Berlin, 15 February 2016

**General position statement of the ZKBS on the “Report of the Ad Hoc Technical Expert Group (AHTEG) on Synthetic Biology” from 7 October 2015**

The German Central Committee on Biological Safety (ZKBS) is a honorary expert committee institutionalized in the German Genetic Engineering Act. The Committee examines and assesses safety-relevant questions of genetic engineering, gives recommendations and advises the Federal Government and the federal states concerning safety relevant questions of genetic engineering. Since 2010, the ZKBS carries out a monitoring on synthetic biology in order to (I) assess the biological safety of current research activities and to (II) evaluate whether these are covered by the German Genetic Engineering Act. We have since held an expert workshop, coorganized with the expert committees from France, Belgium and the Netherlands, resp., [1] and published a first monitoring report [2].

These activities of the ZKBS have considerable overlap with the tasks assigned to the AHTEG, notably the identification of similarities and differences between living modified organisms (LMOs), and organisms, components and products of synthetic biology or the identification of potential risks arising from synthetic biology techniques. Against this background, the following conclusions and recommendations of the AHTEG report are of particular interest for the ZKBS:

* the AHTEG operational definition that defines synthetic biology as “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.”
* the AHTEG statement that living modified organisms developed through applications of synthetic biology are similar to living modified organisms (LMOs) as defined in the Cartagena Protocol
* the AHTEG recommendation to assess potential gaps in oversight under the Convention and its protocols with regard to components and products of synthetic biology
* the AHTEG recommendation to establish a monitoring process.

The operational definition on synthetic biology drafted by the AHTEG is a very broad definition that also includes most applications and techniques generally considered modern biotechnology as defined in the Cartagena Protocol. As the AHTEG stated, most organisms produced through synthetic biology applications today can be considered living modified organisms (LMOs) as defined in the Cartagena Protocol. The ZKBS agrees on this point and would like to point out that these organisms can be assessed with risk assessment methodologies already in place for LMOs. This is why the ZKBS considers the operational definition as too broad. The definition does not allow to discriminate sufficiently, if an LMO has been created by modern biotechnology or by synthetic biology applications. This is illustrated, for example, by “gene drive systems”, which are mentioned as tools of synthetic biology in the report. To our understanding, gene drive systems create organisms with a “novel combination of genetic materials obtained through the use of modern biotechnology” and are thus LMOs that can be assessed by the appropriate risk assessment methodologies (Cartagena Protocol).

“Gene drive systems” can also serve as an example for a risk assessment procedure favored by the ZKBS, in which the produced organism is assessed and not the technique used to create it. Although “gene drive” is seen as a technique of modern biotechnology, organisms produced with this technique may need a more thorough risk assessment. Another example for this product-based risk assessment are organisms, whose genetic material has been altered with the help of modern biotechnology (i.e. genome editing), but cannot be distinguished from organisms resulting from natural variation. These organisms do not pose any risk other than that posed by organisms resulting from natural variation.

Another problem with the operational definition could be the inclusion of non-living entities like “components” and “products”. The AHTEG agreed that “components” and “products” fall under the scope of the Convention, but are not covered by the Cartagena Protocol and therefore recommends assessing potential gaps in oversight with regard to “components” and “products” of synthetic biology. A “component” was defined as a part “used in a synthetic biology process (for example, a DNA molecule)”, while a “product” would be “the resulting output of a synthetic biology process (for example, a chemical substance)”. The ZKBS wants to note that these definitions leave room for interpretation. “Components” as defined by the AHTEG would be tools already frequently used in standard modern biotechnology applications such as (synthetic) genes, plasmids, microRNAs and BioBricks and are therefore not exclusive to synthetic biology. The ZKBS does not consider “components” as a new development, which needs to be addressed in additional regulations. A chemical substance as a “product” of synthetic biology can also be assessed by other regulations (for example REACH).

Finally, the continuous monitoring process suggested by the AHTEG is in accord with the general approach already practiced by the ZKBS. We have so far monitored five research fields (design and synthesis of genes/genomes, design of customized metabolic pathways, xenobiology, minimal cells/protocells and genetic circuits) for synthetic biology applications. The ZKBS concluded that those applications, for the time being, result in LMOs and that no gaps in regulatory oversight have been identified.

**Conclusion:**

The ZKBS acknowledges the challenge to find a definition covering all techniques and applications generally considered as synthetic biology. The definition by the AHTEG is sufficiently broad to cover all these techniques and applications. Yet, it also includes developments of modern biotechnology, which are already covered by existing regulations or which do not need to be regulated at all. Therefore, the AHTEG operational definition should not be used in a regulatory context. The Convention should rather identify organisms, components or products that cannot be regulated by the Protocols of the Convention, but may need further risk assessment and regulation. An example for such an organism could be protocells that replicate independently and pass on their genetic material. It is generally the produced organism that triggers a final risk assessment.

Literature:

1. **Pauwels, K, Mampuys R, Golstein C, Breyer D, Herman P, Kaspari M, Pagès J-C, Pfister H, van der Wilk F, Schönig B** (2013). Event report: SynBio Workshop (Paris 2012) – Risk assessment challenges of Synthetic Biology. *J Verbr Lebensm*. **8**(3):215-226.
2. **Die Zentrale Kommission für die Biologische Sicherheit (Central Committee on Biological Safety, ZKBS)** (2012). Monitoring der Synthetischen Biologie in Deutschland. http://www.bvl.bund.de/SharedDocs/Downloads/06\_Gentechnik/ZKBS/01\_Allgemeine\_Stellungnahmen\_deutsch/01\_allgemeine\_Themen/Synthetische\_Biologie.pdf?\_\_blob=publicationFile&v=3