



## Synthetic Biology Internal Review Process

This section 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, 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 the 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, the JGI Director is required to approve the proposal before work begins. The 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 delays of three weeks or longer. 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

Here are a couple of illustrative scenarios that may assist Investigators as they think about the broader aspects of their proposed research:

A) A plant lab is seeking to better understand plant/pathogen interactions. As part of the research plan, the researchers will develop a plant pathogen strain that no longer stimulates a response in the plant. What are the concerns around an unintentional and/or intentional uncontrolled release of this engineered pathogen? What could and should the plant lab itself do to address these concerns, and who else could and should it collaborate with along these lines?

B) A microbiology lab is seeking to develop a more robust microbe that can break down cell walls of a wider variety of feedstocks, some of which may contain components that can impair cell growth and replication. To this end, the researchers will add exogenous catabolic and solvent-tolerance genes to a non-pathogenic microbe for the purpose of more effectively deconstructing the feedstock biomass. What consequences could result from such work if this engineered organism were to be unintentionally released from the lab? What could and should the microbiology lab itself do to address these concerns, and who else could and should it collaborate with along these lines?

Note that these two illustrative examples are by no means the only issues to consider. It is up to the Investigator (and the Reviewers) to determine the broader aspects of the proposed research.

Thinking about proposed research in a broader light may feel uncomfortable to Investigators that are unaccustomed to doing so. However, 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.

## Responding to Modifications Required by Reviewers

As mentioned above, one possible outcome of the Internal Review process is that the Reviewers may require modifications be made to a proposal before it can be approved. When modifications are required, the Internal Review decision report that the Researcher receives will contain a section entitled “Review Committee Decision Notes” as well as a section entitled “Reviewer Comments.” Researchers should be sure to address the specific modifications requested in the “Review Committee Decision Notes” section. While Researchers may respond to any of the individual comments in the “Reviewer Comments” section, this should not be considered essential. It should be noted that, as described above, Reviewers individually comment on each proposal before discussing proposals together. During group discussion, Reviewers may collectively determine if any of the individual comments must be responded to, and if so, the Reviewers will include these points of concern in their decision notes.

## Summary

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.