



# Ethics Guidelines for Sc2.0



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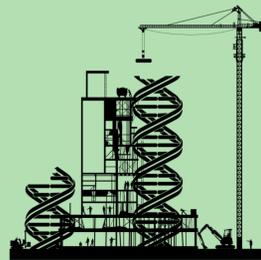
## BACKGROUND

### HISTORY: Asilomar Conference on Recombinant DNA 1975

The discovery of restriction enzymes and Paul Berg's development of a new method allowing for the covalent joining of DNA molecules in the 1970s opened a whole new field for exploration in science. This new rDNA (recombinant DNA) technology allowed for the transfer of DNA between different species. In response to the concerns that were raised and after informal consultation with colleagues, Paul Berg paused his experiments. Less than a year later, a moratorium was called on all rDNA research, pending further discussion and debate. The moratorium and the Asilomar Conference that lifted it were revolutionary in that the biologists conducting the research in question acknowledged that there were potentially substantial risks posed by the new type of research they were doing. They realized that it would be prudent to temporarily halt all research and thoroughly evaluate the situation before proceeding, rather than to allow the research to proceed only to engage with the potential risks after they become actual harms.

### CONTINUING THE TRADITION: SB2.0 2006

Synthetic biology (synbio) research is on a continuum with recombinant DNA research. The SB2.0 Meeting in 2006 continued the tradition of Asilomar, evaluating research in the field in its early stages in an effort to minimize harm and maximize benefit that might come from the science. Maurer, Lucas and Terrell from the University of California-Berkeley drafted a white paper in advance of the meeting outlining options for collective action on biosafety and biosecurity. The paper and the subsequent discussions about it focused on practical steps that the community could take that would build on what was already being done by DNA synthesis companies. While not comprehensive, the SB2.0 recommendations are an excellent starting point upon which to build as the field evolves.

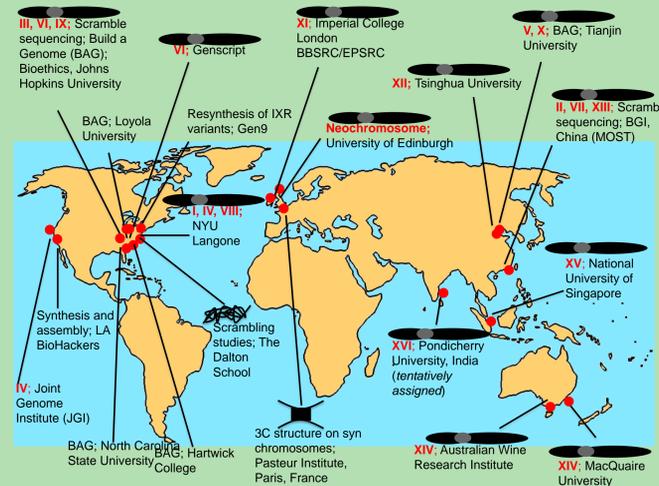


## ETHICAL ISSUES IN SYN BIO

The public is both curious and cautious about synbio. Curious because the science is cutting edge and a fascinating blend of engineering, tinkering and biology. Cautious due to the unknowns that come with any new, emerging technology. Most of the concerns in synthetic biology stem from the fact that many products of synbio that are designed to benefit society could, in the wrong hands, also potentially be used to cause harm ('dual-use'). The discussion around synbio also includes concerns often associated with new technologies, regarding intellectual property and the just distribution of risks and benefits issuing from the research.

## Sc2.0 PROJECT BACKGROUND

In 2010, Craig Venter's team synthesized the entire *Mycoplasma mycoides* genome and transplanted it into another species of bacterium, *Mycoplasma capricolum*, resulting in the first living organism with a fully synthetic genome. In 2011, Dymond *et al.* spearheaded a project similar to Venter's, but on a larger scale. The Sc2.0 project aims to synthesize the genome of *Saccharomyces cerevisiae* and is anticipated to result in the first eukaryotic organism with a fully synthesized genome. The genomic design of Sc2.0 is based on the wildtype yeast sequence; however, a number of genetic changes are included that will be used as tools within Sc2.0 to answer a number of biological questions that we have not, until now, had the tools necessary to be able to answer. Included among these alterations is the addition of symmetric loxP sites throughout the genome that will be used to answer questions about genome structure and evolution, as well as genome-wide codon swaps of all TAGs with TAA that will be used to explore the expansion of the genetic code, for example, by studying addition of a 21st amino acid associated with this now free codon.



## NEED FOR A GOVERNING DOCUMENT

The scope of the Sc2.0 Project is unprecedented. Sc2.0 is a massive, collaborative project that involves diverse scientists from multiple academic and commercial institutions from across the globe. The project also includes a group of motivated citizen scientists from Los Angeles, USA, working at the LA Biohackers lab (<http://www.biohackers.la>). With scientists from such different backgrounds working together on a single project, it is essential that everyone is well informed and conscientious with regard to the ethics and policy issues related to this project. Collaborators are from many different countries where the local and national laws differ greatly. As such, we felt that the project would benefit from a unifying document articulating the major ethical and policy issues related to the project and our collective approach to these issues. These guidelines were finalized after extensive discussion among Sc2.0 members and are summarized below.

## ETHICS AND GOVERNANCE AGREEMENT

### The Sc2.0 Project is for the benefit of society

1. "Peaceful purposes." As scientists and humans, we wish our work on the Sc2.0 project to contribute to the benefit of society and not add to its harm.

2. Transparency and Public Communication. While the Boeke laboratory is primarily responsible for the maintenance of the Sc2.0 Project website, all collaborators will regularly contribute updated information and data to be added to the site. The Boeke lab is also primarily responsible for public outreach and encourages and supports outreach at other Sc2.0 locations. Members of the public are currently involved in this project, including the LA Biohackers and high school students, and such public engagement will continue as the project moves forward.

### Safety

3. Sequence Synthesis Best Practices. All synthetic DNA providers participating in or used by participating partners to generate sequences for this project must be in compliance with the US Department of Health and Human Services' "Screening Framework Guidance for Providers of Synthetic Double Stranded DNA" Guidelines. This will help prevent DNA sequences that can cause harm from being synthesized and shipped to unauthorized individuals.

4. Data Distribution. To reduce the chance of distributing materials to individuals with nefarious intent, members of the Sc2.0 Project will take precautionary steps to verify the identity of individuals requesting materials or data prior to the shipment of any Project materials.

5. Containment. Sc2.0 is designed to be safe to handle within the lab and unlikely to survive outside the laboratory setting. All strains contain a number of auxotrophic mutations that make them dependent on laboratory conditions. Neither Sc2.0 nor its intermediates will be intentionally released into the environment. Further, we are exploring the possibility of adding additional engineered vulnerabilities, further decreasing the likelihood that this organism, or any of its intermediates, would be viable outside of the laboratory.

6. Safety and Dual-Use Training. While we work with *Saccharomyces cerevisiae*, which is Generally Regarded As Safe (GRAS) by the US Food and Drug Administration (FDA) and does not require biosafety training, all scientists working on the Sc2.0 project will receive appropriate training, including in concerns about dual-use technologies.

7. Compliance With National and Local Laws. All work on Sc2.0 is in compliance with laws and policies that apply to synbio across the globe.

### Intellectual Property

8. Intellectual Property. The project encourages innovation and focuses on maximizing the beneficial use of Sc2.0. No intellectual property rights will be exercised on the clones used to generate novel strains, intermediary strains, or the final Sc2.0 strain.

9. Open Access. All data and materials generated by this project will be made available to other researchers, at cost, to promote innovation and maximize the chance of benefits issuing from this research.

### Review

10. The Sc2.0 Executive Committee. The team consists of a team of four interdisciplinary members that are responsible for ensuring that all collaborators are in compliance with this agreement and addressing any safety concerns that arise during the course of this project.

11. Review of this Agreement. As this project and the technologies it uses develop, this document will be revisited to evaluate any risks posed by this work. In addition to the science moving quickly, the local and national policies are also constantly in flux. These shall be reviewed regularly and adjustments to this agreement will be made accordingly.

## CONCLUSIONS

1. This is the first document of its kind (that we are aware of) in this field. It addresses ethical issues that arise in synthetic biology in the context of a large, international collaborative synthetic biology project. It provides a set of recommendations and guidelines to govern the Sc2.0 project to which all collaborators agree to adhere to.

2. As the field grows and evolves, project-specific statements such as this may help catalyze additional collective action in synbio. They also affirm individual commitment to community goals, such as those articulated by the participants in SB2.0.

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## ACKNOWLEDGEMENTS

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For more information, please visit:  
<http://syntheticyeast.org/sc2-0/>