Introduction At the dawn of a new scientific field, it is crucial to consider not only the scientific challenges that will be faced, but also the ethical and policy challenges. Ideally, such consideration takes place in advance of the science, though that is not always possible. Ethical consideration is of particular importance in synthetic biology for a number of reasons, including that many new discoveries hold the potential for both benefit and harm ('dual-use'); the merging of biology and engineering that is a hallmark of synthetic biology particularly appeals to a broad community of citizen scientists and has fostered the development of a host of DIY bio labs that operate outside the usual academic and commercial oversight mechanisms; and finally, the field as a whole is a source of both fascination and concern among the public.

In 2011, Dymond *et al*. spearheaded a major synthetic biology project, Sc2.0, which aims to synthesize the genome of *Saccharomyces cerevisiae*. While we are working with an organism that is Generally Regarded As Safe (GRAS) by the United States Food and Drug Administration (FDA), and not anticipated to have dual-use applications, it is anticipated that this project will produce the first eukaryotic organism with a fully synthesized "designer" genome, and we have a responsibility as scientists and humans to conduct this research responsibly and to be accountable for any concerns it raises. This is a massive, collaborative project involving diverse scientists from academic and commercial institutions across the globe. The project also includes a group of motivated citizen scientists from the United States. With scientists from such different backgrounds working together on this single project, it is essential that everyone involved is well informed and conscientious with regard to the related ethics and policy issues. As such, this ethics and governance document for the Sc2.0 Project, by which all members are bound, was developed to communicate a unified vision about our goals and expectations for this work. We hope that this effort can serve as a model for other similarly collaborative, global endeavors in synthetic biology.

Background The public is both curious and cautious about synthetic biology. Concerns focus on risks to human and environmental health due to intentional or unintentional release of novel organisms, and the possibility that products of synthetic biology designed to benefit society may also be capable of causing harm if placed in the wrong hands ('dual-use'). The discussion around synthetic biology also includes concerns often associated with new technologies, regarding the appropriateness of the research itself, the role of intellectual property, and the just distribution of risks and benefits issuing from the research.

A number of guidelines have been proposed in response to some of these issues[1], most of which focus on biosafety. Currently, the *NIH Guidelines for Research Involving Recombinant DNA Molecules* serves as the main document guiding NIH-funded synthetic biology research. These guidelines focus on DNA synthesis companies as the primary point of intervention; other guidelines focus on the researchers themselves. Here, we endeavor to strike a balance between what individual researchers can do and the responsibilities others must assume, taking into account the details and risk/benefit analysis in the context of the Sc2.0 project, in particular.

Ethics and Governance As participants in the Sc2.0 project, we agree that:

1. *We will conduct and promote our work on Sc2.0 for the benefit of humankind*.

As scientists and humans, we wish our work to contribute to the benefit of society, and not to contribute to its harm. Our work on Sc2.0 will be done only in service to "peaceful purposes"[2]. Further, we will make efforts to ensure that the benefits of Sc2.0 are maximized and any potential harms of Sc2.0 are minimized.

[1] e.g., DHHS (http://www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf); PCSBI (2010: www.bioethics.gov/synthetic-biology-report); DIYbio.org (2011: http://diybio.org/codes)

[2] DIYbio Draft Codes of Ethics (DIYbio.org/codes)

2. *We will participate with the Project's efforts to engage with the public and be transparent and open about our work on Sc2.0.*

We are committed to transparency and public engagement. While the Boeke laboratory holds primary responsibility for the maintenance of the Sc2.0 Project website – our public engagement venue with the broadest reach – all partners will contribute information and data to this resource in a timely fashion. The Boeke laboratory is also primarily responsible for public outreach, though all Sc2.0 participants are encouraged to hold public lectures and will receive support for these activities, such as power point slides and handouts upon request from the Boeke laboratory. Members of the public are already directly involved in the Project, which has partnered with both the LA Biohackers and high school students. This outreach will continue, and all partners are encouraged to make efforts to publicize both the potential and actual benefits of this and other synthetic biology projects, along with the potential risks, in ways the lay public can understand.

3. *All sequence providers generating sequence for use in Sc2.0 shall be in compliance with the US Department of Health and Human Services' "Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA".*

To help prevent DNA sequences that can cause harm from being synthesized and shipped to individuals with nefarious intent, the US Department of Health and Human Services developed guidelines for the providers of synthetic double stranded DNA[3]. These guidelines recommend thorough screening of both the requested sequence for any toxic or pathogenic sequence, and of the requestor, to ensure that the individual is a legitimate customer. While companies are encouraged, but not required, by the US federal government to follow these guidelines, we believe that they are reasonable, prudent, and critical to efforts to maximize benefit and minimize harm from synthetic biology, and therefore support their use.

4. *Members of the Sc2.0 Project will assess individuals requesting Sc2.0 Project data/materials prior to shipment of any such materials, to help reduce the chance that we are distributing materials to those with nefarious intent*.

We wish the fruits of our research only to be used in efforts that are "reasonably justified by a prophylactic, protective, bona fide research, or other peaceful purpose."[4] As such, we will take reasonable efforts, prior to shipment, to ensure that requestors of Sc2.0 Project data/materials are motivated by legitimate goals and have the appropriate training and infrastructure to safely handle the requested data/materials.

5. *Our laboratories, practices and methods will have at their core an ethos of safety for both laboratory workers and the communities outside our institutions.*

While we believe that our experiments do not currently involve significant risks for either the members of our laboratories or the broader community, the Sc2.0 Project embraces and employs rigorous safety practices. Though we currently have no plans to release into the environment the completed Sc2.0, or any intermediaries, all strains contain a number of auxotrophic mutations, rendering them unlikely to be fit enough for long term survival outside the laboratory. However, we acknowledge that it is formally possible that streamlining the genome and making it less likely to undergo rearrangement could confer a growth advantage relative to wild type yeast, at least under laboratory conditions. As such, we are exploring the possibility of additional engineered vulnerabilities to further decrease the likelihood of viability outside of the laboratory in an effort to minimize the chance of harm, should there be an accidental release.

[3] "Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA" (see footnote 1 for URL)

[4] Federal Criminal Code, Title 18, Section 175(b)

6. *All personnel will receive training in biosafety, dual-use concerns, and other ethics issues, as appropriate.*

While biosafety training is generally not required for individuals or laboratories working with organisms, such as *Saccharomyces cerevisiae*, that are Generally Regarded As Safe (GRAS) by the United States Food and Drug Administration (FDA), individuals working on Sc2.0 will receive training in the risks of dual-use technologies, through at least the use of the NSABB's educational module[5] for individual learning and group discussion. Other relevant training will be made available as appropriate to all members of the Project.

7. *Our work on Sc2.0 is in compliance with national and local laws.*

Jurisdictions across the globe have enacted laws and policies that apply to synthetic biology. Insofar as these laws and policies apply to our work on Sc2.0, we will ensure that we are in compliance.

8. *Intellectual property rights will not be taken on Sc2.0 once created, nor on the intermediary clones and strains generated as part of the project.*

We are committed to facilitating innovation and maximizing the beneficial use of Sc2.0. As such, no intellectual property rights will be exercised on the clones used to generate novel strains, intermediary strains, or the final Sc2.0 strain.

9. *Data and materials generated by this project will be made available to other researchers.*

We will make all primary products of the Sc2.0 Project, including the clones used to generate novel strains, intermediary strains, or the final Sc2.0 strain, available to the broader community at cost. Arrangements for deposition of these materials into a repository for distribution to the community are being finalized.

10. *The Sc2.0 Executive Committee will address any issues that may arise with regard to safety or compliance with this agreement*.

At this time, the Sc2.0 Executive Committee consists of Jef Boeke, Debra Mathews, Tim Trevan, and Huanming Yang. The composition of this committee will be modified over time as necessary. The committee will be responsible for addressing any issues that may arise with regard to safety or compliance with this agreement. Such issues may be brought to the Committee's attention by someone within or outside the Sc2.0 project. The Committee has the authority to remove from the Sc2.0 project partners who violate this agreement.

11. *We will revisit this agreement as the project and the technologies it uses develop, to ensure that any risks posed by this work is appropriately matched to the oversight it receives.*

Understanding that the science is moving very quickly and that local and national policies may also shift, we will regularly review this document to ensure that our project policies are appropriately matched to the risks and regulatory status of the project. If the risks increase, so will oversight and our accountability.

[5] http://oba.od.nih.gov/oba/biosecurity/documents/B_Dual_Use_Educational_Module_FINAL.pdf