

*Experiments Involving the Cloning of Toxin Molecules
Frequently Asked Questions*

- **What experiments involving toxin molecules are subject to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*?**

The *NIH Guidelines* apply to certain experiments involving the deliberate formation of recombinant or synthetic nucleic acid molecules containing genes for the biosynthesis of toxin molecules. All experiments subject to the *NIH Guidelines* that involve toxin molecules must be reviewed and approved by an Institutional Biosafety Committee (IBC) prior to initiation. In addition, certain experiments involving genes coding for functional recombinant or synthetic nucleic acid toxin molecules must be registered with OBA, and in some instances approved by OBA prior to initiation.

- **What types of experiments involving toxin molecules must be submitted to OBA?**

Section III-B of the *NIH Guidelines* describes experiments involving the deliberate formation of recombinant or synthetic nucleic acid molecules containing a gene for the biosynthesis of functional toxin molecules lethal for vertebrates at an LD₅₀ of less than 100 nanograms per kilogram of body weight. Experiments such as these require IBC and OBA approval prior to initiation. Examples of toxins that require OBA approval include tetanus, diphtheria, and *Shigella dysenteriae* toxin.

OBA approval is not required when performing experiments involving genes coding for functional toxin molecules having an LD₅₀ of greater than 100 nanograms per kilogram of body weight but less than 100 micrograms per kilogram of body weight. However, Appendix F-I of the *NIH Guidelines* requires that these experiments be registered with OBA in addition to being approved by the IBC. An example of a toxin that would require registration with OBA is *Clostridium perfringens* enterotoxin A.

- **How does an institution obtain OBA approval for experiments subject to Section III-B of the *NIH Guidelines*?**

OBA maintains a list of previously approved toxin experiments. Institutions should review this list to determine if the experiment being proposed is similar to an experiment that has been previously approved as this will inform your application to OBA.

Institutions should provide OBA the following information:

- Details of the proposed experiment (this may be in the form of the IBC registration document);

- Indicate whether the current proposal is similar to an experiment already approved by OBA, and clearly indicate which approved experiment is being referenced; and
- The proposed level of containment under which the experiment will be conducted.

OBA will then make the final determination and grant an approval as appropriate.

If the proposed experiment does not resemble a previously approved experiment, OBA will review the experimental details of the experiment along with the proposal for containment and either approve or disapprove of the experiment. If the experiment is approved, it will then be added to the OBA list of previously approved experiments.

The list of previously approved toxins experiments can be requested by emailing oba@od.nih.gov

- **Is OBA approval required when an experiment subject to Section III-B of the *NIH Guidelines* involves a toxin on the Select Agent list?**

If an institution proposes an experiment subject to Section III-B of the *NIH Guidelines* that involves a toxin on the Select Agent list, OBA defers the approval of that “restricted experiment” to the appropriate regulatory authority, such as the Centers for Disease Control and Prevention (CDC). Once regulatory approval has been obtained, no further approval from OBA is necessary. However, review and approval is still required by an IBC. Guidance on “restricted experiments” can be found on the [National Select Agent Registry](#) website.

Section III-B experiments that would require CDC approval include those involving Botulinum neurotoxins.

- **What information should be submitted to OBA when registering an experiment that involves a toxin subject to Appendix F-I (toxins that have an LD₅₀ of greater than 100 nanograms per kilogram of body weight but less than 100 micrograms per kilogram of body weight)?**

The institution should provide OBA with the following information:

- The IBC-approved registration document that includes the details of the experiment, and
- The level of containment under which the experiment will be conducted.

OBA will acknowledge receipt of the registration.

Registration materials can be sent to oba@od.nih.gov

- **Are there any toxin experiments that do not require either registration with or approval from OBA?**

Experiments involving genes coding for toxin molecules with an LD₅₀ of greater than 100 micrograms per kilogram do not need to be approved by or registered with OBA. However, IBC approval for these experiments is still required.

Additionally, OBA review and approval is not required for experiments that do not result in a functional toxin being expressed.

- **Who can I contact to get additional information or if I have questions about whether OBA approval or registration is required?**

For additional information, or assistance in determining whether a specific toxin experiment requires OBA approval or registration, contact Ryan Bayha, Senior Analyst for Science Policy Outreach, NIH Office of Biotechnology Activities, 301-496-9838, bayhar@mail.nih.gov