Annex

TEMPLATE FOR COMMENTS ON THE REPORT OF THE AD HOC TECHNICAL EXPERT GROUP ON SYNTHETIC BIOLOGY

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Comments on the draft documentation for SBSTTA-22:		
Page #	**Para #**	**Comment**
1	1	[Please note – in this submission text in red comprises the relevant content from the AHTEG report that subsequent comments relate to] The Conference of the Parties noted that the general principles and methodologies for risk assessment under the Cartagena Protocol and existing biosafety frameworks provide a good basis for risk assessment of living organisms developed through synthetic biology, but such methodologies might need to be updated and adapted. The question of whether existing risk assessment and biosafety protocols are adequate for synthetic biology applications was discussed at the 2015 Sackler Forum on *Trends in synthetic biology and gain of function and regulatory implications* (report available here: https://royalsociety.org/~/media/policy/Publications/2016/sackler-report-09-2016.pdf – the Sackler Forum is an annual US-UK scientific forum convened by the Royal Society and the National Academy of Sciences on topics of worldwide scientific concern).

3	17	The recent developments in synthetic biology and the continued pace of development might pose challenges to the ability to understand the possible impacts on biodiversity and human health. There might be a need to consider more thoroughly the potential benefits and potential adverse effects at the ecosystem level, particularly for some developments, such as engineered gene drives. Participants in the 2015 Sackler Forum noted of the importance of research to understand the environmental impacts of synthetic biology. They also endorsed the consideration of benefits as well as risks when assessing new technologies: "The core concepts of regulation are also being examined in the context of emerging biotechnologies. In the US, as in Europe, much of the regulation around GM and the environment are predicated on the concept of risk. This may be changing, with some consideration now also being given to the idea that magnitude of benefit should also be weighed up when making assessments and authorisations." One benefit that might be of particular relevance to the Convention on Biological Diversity is the potential to use gene drives on non-native species. In a speech at the 2017 annual meeting of the AAAS (American Association for the Advancement of Science – speech available here: https://royalsociety.org/~/media/news/2017/venki-ramakrishnan-aaas-speech-gene-tech-18-02-17.pdf?la=en-GB), Royal Society President Venki Ramakrishnan noted: "Research is currently underway into how gene drives could be used to control non-indigenous mouse populations which threaten native biodiversity on islands across the world.[1] [..]Gene drives are also being considered as a way of controlling other invasive species, including wasps in New Zealand[2] and cane toads in Australia[3]."

[1] Cocquet, J, Ellis, P J I, Mahadevaiah, S K, Affara, N A, Vaiman, D, Burgoyne, P S, 2012 A Genetic Basis for a Postmeiotic X Versus Y Chromosome Intragenomic Conflict in the Mouse. PLOS Genetics 8 (9), 1-15

[2] Lester, P J, Beggs, J R, Brown, R L, Edwards E D, Groenteman R, Toft, R J, Twidle, A M, Ward, D F, 2013 The outlook for control of New Zealand's most abundant, widespread and damaging invertebrate pests: social wasps. New Zealand Science Review 70 (4), 56-62

[3] Australian Academy of Science, 2016 Gene Drives in Australia, Acton: Australian Academy of Science

3	18	The development and implementation of well-designed strategies, including physical containment and built-in systems to effectively limit the survival or spread, might be needed to prevent or minimize the exposure of the environment to organisms, components and products of synthetic biology under contained use. These strategies should be commensurate to the risk posed by the organisms, components and products. Participants at the 2015 Sackler Forum discussed ongoing work to promote biosecurity, noting "Multiple layers of enhanced biosecurity would be the major response to curbing any ill effects of accidental escape. This takes two forms: extrinsic biosecurity, that is physical containment measures, and intrinsic biosecurity, that is biologically engineered safety mechanisms. Good practice suggests that such biocontainment safeguards should be multiple and redundant, so that if one fails, another one should stop any potential escapee from taking hold in the natural environment and spreading. Intrinsic safeguards could include measures such as multiple 'kill switches' in essential genes that would be activated in a natural environment or be set off by a lack of a laboratory input. In this way, synthetic organisms can be enslaved to chemistry by altering them so they can only use non-natural amino acids and therefore survive only in synthetic environments. There was some discussion on the need for such multi-lock systems for relatively benign applications of synthetic biology. Some scientists were concerned that current efforts to automatically include multi-lock intrinsic safety systems for everything, might send an incorrect message to the public – that the technology was inherently unsafe and be a waste of resources where they are not necessary. Intrinsic biocontainment is also subject to the powers of evolution, which must be considered in the overall safety design. It was noted that it is important that such systems are developed before they are actually needed and that safeguards are already being worked on in anticipation of future applications. Testing such systems in safe, already contained organisms would be preferable to using them for the first time in 'open system' organisms, it was argued."

1. Completed forms can be sent to Secretariat via e-mail at synbio@cbd.int or submitted online at http://bch.cbd.int/managementcentre/edit/submission.shtml
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4	19	The potential dual use nature of some advances in synthetic biology might raise biosecurity concerns in relation to the three objectives of the Convention. Building on previous discussions of research with dual use potential[4], participants at the 2015 Sackler Forum developed a set of questions to help guide decision making on research of dual use concern. These were: 1) Is there some principled objection to doing this? What is the principle at stake? 2) There may be no such principle, in which case is the work important enough? That is, is there a non-trivial use or purpose for doing the research? 3) Can the research be done safely on an operational level? For example, is the enhanced-BSL3/BSL4 system of laboratories satisfactory for this purpose, and who would ensure that work is done safely? What is the regulatory force? Is there money for oversight? 4) Are there forces in our society now that might make this not the right time, or a difficult time, for emergent technologies? For example, with huge inequalities globally and anxieties over dual use. Even if there is no principled objection and the work has a good purpose, there may be social, ethical or cultural reasons why it might be difficult.

[4] See for example: National Research Council 2004 *Biotechnology Research in an Age of Terrorism*. Washington, DC: The National Academies Press

5	25	Given the current uncertainties regarding engineered gene drives, a precautionary approach and cooperation with all countries and stakeholders that could be affected, taking into account the need for the free, prior and informed consent of indigenous peoples and local communities, might be warranted in the development and release of organisms containing engineered gene drives, including experimental releases, in order to avoid potential significant and irreversible adverse effects to biodiversity. In his AAAS speech, President Ramakrishnan cited the research already underway into possible containment measures for gene drives, and the importance of gaining informed consent from communities where gene drives might be used experimentally: "Despite their potential, gene drives carry considerable risks since the broader ecological consequences of reducing or eliminating a species can be uncertain. Confinement strategies, safeguards and appropriate governance for their use would be critically important[5]. Once a gene drive is released it may be possible to create a 'reversal drive' which can remove the introduced trait[6]. This might not, however, reverse any changes occurring in the ecosystem in response to changes in the target species. Other potential containment mechanisms include limiting the number of generations over which the gene drive operates in order to partially contain it[7]. Even with safeguards in place, it may be a significant challenge to obtain informed consent from those living in an area where a gene drive experiment is being carried out." President Ramakrishnan also noted a specific example of promoting early public debate around the possible use of gene drives: "Another example comes from the New Zealand Department of Conservation, which has released a strategy for New Zealand to be free of the predators introduced to the islands by humans by 2050. The range of options for achieving this strategy includes gene drives to reduce possum numbers[8]."

[5] The National Academies of Sciences, Engineering, and Medicine 2016 Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty and Aligning Research with Public Values. Washington, DC. The National Academies Press

[6] Oye, K, Esvelt, K, Appleton, E, Catteruccia, F, Church, G, Kuiken T, Lightfoot, S B Y, McNamara, J, Smidler, A, Collins, J P 2014 Regulating gene drives. Science 345 (6197), 626-628

[7] Noble, C, Min, J, Loejarz, J, Buchthal, J, Chavez, A, Smidler, A L, DeBeedictis, E A, Church G M, Nowak M A, Esvelt, K M, 2016 Daisy-chain gene drives for the alteration of local populations. BioRxiv (pre-print)

[8] Department of Conservation (New Zealand) 2016 Predator Free 2050. Wellington: New Zealand Government

7	44	The AHTEG further noted that existing risk assessment considerations and methodologies might not be sufficient or adequate to assess and evaluate the risks that might arise from organisms containing engineered gene drives due to limited experience and the complexity of the potential impacts on the environment. The development or further development of guidelines on risk assessment of organisms containing engineered gene drives by the Convention, other international organizations, national governments and professional bodies would be useful in that regard. Participants at the 2015 Sackler Forum noted: "Research on intrinsic safeguards and the population impacts of gene drive on wild type organisms is already under way…For gene drives, proponents suggest that organisms should be assessed on a case-by-case basis for risk, based on lessons learned from non-driving engineered organisms released in nature."
7	45	Some experts noted that a stepwise approach might be appropriate in order to gather information that is needed to fill knowledge gaps and avoid adverse effects or minimise the likelihood of them occurring. However, the step of release into the environment might be irreversible and, therefore, a precautionary approach might be warranted. In his AAAS speech, President Ramakrishnan pointed out the importance of considering the consequences of not acting, saying "All change brings risk. But not changing brings risk too". This relates to the point made in relation to page three, paragraph 17 on needing to take into account benefits as well as risks when assessing whether a new technology should be used.
7	48	Current strategies for risk management and monitoring of LMOs might provide a good basis for managing the risks and monitoring potential impacts of organisms developed through synthetic biology. These strategies might need to be adapted and complemented in order to address specific characteristics of organisms developed through synthetic biology. Please refer to comments on page three, paragraph 18.
8	51c	Internationally agreed standards for effective containment of organisms containing engineered gene drives might be useful in order to avoid the accidental releases from laboratory facilities. Please refer to comments on page four, paragraph 19.

8	57	The importance of addressing the potential socio-economic impacts of the commercialisation of products of synthetic biology that replaced naturally occurring products was noted. Participants at the 2015 Sackler Forum shared this concern, noting "Researchers at the Forum were mindful that these potentially world-changing biotechnologies could have applications which address challenges that public want solved. To this end, most agreed on the need for a close assessment of the field's potential impacts; not just scientifically but in a much broader sense encompassing societal impacts, public perception and acceptance, ecological risks and unpredicted effects, biosafety and biosecurity issues, as well as how regulation and governance may manage these."

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