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| **Contact information** | | | |
| **Surname:** | | | Heinemann |
|  | | |  |
| **Given Name:** | | | Jack A |
|  | | |  |
| **Government** | | |  |
| **(if applicable):** | | |  |
|  | | |  |
| **Organization:** | | | Centre for Integrated Research in Biosafety, University of Canterbury, Christchurch, New Zealand |
|  | | |  |
| **E-mail:** | | | Jack.heinemann@canterbury.ac.nz |
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| **Comments on the Technical Series on Synthetic Biology** | | | |
| **Page #** | **Line #** | **Comment** | |
| 65 | 20-32 | I suggest that the paragraph be revised to separate these falsely conflated alternative viewpoints on the rationale for governance.  The current document perpetuates a particular framing of the perspectives on (1) why gene technologies should be *governed* with (2) how (or why) they should be *regulated*. This is seen in the describing of the viewpoints as “biotechnological developments being inherently risky” or “these technologies not presenting any unique or novel risks”. The former frames the rationale for risk assessment and the latter what is evaluated in a risk assessment, which are not different sides of the same coin. **The inherent property of technology is that it changes the gearing ratio between human activity and the outcome of human activity** (Heinemann et al. 2021).  “Traditional breeding” is generally regarded as relatively slow compared to what can be achieved using gene technologies. The pace of traditional breeding defines the baseline condition of how much human effort is needed to change outcomes. Technology gears up the scale of change by human intervention and along with it the inseparable load of unintended outcomes that are possible because of the process or the product. That is why technology itself is a suitable trigger for regulation (a trigger provided by governance), as it is in a number of other cases where technology catalyses activity with grand geographical scale potential, such as nuclear power and weapons. The equivalent non-sequitur framing there would look like: “nuclear fission developments being inherently risky” ***or*** “these technologies not presenting any unique or novel risks” because after all atoms decay all the time in nature.  The ability of human activity to align atoms with different energy potentials to create a chain reaction, and to concentrate the different species of atoms to achieve a threshold of explosive power, or even to just release radiation (weapons vs medical applications) is the reason why nuclear technology should be regulated. How it should be assessed for risk is then informed by what is expected to be the outcome of the technology (Heinemann et al. 2021).  In this regard, synthetic biology is like any other manifestation of gene technology. | |
| 65 | 33-44 | The above would align better with this paragraph which in essence is saying the use of syn bio will likely be assessed for risk. The question then is not whether to govern, but whether assessment currently is suited to predicting the likelihood of adverse effects from all applications of synthetic biology. | |
| 65-  -66 | 46  8 | These sentences are internally inconsistent and contradictory. The paragraph begins by saying both that a wide range of positions have been taken (and thus implying that there are a substantial number of countries taking positions) to a sentence or two later saying that almost no countries have declared a position but where they have it is based on just one, the metaphor of a mimic of nature. Either a wide range, or a narrow range, which is it?  The loudest voices, and countries with the resources to make their voices loud, have been those who argue some nature equivalence logic. (See comment below related to text on page 86.) In my view the number of countries taking a position has been small and are defined by a narrow spectrum of economic interests and cultural similarities. | |
| 66 | 9-33 | What this paragraph demonstrates is that there is no internally consistent approach being taken by the example countries. Their choices of inclusion or exclusion are case-by-case, as in plants vs animals in the US. The Japanese and Brazilian examples leave the reader unclear as to whether the determinations deregulate all plants or just those two mentioned, one in each country. This also applies to lines 41-47.  In short, this paragraph looks contrived to use a variety of disjointed observations to fit a predetermined narrative. I suggest deleting lines 9-33. Same for 41-47. Lines 34-40 are succinct summaries of the facts and the paragraphs p 66 line 48-67 line 10 follow consistently from 34-40. | |
| 66 | 40 | Please balance the article reference Fritsche, S., Poovaiah, C., MacRae, E., & Thorlby, G. (2018) with the CBD initiated book chapter: Heinemann, J.A., Coray D.S. and Kurenbach, B. GMO Rules and Regulations in New Zealand In GMOs: Implications for Biodiversity Conservation and Ecological Processes. Edited by D.L. Hawksworth and A. Chaurasia. Springer-Nature https://doi.org/10.1007/978-3-030-53183-6 | |
| 66 | 6-8 | This section should have more recent references. | |
| 66 | 16-17 | This line would be strengthened by a reference. It could be (Heinemann et al. 2021) among others. | |
| 68 | 1-3 | This line would be strengthened by a reference. I suggest (Heinemann 2019) which is already used in other places. | |
| 68 | 5-7 | This sentence projects a pre-determined conclusion as if it were a fact. In saying that topical treatments are non-transgenic, the report is implying that this is a settled issue of science. It is not. Instead it draws upon unofficial definitions of what are genes and other genetic material are as held by some. In fact, in two peer reviewed publications, we demonstrate that both the scientific literature and industry patent claims (with included experimental evidence) converge on the heritability of topical RNA treatments both via long lived (hundreds of generations so far) effects from single exposure treatments and RNA-RNA recombination in eukaryotic organisms with stable RNA components of their genome (ie, fungi) (Heinemann 2019; Heinemann and Walker 2019). Both of these publications are known to the AHTEG and are cited elsewhere in the report (although for side points), so it should be possible to balance this paragraph appropriately with the contrasting point of view and extensive evidence for it. The AHTEG cannot ignore away inconvenient science.  The key analysis missing in this section is that there is no basis for assessing the risk of topical (spray, ingestion etc) exposures because they violate point one of Annex III of the Protocol:   * “An identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health;”   because by definition many topical applications will not control exposures, particularly to small and ubiquitous organisms that do inherit the modification. This includes fungi and importantly protozoa, many of which are not even yet described.  The AHTEG should feature this particular issue with no less fairness than it did the gene drive section where exposure analysis is challenged, and in the case of RNA technology, probably impossible in open air use. | |
| 68 | 14-27 | I would also point out that by Australia’s decision to exempt a highly defined and limited scope of external treatments of organisms with dsRNA from the GMO regulations, *they had not arrived at the conclusion that treatments do not create genetically modified organisms under regulations*. Indeed, the list of limitations to the exemptions make clear that the technology can produce GMOs, as per the conversion of the RNA into DNA or through direct transfer of viruses or the potential for RNA-RNA recombination of even partial viruses. Therefore, they have made a decision with specific relevance to how to regulate rather than whether to govern. (See comment above related to page 65 lines 20-32).  Moreover, this is entirely different to what New Zealand did. Note, that New Zealand recalled that decision and issued a new determination with much more limited scope. | |
| 68 and elsewhere |  | Please do not reduce the external use of dsRNA to “sprays”. External use can be achieved using a variety of very different mechanisms and this should be acknowledged and explained to avoid oversimplification and ongoing use of semantics to narrow the discussion. For example, uptake of pesticidal dsRNA via roots may not be a spray, but still could result in a variety of different exposure pathways depending on organism, from ingestion by pests to contact by fungi. | |
| 70 | 12-13 | Not toxic genes. Genes that would result in the production of toxins. | |
| 70 | 14-18 | This is a particular interpretation of the post Asilomar time. In fact, Asilomar participants had a variety of views (Russell 1975). What is missing in this and later paragraphs is the view of Brenner and others that the essence of the need to regulate was in the ability of gene technologies to allow rapid changes across many dimensional scales. Reported at the time was the fear of some scientific leaders, such as James Watson, Joshua Lederberg and David Baltimore, that without ‘self-governance’ a hypothetical bureaucracy would imposed governance. As Baltimore said at the time “We have to do what we're doing. Otherwise someone else will come in and do it for us” (Russell 1975). This was not a reflective endorsement of the efficacy of self-governance, but instead as Lederberg put it, an attempt to avoid even guidance because it might become “crystallized into legislation” (Russell 1975). | |
| 72 | 7-37 | Is this a paid advertisement? Why doesn’t ETC get a nice explanatory endorsement too? What is the purpose of section 7.3.4? If it is an attempt to illustrate spontaneous self-regulation, then it needs to have a research basis where its anticipated risk mitigation tactics have been independently verified and effectiveness thoroughly investigated. | |
| 72 | 13-15 | Here is an example of the uncritical nature of this section. It describes a framework that already *endorses* a commercial-technological vision while cementing a view of risk narrowly defined by that described by a certain subset of technical experts (Herrero et al. 2015; Montenegro de Wit 2020; Roberts et al. 2020). | |
| 73 | 8-10 | This single publication is insufficient to justify the conclusion that regulatory hurdles are the more important barrier to “pro poor” technology. The view is highly contested and there are numerous papers on either side. This paragraph is highly leading.  Even the AHTEG does not believe it as they point the finger to IP costs in lines 44-46 as being substantial. However, here all that is being accounted for is patent registration fees. These are the smallest costs of IP. The much larger costs come from defending claims. Therefore, when a true accounting of IP costs is made, it will both undermine the statement in lines 8-10 and dwarf the figure stated in lines 44-46. | |
| 86 | 1-4 | *It is more than* “modifications that would not otherwise naturally arise”. The point is that they would not occur in nature without the assistance of the technology to design, create and *amplify them to a scale that can cause harm*. For something to occur in nature requires **more than mutation**. Despite the genetic deterministic fantasies of X-men and Superman, mutation is not evolution. What occurs in nature requires both mutagenesis to provide variation, and natural selection (in the case of humans, technology) to act on the variation to increase the proportion of some genotypes relative to others. It does not matter for a governance framework whether or not a dangerous phenotype could be caused by the same mutation occurring spontaneously (naturally arise) or through gene technology if the former was never fit enough to increase to numbers that caused harm (Heinemann et al. 2021).  This mistake of failing to differentiate between mutagenesis and evolution as the baseline metaphor is being made with frightening frequency. In fact, it is occurring so often it could be said to be evolving. | |

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

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