European Biosafety Association
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Summary[1] Break-out Discussion
Synthetic Biology – have we got it covered

Moderators: Dr. Cécile van der Vlugt, National Institute for Public Health and the Environment, Bilthoven, The Netherlands; Dr. Michael A. Skinner, Imperial College London, UK; Chair of the Health & Safety Executive's Scientific Advisory Committee on GM (CU).

About 35 participants were present, most of whom were biosafety professionals, with small numbers of occupational health professionals, scientists and governmental risk assessors or inspectors.

Most felt they had a pretty good idea of what SynBio represents but acknowledged the common, initial tendency to contrast it with genetic modification (GM). In fact, consideration of a list of potential applications confirmed that while most SynBio is clearly GM in practice, most modern and new techniques were far more likely to be described as SynBio rather than GM, not least for fundability and impact. A clear example of this is the common description of GM sterile mosquitoes, created by Sterile Insect Technology, as a SynBio application in contrast to the multitude of knock-out and sometimes sophisticated mutant mice, which are only ever described as GM. The participants considered it a common misconception to confuse the use of 'synthesized DNA' with SynBio applications. The former is merely one of the tools that has, for many years, been applied to GM.

Although most of the techniques commonly described as 'SynBio' were recognized by the participants as applications or extensions of GM, there were some exceptions. One such exception is DNA origami – not least because it did not result in a "living" organism (whether replicative or non-replicative). Another area is protocell design, although one participant mentioned that her work on artificial lipid membranes was not even regarded by her institute biosafety officer as SynBio. She wondered whether, at some point, this line would be crossed and what that would mean for risk assessment.

The discussion therefore focused on trying to define areas that were not covered by GM risk assessment as these might require new or modified EC regulations to fill in the gaps between existing regulations (such as the EC directives on Contained Use and Deliberate Release GM) to avoid different approaches and interpretations by the various member states.

However, even an organism with a "minimal genome", or an organism with a newly designed, completely novel metabolic pathway, is still a product of GM (even if it were labeled as SynBio). Truly novel, synthetic organisms are not yet within reach (although synthetic viruses, possibly as bacteriophages for the control of antibiotic resistant bacteria, might not be so 'far-fetched'). Although novel, synthetic organisms (with no obvious progenitors) initially might not fall under

[1] This summary reflects the discussion and recommendations as noted by the moderators. While the views expressed in this summary can assist EBSA in determining what further action is possible, they do not necessarily represent EBSA's position on the matter and should not be presented as such.

the control of GM legislation, they would then only need to be recognized as an organism for any subsequent modification of their genetic material to generate a GMO.

The workshop did not spend long addressing the issue of targeted mutagenesis (using TALENs and the CRISPR Cas approach) and its potential application in "gene drives" as this poses as much of an issue for definition of GMOs as it does for its role in SynBio. The workshop did address the issue of orthogonal systems and xenobiology, both in the form of altered nucleic acids and as altered genetic codes. It was generally felt these would be covered under GM risk assessment procedures but that issues concerning their persistence and control might cause problems for risk assessment in practice, even though these systems were being themselves developed to help limit the persistence and spread of SynBio organisms in the environment.

The workshop also discussed other issues that might significantly affect risk assessment of SynBio, namely (i) assessment of ultra-wide-scale, low-risk activities and (ii) potential problems from divergence of scientific background, approach and technical language. The general opinion was that the first of these was unlikely to be a significant problem but that the second was already beginning to have impact. SynBio is aimed to integrate new disciplines and to encourage scientists with different scientific background to cooperate, e.g. biologists and engineers. However, they use different language (promoters and operons, *etc* versus oscillators, toggle switches, *etc*) and it is the language of biology that is currently in use for GM risk assessment Routinely they deal with very different types of risks (those from engineering typically being more stable and predictable than those from biology) and so their relative perceptions of biosafety are likely to be divergent. The presence of biologists or biosafety experts in the SynBio teams should help – but they might not always be recruited.

Overall there was broad consensus that:

(i) existing GM regulations (for Contained Use and Deliberate release) cover the vast majority of existing and proposed Synbio work;

(ii) most non-GM SynBio activities and applications will be covered by other legislation (whether from the EU or specific to member states), at least for the moment.

Recommendations to the EBSA board

- That EBSA should hold regular sessions on risk assessment of new techniques and SynBio applications, aiming at a European consensus.
- That EBSA should help review whether new developments fall into a gap in current legislation and whether they constitute a significant risk requiring new or modified EC legislation.
- That EBSA should help prepare guidance on interpretation of existing directives as they apply to the planning, risk assessment, conduct and oversight of SynBio.