**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 | 1. The Technical Series No. 82 tries to identify developments in synthetic biology as well as potential gaps in the regulation of synthetic biology. However, it is very difficult to identify gaps without a widely accepted and clear definition of synthetic biology. The operational definition used by the CBD for deliberations has not been acknowledged by the COP as there was disagreement as to whether the definition can describe synthetic biology adequately. This definition was often described as too broad and covers all major areas of biotechnology including also traditional research and development projects which lack the novel aims and constructive endeavours characteristic of synthetic biology. These conventional and other biotechnology issues are long known, often use classic gene technology and are, if applicable, under the scope of the Cartagena Protocol. The German Central Committee for Biological Safety (ZKBS) substantially shares the concerns of a too broad definition of synthetic biology. In this regard, LMOs mentioned here include, for example, genetically engineered bacteria for agriculture, genetically engineered sorghum and oilseed rape, or genetically engineered bacteria for environmental applications. Further, genome-edited organisms cannot be considered synthetic biology, but are either exempted from GMO regulations (as decided by some Parties) or are LMOs (as decided, for example, by the EU). Furthermore, transient modification techniques such as “RNAi sprays” do not modify an organism´s genome and should not be considered synthetic biology either.  The CBD may concentrate its efforts and resources on the identification of organisms, components and products that are not conventional LMOs and therefore cannot be dealt with under the scope of the Cartagena Protocol.  2. The ZKBS likes to emphasize that organisms containing engineered gene drive applications to circumvent agricultural pests or human diseases, e.g. malaria, and organisms resulting from genome editing must be kept apart and are both not per se an item of synthetic biology. | |
| 10 | 46 | The sentence “It is expected that some other genome edited organisms and potentially those containing engineered gene drives could reach the market in a few years.” implies that organisms containing engineered gene drives are genome edited. However, to cause a gene drive, a substantial, genetically complex insertion into the genome of an organism is needed. This is not what is usually understood by “genome editing” where only small insertions/deletions or changes of a few nucleotides are made. The sentence should be changed to: “It is expected that some other genome edited organisms and ~~potentially those~~ *organisms* containing engineered gene drives could reach the market in a few years”. Again, the ZKBS would like to strengthen that “gene drives” are not per se an item of synthetic biology. | |
| 12 | 8-23 | 1. The dual-use discussion is not inherent to synthetic biology. For example, dual-use concerns are discussed for genetic engineering as well. This is more likely a topic for the Cartagena Protocol or a general topic for the CBD.  2. Do-it-yourself biology is not an issue of synthetic biology and usually uses standard methods of genetic engineering leading to the creation of LMOs. | |
| 12-13 | 47-7 | 1. The document states under point 14 that synthetic biology is a new discipline. This is not agreed upon by all CBD Parties and other stakeholders. In dec. 13/17, it was concluded “that living organisms developed through current applications of synthetic biology, or that are currently in the early stages of research and development, are similar to living modified organisms as defined in the Cartagena Protocol;”. Several Parties have the opinion that synthetic biology is a new kind of modern biotechnology and that regulatory mechanisms in place for living modified organisms are adequate to address synthetic biology. Point 14. needs to be rephrased accordingly.  2. A regular monitoring of the scientific progress in synthetic biology would be adequate to identify necessary adjustments of national and international regulation. The German ZKBS has been carrying out such a monitoring, including a risk assessment of the applications identified, for almost 10 years (see <https://www.zkbs-online.de/ZKBS/EN/Home/home_node.html> 🡪 Synthetic Biology). It should be added to the text that a perpetual horizon scanning process is already established nationally in Germany. | |
| 19 | 27-28 | The sentence “A gene drive is a phenomenon in which selfish genetic elements circumvent Mendel’s laws of independent assortment and favour their own inheritance” is phrased too colloquially. It should be rephrased more scientifically as in line 35/36: “…engineered gene drives are genetic elements that are inherited more frequently than expected based on Mendel’s laws alone.” The ZKBS would like to point out repeatedly that “gene drives” are not per se an item of synthetic biology. | |
| 43 | 5-8 | Ethically, the following sentence does not correspond to international values and should therefore be deleted: “Further, although not specific to synthetic biology approaches, the reduction or elimination of human malaria from geographical areas may lead to demographic and land-use changes, potentially impacting biodiversity conservation (Redford et al. 2019)”. | |
| 46 | 18-20 | Concerning the sentences: “A recent example is the ongoing conversation about the responsible application of CRISPR that is taking place at both national and international levels concerning the limitations of current global governance structures to safeguard its use. Largely missing from this conversation however, is attention to local communities in decision-making which are likely to be the first to feel any potential impact from these applications (Kofler et al., 2018)” 🡪 CRISPR itself is a technique that can be applied for a variety of purposes. Only one of its applications is the creation of organisms containing an engineered gene drive that may affect local communities. The text should be specified accordingly. | |
| 64 | 27-31 | The methods described in Chhalliyil et al. 2020 and Peng et al. 2020 can specifically detect a point mutation introduced into a crop plant. However, these methods do not allow the identification of a genome-edited plant, because solely identifying a given point mutation does not allow to disclose the method used for the creation of specific point mutations. Consequently, the methods described in Chhalliyil and Peng do not allow for the discrimination between a genome-edited plant and a plant having acquired the same point mutation spontaneously or through traditional mutagenesis e.g. by radiation or chemical treatment of seeds. The following text, which is scientifically incorrect and grossly misleading, should therefore be deleted: “Despite this concern, recent developments have demonstrated the potential possibility of detecting and quantifying genome edited canola and rice utilising real-time quantitative PCR and droplet digital PCR, respectively (Chhalliyil et al., 2020; Peng et al., 2020). In particular, the method for detecting the genome edited oilseed rape demonstrated consistency with ISO1702532 standards (Chhalliyil et al., 2020).“  For reference, please see the statement made by the ZKBS on its homepage (see <https://www.zkbs-online.de/ZKBS/EN/Home/home_node.html> 🡪 Commentaries). | |
| 67 | 12-15 | The described detection methods do not allow the identification of a mutant plant as a genome-edited plant (see comment above for page 64). The sentence “However, recent advances in detection methodologies, including the adaptation of techniques already in use by laboratories, such as quantitative PCR and digital PCR, could facilitate the detection of genome-edited events more readily (Chhalliyil et al., 2020; Peng et al., 2020; Ribarits et al., 2020)” should therefore be deleted. | |
| 74 | 18-20 | The text should read “including the operational definition developed by the Ad Hoc Technical Expert Group on Synthetic Biology and ~~acknowledged by the Conference of the Parties~~ *considered useful by the Conference of the Parties as a starting point for the purpose of facilitating scientific and technical deliberations under the Convention and its Protocols*;” The operational definition was not acknowledged by COP. Instead, the COP acknowledged that the outcome of the work of the Ad Hoc Technical Expert Group on Synthetic Biology on the operational definition is “synthetic biology is a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems” | |
| 82 | Table 1 | Dec. 13/17 (2016): on the operational definition it must read “~~Acknowledged the operational definition of “synthetic biology” and~~ considered *the operational definition* as a useful as a starting point for the purpose of facilitating scientific and technical deliberations under the Convention and its Protocols.” The operational definition was not acknowledged by COP, instead the COP acknowledged that the outcome of the work of the Ad Hoc Technical Expert Group on Synthetic Biology on the operational definition is “synthetic biology is a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems” | |
| 89 | 29-32 | The SARS-CoV-2 vaccines developed so far are not an issue of synthetic biology, but of classical and contemporary genetic engineering (reference Forni & Mantovani 2021). This statement has to be corrected or rather, the sentence should be deleted. | |
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Please submit your comments to [secretariat@cbd.int](mailto:secretariat@cbd.int).