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Swiss Expert Committee for Biosafety SECB

SECB opinion

Risk-related criteria to assess activities in the field of synthetic biology and its regulation

October 2018

1 Introduction

Synthetic biology comprises many different specialities and fields of activity and pursues the aim of generating new types of biological systems. In contrast to traditional gene technology, in which individual genes are modified or transferred from one organism to another, synthetic biology intends to construct complete artificial systems, such as new metabolic pathways.

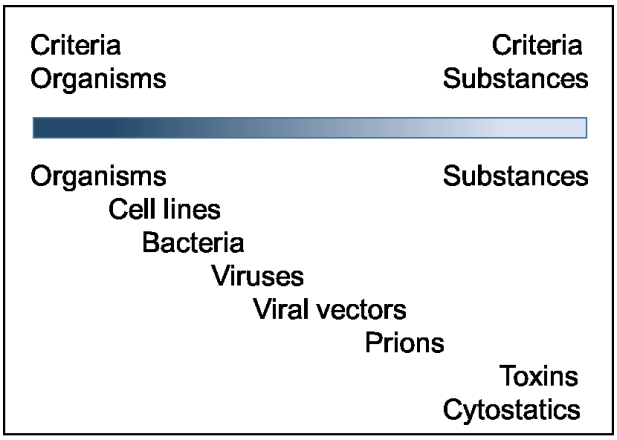

Figure 1: Continuous transition between organisms and substances

One of the challenges for activities in synthetic biology is regulation: for each activity in Switzerland it has to be decided whether it involves a (living) organism, which is covered by legislation on organisms (Gene Technology Act, Containment Ordinance etc.), or a (dead) substance, which is regulated by legislation on substances (Chemicals Act). Often the boundary between organism and substance is continuous, and thus certain applications in synthetic biology are located in a grey area (Figure 1), in which various criteria and properties must be used to decide which legislation applies. Another difficulty is that there are organisms that are regulated according to substances legislation (e.g. microorganisms as biocidal products are covered by the Ordinance on Biocidal Products), and conversely, substances may also fall within the scope of legislation on organisms.

In the SECB's view a case-specific risk assessment is crucial, based on the effective potential for damage, and not a classification by category using the criteria of organism or substance.

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2 Properties of living organisms and substances

A substantial difference between substances and living organisms consists in the development over time of the hazard potential. This decreases over time for substances, but for organisms that reproduce the hazard potential remains constant or can even increase (simplified depiction in Figure 2).

Important criteria that define a (living) organism are spontaneous reproduction or the potential to reproduce, growth in size, independent metabolism and energy turnover, interaction with the environment, the ability to change its conformation etc. – this list is not exhaustive. Nevertheless each individual criterion is not sufficient to make a "thing" into an organism. Substances, too, can demonstrate various of the mentioned properties, such as interaction with the environment, the ability to change its conformation, or energy turnover.

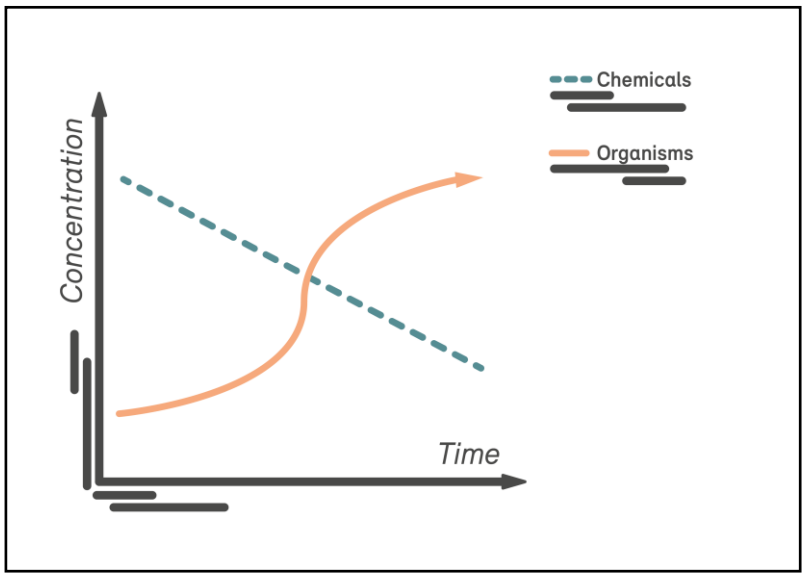

Figure 2: Reproductive capability of organisms and persistence of substances

3 Risk assessment

The protection objectives are humans, animals and the environment.

The risk assessment should take account of the following criteria.

3.1 Risk-related criteria of (genetically modified or pathogenic) organisms regulated in Switzerland

- Harmful properties
  - Pathogenicity
  - Invasiveness
  - Potential for gene transfer
    - Crossing out
    - Horizontal gene transfer
    - [Vertically to offspring (not a harmful property in the proper meaning of the word))]
- Type and extent of a leakage
- Harmful quantities / concentrations
- Is something new and known or something new and unknown being created?

The following properties and their possible effects should also be considered:

- Multiplication and dissemination (including actual gene transfer):
  - Hosts
  - Vectors
  - Non-target organisms
  - Climate conditions
  - Persistence in the environment

3.2 Risk-related criteria of substances

- Harmful properties
  - Toxicity
  - Carcinogenicity, tumorigenicity
  - Reproductive toxicity
- Type and extent of a leakage
- Harmful quantities / concentrations
- Is something new and known or something new and unknown being created?

The following properties and their possible effects should also be considered:

- Abiotic and biotic degradation
  - Metabolites produced by hydrolysis, photolysis, photochemical reactions, biodegradation etc.
  - Degradation rate

3.3 View of the SECB on the risk assessment

For the SECB, a risk-based evaluation is crucial in each case. Primarily the safety of the product (organism or substance) should be assessed (protection of the environment, population and consumers). In addition when manufacturing and processing the product, the safety of these processes should also be included in the assessment (protection of workers, population and environment).

For the risk assessment it is important whether the product/organism is able to pass on information or to interact with other organisms. Attention should be paid to molecular interactions (crossing out, gene transfer) as well as ecological interactions (competition for food and space, occupation of ecological niches etc.), taking into account the precautionary principle.

For handling “new” organisms (for example those containing synthetic macromolecules such as xeno or peptide nucleic acids), it be done initially in safety level 2 laboratories (BSL2). Such new components could be able, at molecular level, to form new bonds, the properties of which are as yet unknown and which, therefore, hinder the risk assessment.

4 Examples

A few recent applications are listed here as examples of what the SECB views as relevant. The list does not claim to be exhaustive. The report by the German Central Committee on Biological Safety (ZKBS) provides a comprehensive overview of current developments in synthetic biology[1].

- New generation vaccines: These are vaccines based on synthetically produced proteins which act similarly to inactivated vaccines, but for which in some cases a larger dose of antigen must be given as they are less immunogenic.
- Nano-CRISPR/Cas: Nanoparticles transport Cas9-ribonucleoprotein (RNP) complexes into the cytoplasm and into the nucleus of cells in a targeted and efficient way. A promising method for the future treatment of genetic diseases such as cystic fibrosis, muscular dystrophy or haemophilia.

[1] Synthetic Biology : 2nd Interim report of the German Central Committe on Biological Safety, June 2018, https://www.zkbs-online.de/ZKBS/SharedDocs/Downloads/01_Allgemeine%20Stellungnahmen/01_Allgemeine%20Themen/2.%20Bericht%20der%20ZKBS%20zur%20Synthetischen%20Biologie%20(2018).html;jsessionid=490C06E764789C428A83AEFF8EC5E4DC.1_cid350?nn=10959216

- "Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments"[2]. The virus has been assembled completely via DNA synthesis, and has been the subject of controversy for reasons of biosecurity and the dual-use problem.
- siRNA in plant protection, for example for potatoes. Depending on the use, this example would come under the Ordinance on Plant Protection Products or the Ordinance on Biocidal Products.
- Recombinant viruses, such as viral vectors for gene therapy applications.
- Minimal cells in system biology research.
- Synthetic bacteriophages for therapy, diagnostics or the food industry.
- Synthetic biology for improving the microbial synthesis of "green" biopolymers[3].

5 Conclusions

For activities in the field of synthetic biology, the SECB recommends a case-specific risk assessment with a focus on the protection objectives of humans, animals and the environment. Classification into the category of organism (legislation on organisms) or substance (legislation on chemicals) is not necessarily required. It is more important that all risk-related criteria, in particular the ability to multiply and disseminate, are taken into account.

[2] Noyce, R.S et al. (2018). Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments. PLOS ONE, published 19 January 2018: http://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0188453&type=printable

[3] Anderson, L.A. et al. (2018). Synthetic biology strategies for improving microbial synthesis of "green" biopolymers. Journal of Biological Chemistry, first published 16 January 2018, doi: http://www.jbc.org/content/early/2018/01/16/jbc.TM117.000368.full.pdf