

## **The Joint Genome Institute's Synthetic Biology Internal Review Process**

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Synthetic biology has the potential to accelerate science and bolster economic growth. However, like any new technology, synthetic biology could be misapplied or result in unintended consequences. Serious concerns have been raised over the possible intentional use of synthetic biology approaches to engineer pathogenic organisms as well as the possible accidental environmental release of genetically engineered organisms. Scientists pursuing synthetic biology research must diligently consider issues such as these.

The U.S. Department of Energy (DOE) Joint Genome Institute's (JGI) Synthetic Biology Internal Review process seeks to assess, beyond technical and scientific merit, certain broader aspects (e.g., environmental, biocontainment, biosafety, or biosecurity) of the research proposals associated with the JGI's DNA synthesis program (<http://jgi.doe.gov/our-science/science-programs/synthetic-biology/>). The purpose of this internal review process is two-fold: 1) to assess the broader aspects of the research, request proposal modifications if issues of concern are not sufficiently addressed in the proposal, reject research proposals where issues of concern are not or can not be satisfactorily addressed, and output a paper-trail audit of the review process; and 2) to encourage and educate researchers to more extensively consider the broader aspects of their research, including beyond the immediate research itself.

All JGI DNA synthesis proposals (including those from the JGI Community Science Program and from the DOE Bioenergy Research Centers) contain a broader implications section dedicated to a brief discussion of these broader aspects. This broader implications statement should address not merely the possible rewards but also a considered statement of the risks associated with the work. These statements serve as a useful tool to protect not only the public, but the Investigators (and their institutions), as well as JGI itself. These statements are proof of consideration and deliberation - proof of the responsible application of science. As members of the research community, we must consider risks, and be able to show our consideration of those risks - even if they are demonstrably small.

After a synthetic biology research proposal has successfully passed technical feasibility and scientific merit review, the proposal enters the JGI's Synthetic Biology Internal Review process. A JGI system administrator uploads the proposal to the Synthetic Biology Internal Review System (SBIRS, <http://jgi-sbirs.jgi-psf.org>) and assigns a minimum of 3 Reviewers to it. Each Reviewer reads the full proposal, makes comments on the proposal in the SBIRS, and votes in the SBIRS to either approve the proposal or to discuss it further with the other assigned Reviewers. If not unanimously approved, the assigned Reviewers discuss the proposal in person or via telephone, and decide to approve or reject the proposal, or to require that modifications be made to the proposal to address the Reviewers' concerns. The Reviewers email the decision to a system administrator, who records the decision in the SBIRS. If the Reviewers decide to approve the proposal after discussion, a JGI Director is required to approve the proposal before work begins. A JGI Director can reject any proposal, and can require that additional modifications be made to any proposal. The entire Synthetic Biology Internal Review process should take three

weeks or less (unless modifications are requested, which could delay the process by an additional three weeks or more).

Investigators are strongly encouraged to use the broader implications section of the proposal to make it clear to the Reviewers that the Investigators are actively thinking about the broader implications (noted above, primarily environmental, biocontainment, biosafety, or biosecurity) of their research, and that they have mitigation strategies in place to address outstanding issues of concern. Note that Investigators are not expected to provide an in-depth analysis (e.g., full socio-economic analysis) of their early-stage research, but Investigators should demonstrate that they are currently considering the implications of their research, and that more in-depth analyses can and will be pursued as their research matures. Investigators should not merely write "None" or "All research will be conducted in a safe manner according to Federal regulations" in the broader implications statement, as this will lead to the Reviewers asking for proposal modifications, incurring three week or longer delays.

Investigators must explicitly state if their proposed research would:

1. Demonstrate how to make a vaccine ineffective
2. Confer resistance to antibiotics or antiviral agents
3. Enhance a pathogen's virulence or make a non-virulent microbe virulent
4. Increase transmissibility of a pathogen
5. Alter the host range of a pathogen
6. Enable a pathogen's ability to evade diagnostic or detection modalities
7. Enable the weaponization of a biological agent or toxin

Investigators are encouraged to think broadly about the aspects of their research. This will make sure that JGI DNA synthesis is not delayed, and it will start to nudge the collective research community's cultural mindset in the right direction. Reviewers should assess whether Investigators are actively thinking about the broader implications of their research, and whether the Investigators have mitigation strategies in place to address outstanding issues of concern. Reviewers should request proposal modifications if issues of concern are not sufficiently addressed in the proposal, and reject research proposals where issues of concern are not or cannot be satisfactorily addressed.

JGI Synthetic Biology Internal Review Process Statistics (as of Oct.7, 2014):

- 22 proposals reviewed
  - 12 from DOE BioEnergy Research Centers
  - 10 from the JGI's Community Science Program
- 74 Reviewer comments
  - General [33], BioSafety [17], BioSecurity [6], Ethical [2], Legal [2], Social [6], Environmental [8]
- 13 proposals unanimously approved by Reviewers
- 6 proposals discussed and approved by Reviewers
- 3 proposals discussed and modifications requested by Reviewers
  - 2 revised proposals unanimously approved by Reviewers
  - 1 proposal pending modification and resubmission
- 21 proposals approved by JGI Director