Comment on the Preliminary Opinion on Synthetic Biology III
(Research priorities)

Verband | Biologie, Biowissenschaften & Biomedizin in Deutschland

Background
The preliminary opinion on Synthetic Biology III (Research priorities) was prepared by
- Scientific Committee on Health and Environmental Risks SCHER
- Scientific Committee on Emerging and Newly Identified Health Risks SCENIHR
- Scientific Committee on Consumer Safety SCCS

Available under http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_050.pdf

German Life Science Association (VBIO e. V.) participated in the public consultation submitting this comment to the scientific committee on September 16th 2015

VBIO comments on the "Executive Summary"

General remarks

„Genetic part libraries and methods", „Minimal cells and designer chassis", „Protocells and artificial cells", „Xenobiology", „DNA synthesis and genome editing" and „Citizen science" have already been defined as key application areas of SynBio in previous opinions I and II. Besides reasons of consistency there is no rationale why these areas have been identified as particularly relevant to the objectives of the CBD.

For matters of consistency we would have had expected to see the six novel SynBio developments as bullet points in all chapters of the opinion, which, however, is not the case. For example, there is no pronounced statement on "DNA synthesis and genome editing" in the Opinion or in the corresponding executive summary although a lack of knowledge is mentioned on pages 30 and 44ff.

Suggested edit: Adjust the structure of the opinion.

Social, governance, ethical, and security implications of SynBio are explicitly outside the scope of preliminary opinion III. However, within the text several references to these issues can be found.

Suggested edit: Delete these passages throughout to arrive at a more concise opinion that focuses on the original scope.

As terms are not consistently used throughout the text we suggest proper copyediting. In particular, the terms "genetic modification" and "genetic engineering" seem to be used synonymously to mean synthetic biology.

P7, line 30-33

Yet, SynBio does not produce "varieties of organisms, including de-extincted species" Especially research on de-extinction is speculative and clearly beyond the timeframe of opinion III (2020).

Suggested edit:
"Beyond 2020, SynBio may lead to products or organisms, which could destabilise conservation efforts and diminish support for conservation due to reduced focus on species and habitat preservation".

P8, line 4-6
New approaches are only needed if it is likely, that the organism, process or product developed with SynBio might cause harm.

Suggested edit:
"New approaches such as new forms of biocontainment and new biocontainment strategies to manage environmental and health risks will be necessary where such risks are identified for a particular SynBio product."

P8, line 26-29
Chemical and radiation mutagenesis, besides others, are well established methods for genetic modifications that result in large, simultaneous and pervasive changes in the genome of the treated organism. Thus, the statement „The use of genome editing methods allows (…) a more pervasive change to the genomes of living organisms than those obtained by traditional genetic modification techniques" is incorrect.

Suggested edit:
"The use of genome editing methods in a multiplexed fashion allows the simultaneous generation of a large number of variants, the genome-wide modification of organisms and a pervasive change to the genomes of living organisms comparable to the products of already established mutagenesis techniques with safe use."
And delete sentence "This might create additional challenges for risk assessment".

P9, line 1-2
The idea of streamlining and standardising across EU member states the methods for submitting genetic modification data and genetic parts information to risk assessors has been mentioned in Opinion II already. VBIO supports the idea of transparency. However, it has to be considered that a forced complete disclosure might discourage scientists to submit confidential business information to the risk assessors. In this context, the scope of the data collection (industrial applications or environmental releases) should be defined more precisely.

P9, line 28-30
To characterise xenobiologic organisms the existing GMO risk assessment frameworks can be used. So far there is no necessity to establish a new framework.

VBIO comments on "3.1.3 potential impacts of SynBio applications on conservation and sustainable use of Biodiversity"

General remarks
This chapter gives a concise overview about the possible impact of SynBio with relevance to certain applications. Nevertheless we would have preferred a more elaborated presentation of direct and indirect effects as well as of accidental and planned effects. For example, the negative impact of an accidental release of organisms is only mentioned for bioenergy applications (page 14, 46-47), but not for the other applications.

P14, line 21 ff
We like to mention, that a number of consequences depicted for SynBio applications to bioenergy (like biomass extraction or loss of biodiversity) are a matter of land use and producing systems and thus is not exclusive to SynBio products.

P15, line 13-29
Wildlife-targeted applications of SynBio aiming at the restoration of extinct species are far beyond the time frame of this opinion (2020). They should be mentioned as future issues only.

P 17-23 (Table 1)
Development of SynBio might interfere with Aichi targets. But it is doubtful whether the Aichi targets (2020) are the right framework to judge possible long-term impacts of SynBio on biodiversity. In addition, Aichi targets include socioeconomic issues, which are outside the scope of this opinion making it difficult to align them to the six key areas of SynBio. A number of comments are not biunique to one of the six areas or are general to SynBio.
Please note, that within the systematics of Aichi targets no accidental impact of SynBio organisms can be mapped, which biases the overall evaluation.
The general content of table 1 does not deliver a compulsory assessment but is more anecdotic. The bullet points are general and in a substantial number of cases not exclusive for SynBio. Often the comments are speculative and not based on references to scientific literature.

We suggest to revise table 1 as follows:

Aichi target 5
No content?

Aichi target 7
Reduction of pesticides through genetically modified organisms (SynBio products?) is only one element of sustainable management. Thus, the statement for „genetic parts“ is only anecdotic and may be misleading.

Aichi target 8
The statement “Industrial processes that produce a lot of pollution could be superseded by more environmentally friendly biological replacements” is much too general. The specific relevance of SynBio is not clear.

Aichi target 14
Spreading of general biological knowledge on biodiversity and sustainable management definitely contributes to the empowerment of women, indigenous and local communities, poor and vulnerable groups - But there are no references in literature, which confirm this with respect to specific knowledge of synthetic biology.

Aichi target 16
DNA sequencing and synthesis could provide a loophole to the Nagoya Protocol and its implementation regulations. This is due to weaknesses of the Nagoya Protocol and its implementation rather than a risk specifically arising from SynBio techniques. Although legal aspects are not the primary scope of this preliminary opinion, we claim, that this issue has to be monitored carefully. Solutions have to be found which do not hamper basic research.

Aichi Target 18
The comments should be removed because this target addresses questions outside the scope of preliminary Opinion III

Aichi target 19
There is no specific attribution of the statement “None, possibly positive…” to any of the head of columns. Does this mean that this statement is true for each of them?

VBIO comments on "3.1.4 Specific risks to the environment per research area"

P24, line 9-15
The risk for antibiotic resistance transfer in waste water plants also apply to natural microorganisms exposed to antibiotics and GMMs. It is not specific to SynBio organisms.

P24, line 22-23
SynBio activities concerning „de-extinction" will have an impact on biodiversity and ecosystems but this will not be relevant within the time scope of the opinion (2020)

Suggested edit:
"IN THE LONG RUN: Potential impacts on biodiversity and ecosystems from "de-extinction" (…)

P24, line 27
As of their nature "emergent" properties cannot be ruled out in advance. But this emergence can also occur in strains modified by any other technique (e. g. chemical or physical mutagenesis).

P26, line 4

Suggested edit:
Replace "New variants must be tested for risk to…" with "New variants must be assessed for potential risks to…"

P26, line 8-9
The SCs should specify what is meant by "particular auxotrophies" of xeno-systems.

P26, line 10-14
The claim that DNA synthesis and genome editing accelerate genetic modification and increase the range and number of modifications is not correct. What might be different in comparison to other methods of mutagenesis is the very high precision and specificity.

Suggested edit:
"*The new technologies for DNA synthesis and genome editing improve the precision and accuracy of genetic modification and increase the range and number of modifications that are possible*".

VBIO comments on "3.3.1 Research recommendations related to the gaps in the six novel SynBio developments"

P31, line 33-37
It is not clear to us, what exactly is addressed by this bullet point: contained use, industrial application or environmental release?

Suggested edit:
The SCs should specify the scope of this bullet point.

P32, line 16
The SCs suggest the establishment of a public repository of well characterised engineered safe chassis and safety devices as such a public repository might help to minimize risks. We hesitate to support this suggestion before all relevant stakeholders agreed upon a clear concept as to how this repository is organized and managed, how IP rights should be handled, etc.

P32, lines 25ff
We are well aware that while adding modules might make the chassis less fit, increasing bioreactor robustness might also increase environmental robustness. We also see the demand for additional research to establish the best approach to deal with this trade-off. But as of principal reflections we want to underline that in practise there is no complete escape from this dilemma. Limitation of the trade-off will be an approximation only.

P32, lines 31-32
As a matter of transparency we ask the SCs to exemplify, which level of regulation is intended and which time frame has to be expected. We want to express our view that acceptance of these standards will be higher, if they are lean and a direct safety benefit can be seen.

P32, line 42
We like to emphasize that there is a trade-off between the demands of increased genetic robustness and decreased environmental robustness, which can not be solved completely. We therefore suggest that further research should not alone focus on quantifying evolutionary change, but in addition should include „qualifying“ measures of evolutionary change as well.

P34, line 14
VBIO already expressed in its statement on preliminary opinion II that the inclusion of Citizen Science (e.g. Do-It-Yourself Biology - DIY Biology) seems misguiding as it is neither a technology nor a method of engineering. Citizen Science is specified by the person doing science (Synthetic Biology) in a certain framework of facilities in the absence of a professional research infrastructure. We agree that DIY Biology raises questions on training, safety, security, compliance and supervision that need to be addressed.
We would have preferred a longitudinal approach including special considerations about Citizen Science in the recommendations wherever necessary und useful. The SCs recommend the development of strategies to further increase and maintain the compliance of citizen scientists with national biosafety rules and codes of ethics, including collaboration with traditional institutions and training.
As a matter of transparency we ask the SC to exemplify, who should promote this strategic process, which stakeholders to include, what level of regulation to achieve and which time frame to expect.

VBIO comments on “4. Opinion”

P35, line 20 & P35, line 33-34
As a matter of consistency we suggest to add the relevant CBD references.

P35, line 21
Suggested edit:
Please insert the word ‘PLANT’ before ‘varieties’.

P35, line 25-29
Suggested edit:
Please delete this paragraph as „De-extinction“ is beyond the time frame of this preliminary opinion.

P35, line 35
We agree that “SynBio alternatives for chemical products and industrial processes might not *per se* be more sustainable than traditional products”. But placing this general statement under the headline of “biological diversity and conservation” is entirely misleading as sustainability is much more comprehensive.

P36, table 2
Suggested edit:
Protocells: Add "... might mutate OR BE HORIZONTALLY TRANSFERRED ..."

P36, line 20-22
Suggested edit:
“However, no single technology reliably manages all biosafety risks and new approaches AND COMBINATIONS OF EXISTING AND UPCOMING NEW STRATGIES will be necessary (…)”.

P38, line 25
A Biosafety clearinghouse mechanism on bioparts, devices and systems to support risk assessment of genetic circuits generated with biological parts, devices and systems might be useful in some fields of SynBio although it is not clear what kind of information has to be passed at what stage and in what detail. We would like to stress that acceptance of a Biosafety clearinghouse mechanism will be much higher, if structures are lean and linked to an existing international organisation.

P38, table 3
a) Genetic parts:
The statements are not exclusive to SynBio

b) DNA synthesis and genome editing:
The statement “*Lacking risk assessment for organisms with pervasive changes to the genomes produced by MAGE/CRISPR/zinc finger protein techniques*.” is not correct. These techniques are instruments to secure precise changes in the genome at exact spots. This makes risk assessment more easy compared with traditional methods of genetic engineering.
Suggested edit:Deletion of this statement

P39, line 15-17
It should be stressed, that there is a bottleneck in fundamental knowledge about functional mechanisms of biological parts and interactions between biological components.

P40, line 10-14
Any threshold depends on the environment and the engineered system. Therefore the justification for setting 10^{-11} seems to be weak. Please provide a reference to scientific literature.

P 40; line 26ff
The research recommendations are of high significance for the improvement of risk assessment. Having in mind that the research priorities given in this Opinion might have consequences for future resource allocation, we suggest to make it more explicit, how this additional recommendations relate to the recommendations of SynBio developments 1)-6). Furthermore, we see a need to prioritise within the chapter “additional research recommendations”.

We want to indicate a certain fuzziness between the research recommendations in the executive summary and in the opinion chapter. In the latter case, questions concerning differences in physiology, vertical or horizontal gene flow, survival, persistence, ecological fitness and the rate of evolutionary change are (only) subsets of research on the impact of introductions of SynBio organisms into the environment.

P40, line 30-31

Suggested edit:

"Research on impacts…of Synbio organisms THAT ARE LIKELY TO CAUSE HARM…."

P40, line 37-38

Suggested edit:

"Research on containment strategies…. To organisms resulting from Synbio techniques IF THEY ARE CLASSIFIED AS DANGEROUS OR MAY CAUSE HARM."

VBIO comments on "7. References"

Publications of NGOs that are campaigning against GMO or synthetic biology are cited under the headline „scientific literature" (e. g. ETC 2010, FOE 2010, FOE 2012). Please make transparent the character of this material in the reference list as well as on page 12.

Please verify the reference list:
1) Some publications like ETC 2013 (page 14) and ETC 2013a (page 15) are cited but not included in the reference list

2) Duplicate
Page 51, 5-7: Presidential Commission for the Study of Bioethical Issues (2010). New directions: The 5 ethics of synthetic biology and emerging technologies. Washington DC. 6
http://bioethics.gov/sites/default/files/PCSBI-Synthetic-Biology-Report-12.16.10_0.pdf
Page 53, 36-37: US Presidential Commission for the Study of Bioethical Issues (2010). New directions, Ethics of Synthetic Biology and Emerging Technologies. www.bioethics.gov

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