameworks for coordinated review of gene drive applications. South Africa therefore recommends continued capacity building in this area.
 |
| 31 | 38 | Clearly described issues | **Comment:**Discussions on this topic should focus on risk assessment of gene drives LMOs and not generic risk assessment. This means all features that would be considered in risk assessment, including the gene drive system, the genes, the host organism, the introduced trait, the target organism, the receiving environment.  |
| 32 | 1 | Specific issues for engineered gene drives | **Comment:**Literatures proposes release of reversal drives to mitigate unintended negative impacts of gene drives on the environment, yet there are no studies that have researched adverse ecological effects that these reversal drive constructs may also introduce to the environment. |