**Synthetic Biology Internal Review Process**

**Investigator Guidelines**

*Purpose of this document*

This document provides guidance for Investigators as they prepare their JGI DNA synthesis proposal submissions in anticipation of the Synthetic Biology Internal Review process.

*Background*

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. Legitimate concerns have been raised over the intentional use of synthetic biology approaches to engineer pathogenic organisms and the accidental environmental release of genetically engineered organisms. Scientists pursuing synthetic biology research must diligently consider issues such as these.

*Overview of the JGI Synthetic Biology Internal Review Process*

The JGI Synthetic Biology Internal Review process seeks to assess, beyond technical and scientific merit, the broader aspects (e.g., environmental, ethical, legal, social justice, biosafety, biosecurity) of the research proposals associated with the JGI’s DNA synthesis program. 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) 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).

*Guidelines for Investigators*

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 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. In addition, Investigators are requested to check over their proposals for spelling and grammar mistakes, which will not favorably contribute to the review process.

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

Thinking about proposed research in a broader light may feel uncomfortable to Investigators that are unaccustomed to doing so. This is perfectly normal. Investigators should recognize that there are broader aspects, positive and negative, to all research, and that in some cases, actively considering these aspects enables the placement of mitigating strategies so as to avoid unwanted outcomes.