Institutional Biosafety Committee (IBC)
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Research requiring NIH OBA Review

The National Institutes of Health Office of Biotechnology Activities (NIH-OBA) is the administrative branch of the NIH responsible for carrying the orders of the NIH Director with regard to recombinant or synthetic DNA. An advisory committee, the Recombinant DNA Advisory Committee (RAC), is involved in establishing policies for recombinant and synthetic DNA. In addition to review by the OHSU Institutional Biosafety Committee (IBC) some research may require review by NIH-OBA and/or the RAC.

This document provides guidance on when additional review by NIH-OBA and/or the RAC may be necessary so you may appropriately time the submission of IBC paperwork so reviews are conducted and approvals are in place prior to start of work. The review process can be initiated by completing and submitting a Recombinant DNA Research Questionnaire (RDRQ) to the OHSU IBC or when there is uncertainty on whether or not the project requires IBC review, the Initial Classification From should be submitted first. The current versions of these forms can be found on the IBC Policies and Forms webpage.

Antibiotic Resistance Genes

If an antibiotic resistance gene is being used, this needs to be addressed as outlined in Question 4 of the RDRQ. Most antibiotic resistance genes used in research do not pose a concern. But RAC review and approval from the NIH Director is required if a drug resistance trait is deliberately transferred into microorganisms that are not known to acquire the trait naturally and *if such acquisition could compromise the use of the drug to control disease agents in human or veterinary medicine or agriculture*. More guidance on this topic is available in NIH-OBA's Major Action FAQs.

DNA encoding a biological toxin

If DNA encoding a biological toxin is being used, the toxin gene and its LD50 are to be identified in Q11 of the RDRQ. If DNA encodes a biological toxin with an LD50 in vertebrates of <100 µg/kg, additional registration or review by NIH-OBA may be required:

- Recombinant or synthetic DNA molecules that result in the biosynthesis of toxins (or the active subunit of a toxin) with an LD50 in vertebrates of **< 100 ng/kg** require containment to be reviewed and approved by the NIH-OBA prior to initiating work, as detailed in Section III-B-1.
- Recombinant DNA molecules that result in the biosynthesis of toxins (or the active subunit of a toxin) with an LD50 in vertebrates of **> 100 ng/kg but <100 µg/kg** require registration with NIH-OBA prior to initiating work as detailed in Appendix F.

The OHSU Fact Sheet on Biological Toxins includes a table of toxins and their LD50s can be found on the IBC Policies and Forms webpage..

Work with DNA from restricted agents

NIH Guidelines Section V-L defines three agents as restricted agents, alastrim (variola minor), smallpox (variola major), and whitepox (a virus related to smallpox).

- Work with these restricted agents in their entirety is not permitted at OHSU.
- Any work with recombinant or synthetic DNA encoding portions of these restricted agents (regardless of the size of the DNA fragment or the function of the gene) must be described in Question 8 of the RDRQ and requires NIH-OBA review to set containment conditions for the work (NIH Guidelines Section III-D-2-b).

The World Health Organization (WHO) has also issued guidelines regarding work with smallpox and recombinant or synthetic DNA encoding smallpox sequences, WHO recommendations concerning the distribution, handling and synthesis of Variola virus DNA. WHO review and approval of the work is required if the DNA fragment encoding smallpox is greater than 500 bp.

Work with 1918, H2N2 (1957-1968) or HPAI H5N1 Influenza

The NIH Guidelines include specific requirements for experiments with influenza viruses utilizing recombinant or synthetic methods. All such work must be described on the RDRQ.

Experiments with 1918 H1N1, human H2N2 (1957-1968) or HPAI H5N1 that are designed to create resistance to neuraminidase inhibitors or other effective antiviral agents (including investigational antiviral agents being developed for influenza) would be subject to Section III-A-1 (Major Actions) and require RAC review and NIH Director approval.

Human Subjects Research

For human gene transfer studies a completed Appendix M must be submitted to NIH-OBA for review. This is typically submitted by the sponsor or institution serving as the central site for multi-site clinical trials. Researchers must submit to the OHSU IBC a memo from NIH-OBA certifying RAC review is complete and any additional RAC questions with responses.

Appendix M-VI-A allows for exemption from RAC review if the study is designed for the induction or enhancement to a vector-based microbial immunogen, if an immune response has been demonstrated in an animal model and persistence of the vector encoded immunogen is not expected to persist.

Additional guidance on the documents required for OHSU IBC review of human gene transfer studies is available on the OHSU IBC website:
http://www.ohsu.edu/xd/research/about/integrity/ibc/gene_transfer.cfm.

Questions or uncertain if this applies to your research?

Please contact the IBC office at ibc@ohsu.edu or 503-494-7887, option 1. The IBC administrative staff will assist you in determining if your research falls into any of the above categories.