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Investigate, evaluate, protect

Comments on the draft scientific opinions on synthetic biology

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Microbial characterisation and ERA of SynBioMs (WP1)

An international definition for « synthetic biology » is needed

Knowledge gaps

- Poor knowledge of the interactions within complex microbiomes.
- Too much unknown factors in Xenobionts biology to even imagine them in the environment?

⇨ Huge challenge to assess the safety of these new organisms.
⇨ A serious risk-benefit assessment would be necessary.

Measures to control the risk?

- Unlike plants, the dissemination of such microorganisms will be difficult to limit to one country or continent.
- What about an irreversible environmental deleterious effect if there is no way to turn back?

⇨ Should we request a sufficient margin of action in case things go wrong?
⇨ Should elements to control the microorganism after its dissemination (safe-by-design principle, firewalls, barcoding) be compulsory?

Microbial characterisation and ERA of SynBioMs (WP1)

Context

• To document potential hazards and risks of SynBioMs, information about the situation and experience gained in and outside Europe would help.

• Proposal to:

⇨ Broaden the introduction to the international context.

⇨ Detail feedbacks from countries already experimenting current and new GM microorganisms.

Structure of the document

• Document of high scientific quality.

• Last part, prospective, really well done and much appreciated: in-depth analysis of complex environmental microbial ecosystems.

• Proposal to invert the 2nd and the 1st part:

⇨ More logical to have the presentation of the new risks first and then judgements about the adequacy of current guidance.

⇨ Better understanding of the arguments about the adequacy or not of the current guidance for evaluating the new SynBioMs.

Molecular characterisation and ERA of SynBio GMPs (WP2)

Limits of the existing risk assessment methodologies

• Existing risk assessment methodologies will need to be revisited at regular intervals and improved when necessary: yes, but who will decide when such updates are necessary and according to which procedure and criteria?

• For GMPs containing stacked events, analysis of the expression levels of the newly expressed proteins (NEPs) may become a challenge that will increase with the number of NEPs. The same will go for the study of the interactions (potential additive, synergistic, and antagonistic effects) and for the risk assessment of each event before they are stacked.

⇨ Should we consider putting a threshold on the number of genes stacked?

Molecular characterisation and ERA of SynBio GMPs (WP2)

Off-target effects: a question set aside too quickly

- "The analysis of potential off-targets on a regular basis would be of very limited value for the risk analysis": Anses disagrees and considers that the identification of the off-targets is necessary to analyse potential new hazards and risks resulting from them, since there is not yet a scientific consensus on this question.

- "In addition, back crossing steps following DNA modifications may allow removal of most of these potential off-targets from the final product assuming they are not genetically linked to the target site.": same comments as for the draft scientific opinion on genome editing regarding the feasibility and the demonstration of the removal.

⇨ Proposal to use whole genome sequencing (WGS), especially for the introduction of point mutations.

⇨ Research efforts needed to develop methods and tools for the identification of off-targets even in the most complex cases.

Molecular characterisation and ERA of SynBio GMPs (WP2)

Editorial comments

- Document well written and of high scientific quality.
- Choice and use of cases studies particularly appreciated.

⇨ Information about the documents used as reference documents should be made more comprehensive (some important references are missing), clearer and consistent throughout the opinion.

⇨ Clarification needed about what was done by the contractor and by the working group respectively.