Bigelow | Laboratory for Ocean Sciences

Policy on Genetic Modification

1. Purpose

Genetically Modified Organisms (GMOs) have become essential research tools in all facets of the life sciences. Genome sequencing, particularly over the past decade, has yielded massive amounts of information from all branches of the universal 'tree of life'. The prominence of new molecular editing tools is the result of this rapid expansion in genome sequencing capacity and the 'mining' of these genomes to discover the functions of naturally occurring proteins encoded therein. GMOs provide the critical, living biological models for genome-based hypothesis testing and can also be the source of new bio-products, disease diagnostics and therapies.

Bigelow Laboratory for Ocean Sciences takes the issue of working with genes and their host organisms, including their modification, very seriously. This document outlines the procedures to be followed when working with genes, including the process of deciding whether to engage in a project that involves genetic modification or genetic engineering.

For clarity, it is necessary to distinguish between genetic modification and genetic engineering.

Genetically Modified Organisms (GMOs) are organisms in which the DNA from another genus (or higher taxonomic level) has been inserted into an organism in a laboratory. Genetically Engineered (GE) organisms are strains, which have been genetically-altered in the lab but do not contain artificially-inserted DNA from another organism. GE organisms are created instead through exposure to a DNA mutagen (e.g., ultraviolet light, chemical agents), by directed gene 'knock-outs', or by targeted gene editing. In practice, most of the existing federal guidelines for biosafety have been written with GMOs in mind, but there is still sometimes ambiguity around what exactly is meant by a GMO. For the purposes of this document, Bigelow Laboratory will adhere to the definitions above.

The steps outlined below are above and beyond what is required by federal funding agencies or by private industry. We have implemented this process, however, to ensure that we conduct our research in a professional manner, following all accepted protocols, and in a thoughtful way that acknowledges the importance of, and responsibility that is inherent in, working with genetic material.

This policy is purposely written in non-technical language to provide all Principal Investigators, Staff, Trustees, and interested members of the public with information governing Bigelow Laboratory's approach to research and contracts involving the use of GMOs and GEOs.

This policy defines the review mechanisms, decision making responsibility and monitoring requirements for GMO/GEO work at Bigelow Laboratory. The policy references two key documents that contain much greater detail on both the legal and procedural status of GMO research in the United States. These are: *Restrictions on Genetically Modified Organisms: United States*[1] authored by The Law Library of Congress, and the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*[2]. Both are subject to periodic revision. It is the responsibility of the researchers involved with GMO/GEO work to be familiar with their contents.

2. Brief Overview of GMO policy and use[3]

The United States does not have any federal legislation that is specific to genetically modified organisms (GMOs). Rather, GMOs are regulated pursuant to health, safety, and environmental legislation governing conventional products. *The U.S. approach to regulating GMOs is premised on the assumption that regulation should focus on the nature of the products, rather than the process by which they were produced.*

The development of a regulatory framework concerning genetic engineering began in 1975, at Asilomar, California. The first use of Recombinant DNA (rDNA) technology had just been successfully accomplished by Stanley Cohen and Herbert Boyer two years previously and the scientific community recognized that, as well as providing benefits, this technology could also pose some risks. The Asilomar meeting recommended a set of guidelines regarding the cautious use of recombinant technology and any products resulting from that technology. The Asilomar recommendations were voluntary, but in 1976 the US National Institute of Health (NIH) formed an rDNA advisory committee. This was joined by other regulatory offices (the United States Department of Agriculture (USDA), Environmental Protection Agency (EPA) and Food and Drug Administration (FDA). In 1982 the Organization for Economic Co-operation and Development (OECD) released a report into the potential hazards of releasing genetically modified organisms into the environment as the first transgenic plants were being developed. As the technology improved and genetically organisms moved from model organisms to potential commercial products the USA established a committee at the Office of Science and Technology (OSTP) to develop mechanisms to regulate the developing technology. In 1986 the OSTP assigned regulatory approval of genetically modified plants in the US to the USDA, FDA and EPA.

The Cartagena Protocol on Biosafety was adopted on 29 January 2000 and entered into force on 11 September 2003. It is an international treaty that governs the transfer, handling, and use of genetically modified (GM) organisms.

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[1] http://www.loc.gov/law/help/restrictions-on-gmos/usa.php

[2] http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines

[3] from Wikipedia and other sources. Mouse over for follow up references.

It is focused on movement of GMOs between countries and has been called a *de facto* trade agreement. One hundred and fifty-seven countries are members of the Protocol and many use it as a reference point for their own regulations. The US is not a party to the Cartagena Protocol on Biosafety. As a signatory but a nonparty to the parent Convention on Biological Diversity, it cannot become a party to the Protocol. However, it has participated in meetings as a nonparty observer.

Like most other countries, the USA has developed a classification system for research involving GMOs. Work that poses only a low risk includes that using standard laboratory strains as hosts (e.g., *Escherichia coli*, *Saccharomyces cerevisiae*), recombinant DNA that does not code (i.e., impart the genetic blueprint) for a vertebrate toxin, or is not derived from a microorganism that can cause disease in humans or animals. **Exempt dealings** usually do not require approval from the national regulator. GMOs that pose a low risk, if certain management practices are complied with, are classified as **notifiable low risk dealings,** which means that researchers must notify the applicable regulatory agency. The final classification is for any uses of GMOs that do not meet the previous criteria. These are known as **licensed dealings** and include cloning any genes that code for vertebrate toxins or use hosts that are capable of causing disease in humans. Licensed dealings require the approval of the national regulator.

Work with exempt GMOs does not need to be carried out in certified laboratories. All other work must be carried out in a Physical Containment level 1 (PC1) or Physical Containment level 2 (PC2) laboratory. GMOs classified as low risk include knockout mice (a genetically modified mouse which researchers have inactivated, or 'knocked out' an existing gene by replacing it or disrupting it with an external segment of DNA), as long as the modification does not confer an advantage to the animal or it does not secrete any infectious agents. If a laboratory strain is used that is not covered by exempt dealings or if the inserted DNA could code for a pathogen-encoding gene it must be carried out in a PC2 laboratory.

The approaches taken by governments to assess and manage the risks associated with the use of genetic engineering technology and the development and release of GMOs vary from country to country, with some of the most marked differences occurring between the United States and Europe. The U.S.' regulatory policy is governed by the *Coordinated Framework for Regulation of Biotechnology*. The policy has three tenets: (1) U.S. policy would focus on the product of genetic modification (GM) techniques, not the process itself, (2) only regulation grounded in verifiable scientific risks would be tolerated, and (3) GM products are on a continuum with existing products and, therefore, existing statutes are sufficient to review the products. In contrast, the European Union enacted regulatory laws in 2003 that provided possibly the most stringent GMO regulations in the world. All GMOs, along with irradiated food, are considered

'new food' and subject to extensive, case-by-case, science-based evaluation by the European Food Safety Authority.

3. Hierarchy of responsibility for GMO research and contracts at Bigelow Laboratory

Trustees, Chair and Vice-Chair of the Board: overall responsibility for the fiduciary, legal and reputational activities of the laboratory. The Board may delegate its scientific review of GMO work to the ORCA Subcommittee, and the legal/reputational considerations to the Governance Committee.

Executive Director: delegated responsibility from the Board to monitor GMO research, ensure that policy and procedures are followed, receive advice from the Institutional Biosafety Committee, and review and sign-off on ALL non-exempt proposals and contracts involving GMO work or collaboration with organizations conducting GMO studies.

Institutional Biosafety Committee: review all GMO proposals currently chaired by Dr. Mike Lomas (see below), and makes recommendations about the appropriate category classification of a given procedure and specifies whether further review may be required. Decisions on non-exempt processes revert to the Executive Director for his consideration. The NIH guidelines define the IBC as: "The Institutional Biosafety Committee must be comprised of no fewer than five members so selected that they collectively have experience and expertise in recombinant or synthetic nucleic acid molecule technology and the capability to assess the safety of recombinant or synthetic nucleic acid molecule research and to identify any potential risk to public health or the environment. At least two members shall not be affiliated with the institution (apart from their membership on the Institutional Biosafety Committee) and who represent the interest of the surrounding community with respect to health and protection of the environment (e.g., officials of state or local public health or environmental protection agencies, members of other local governmental bodies, or persons active in medical, occupational health, or environmental concerns in the community)."

Principal Investigator: comply with the Bigelow Laboratory policies ensure that all of his/her staff members working on the project also comply with those policies, inform all his/her staff working on the project about the procedures that will be followed, inform the Director of Communications and Director of Research and Education of the work before commencement, act responsibly and work with all the responsible persons above to ensure safe, transparent and responsible use of our science.

4. Role of the Institutional Biosafety Committee and the Principal Investigator

Prior to the initiation of an experiment that involves GMOs, the Principal Investigator must submit a **registration document** to the Institutional Biosafety Committee, which contains the following information: (1) the source(s) of DNA; (2) the nature of the inserted DNA sequences; (3) the host(s) and vector(s) to be

used; (4) whether an attempt will be made to obtain expression of one or more foreign genes, and if so, the proteins that will be produced; and (5) the containment conditions that will be implemented as specified in the *Bigelow Laboratory GMO Policy Appendix 1,* and the NIH Guidelines.

The registration document shall be dated, signed by the Principal Investigator, and filed with the Institutional Biosafety Committee. The Institutional Biosafety Committee shall review and approve all experiments in this category prior to their initiation. Requests to decrease the level of containment specified for experiments in this category will be considered by Executive Director, and with reference to the NIH guidelines.

5. Role of the Executive Director and the Principal Investigator
The Executive Director will review all contracts submitted by external organizations involved in GMO work that propose to collaborate with or receive services from any PI or Core Laboratory at Bigelow Laboratory. The ED may seek advice from the Institutional Biosafety Committee under strict confidentiality, and will provide a written determination on the approval/ decline of the project for review by the Chair/Vice-Chair and PI. Contracts can only move forward with the ED's positive determination and signoff. All approved contracts will be signed by the ED, countersigned by the PI. The ED and PI will inform the Director of Communications on the general nature of the work, subject to full confidentiality.

6. Areas of GMO non-exempt research that will require further review by IBC (based on, but not exclusively, NIH Guidelines)

- The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine or agriculture (including the terrestrial and marine environment);
- Deliberate formation of recombinant or synthetic nucleic acid molecules containing genes for the biosynthesis of toxin molecules lethal for vertebrates at an LD_{50} of less than 100 nanograms per kilogram body weight;
- The deliberate transfer into human research participants of either recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules;
- DNA from Risk Group 3, 4 [*NIH definition*], or restricted organisms or cells known to be infected with these agents;
- Whole plants[4] regenerated from plant cells and tissue cultures that do not remain as axenic cultures;

[4] Herein plants include those species listed in the USDA PLANTS Database: USDA, NRCS. 2016. The PLANTS Database (http://plants.usda.gov, 5 February 2016). National Plant Data Team, Greensboro, NC 27401-4901 USA.

- Large scale experiments with GMOs (more than 10 liters of volume in a single culture vessel); and
- Deliberate introduction of genes coding for the biosynthesis of molecules that are toxic for vertebrates with an LD_{50} greater than 100 nanograms/kg but less than or equal to 100 micrograms/kg.

Note that PIs and the IBC cannot make the determination that a class of experiments other than the ones listed in NIH Guideline Section III-F-8, and FAQ:http://osp.od.nih.gov/sites/default/files/Experiments_that_are_Exempt_from_the_NIH_Guidelines.pdf **pose no significant risk.**

Bigelow Laboratory will also consider reputational risk and balance its responsibility to promote high quality, well-documented research and contracts in considering whether a particular GMO project should progress.

7. Operational procedures and containment practices
Bigelow Laboratory places a very high priority in ensuring that operational procedures and containment practices are fully maintained at all times. Procedures and practices are described in the accompanying appendices.

Bigelow | Laboratory for Ocean Sciences

Institutional Biosafety Committee (IBC)
Procedures for Exempt Experiments with GMOs

1. Exempt dealings with GMOs will be conducted in a laboratory that is a fully enclosable space bounded by walls, doors, windows, floors and ceilings. NOTE: The walls, doors, windows, floors and ceilings form the physical containment barrier around the area where exempt dealings with GMOs will be conducted.

2. Floors and benches in the laboratory should be cleanable, easily decontaminated and resistant to damage by the cleaning agents and/or disinfectants that will be used in the laboratory.

3. The laboratory should contain either a washbasin or some other means of decontaminating hands using approved biocidal handwash. NOTE: Decontamination of hands is considered an important means of preventing unintentional release of GMOs. Alternatives to wash basins, such as dispensers filled with decontaminant solutions, are considered suitable.

4. Specific precautions for mobile containment (e.g., double bagging cultures) is required when moving exempt GMOs from one laboratory to another through public spaces. This movement requires approval through the GMO registration form.

5. Access to the laboratory should be restricted to persons authorized to enter.

6. Dedicated “emergency only” exits should not be used except in emergencies.

7. Persons performing procedures with GMOs in the laboratory should wear protective clothing to protect the front part of the body from exposure to the GMOs.

8. Protective clothing should be removed and disposed of, or stored, before leaving the laboratory. NOTE: Consideration should be given to the provision of hooks or other storage for protective clothing.

9. Protective clothing contaminated or suspected to be contaminated with GMOs should be removed as soon as reasonably possible and decontaminated prior to reuse. Protective clothing that has not been contaminated with GMOs may be washed using normal laundry methods.

10. Precautions should be taken to minimize the production of aerosols where procedures involving GMOs are carried out on an open bench.

11. All cultures of GMOs must be clearly labeled. NOTE: Labeling assists the separation of GM work from non-GM work and enhances the control of GMOs within the laboratory.

12. Cultures of GMOs should be decontaminated prior to disposal by an acceptable and verifiable method. NOTE: If using the autoclaves to sterilize cultures, ensure that the autoclave is functioning properly (i.e., getting to the proper temperature and pressure). Verification of proper function should be done with a commercially available *Bacillus subtilus* spore test kit.

13. Liquid and solid wastes potentially containing GMOs should be decontaminated prior to disposal.

14. Work benches, surfaces and equipment where procedures involving GMOs have taken place should be decontaminated when the procedures are completed. NOTE: This is to minimize any persistence of GMOs inside the laboratory and minimize cross-contamination with any other work.

15. Any equipment that is, or may be, contaminated with GMOs should be decontaminated prior to being removed from the laboratory.

16. Decontamination can be achieved by any method effective in rendering the GMO non-viable, including autoclaving or other heat treatment; chemical treatment; or incineration. Within the seawater facility this may also include the use of UV light irradiation, followed by chemical bleaching, and a holding tank reservoir, before release to the environment.

17. A supply of disinfectant(s) effective against the GMOs used in the laboratory should be available in the laboratory for decontamination purposes. Containers of disinfectant(s), including any solutions for decontaminating hands, should be clearly labeled with the contents and, where necessary, the expiry date. Solutions should not be used after the expiry date.

18. All cultures of GMOs being stored inside the laboratory should be sealed during storage to prevent dissemination of the GMOs. NOTE: The type of containment necessary to prevent the GMOs from escaping will vary depending on the type of GMO being stored.

19. Persons who have been performing procedures with GMOs in the laboratory should decontaminate their hands before leaving the laboratory. NOTE: This may include the use of soap and water, if appropriate.

20. GMOs may be stored outside the laboratory in a storage unit (freezer, fridge, controlled temperature room or other container) provided that: (a) access to the storage unit is restricted or controlled to prevent unintentional release of GMOs into the environment and that the GMOs are stored in a labeled, sealed,

unbreakable primary container to prevent the escape or release of the GMO. In the case of GM organisms stored in the Building A Freezer Farm room, the appropriate freezer must be locked to restrict access.

21. If any spills of GMOs occur inside or outside the laboratory, the contaminated surfaces should be decontaminated as soon as reasonably possible, and notified to the Laboratory Safety Manager, the chair of the Institutional Biosafety Committee, and the Executive Director.

Bigelow | Laboratory for Ocean Sciences

Institutional Biosafety Committee (IBC)
Procedures for Limited non-Exempt Experiments with GMOs

1. Non-Exempt dealings with GMOs will be conducted in a fully enclosed laboratory.

2. Floors and benches in the laboratory must be cleanable, easily decontaminated and resistant to damage by the cleaning agents and/or disinfectants that will be used in the laboratory.

3. The laboratory must contain either a washbasin or some other means of decontaminating hands using approved biocidal handwash. NOTE: Decontamination of hands is considered an important means of preventing unintentional release of GMOs. Alternatives to wash basins, such as dispensers filled with decontaminant solutions, are considered suitable.

4. Non-exempt GMOs are not allowed to move from one laboratory to another through public spaces unless they are in redundant containers (e.g., double bagged, or double boxed) and the outermost containers is verified to be non-contaminated.

5. Access to the laboratory must be restricted to persons authorized to enter.

6. Dedicated “emergency only” exits must not be used except in emergencies.

7. Persons performing procedures with GMOs in the laboratory must wear protective clothing to protect the front part of the body from exposure to the GMOs.

8. Protective clothing must be removed and disposed of, or stored, before leaving the laboratory. NOTE: Consideration should be given to use of disposable laboratory coats or the provision of hooks or other storage system for protective clothing.

9. Protective clothing contaminated or suspected to be contaminated with GMOs must be removed as soon as reasonably possible and decontaminated prior to reuse by an verifiable and acceptable method (e.g., autoclave). Protective clothing that has not been contaminated with GMOs may be washed using normal laundry methods.

10. Precautions must be taken to minimize the production of aerosols where procedures involving GMOs are carried out on an open bench, e.g., use of a filtration hood appropriate for the task.

11. All cultures of GMOs must be labeled. NOTE: Labeling assists the separation of GM work from non-GM work and enhances the control of GMOs within the laboratory between exempt and non-exempt.

12. GMOs cultures and Liquid and solid wastes potentially containing GMOs must be decontaminated prior to disposal using a verifiable and appropriate method. NOTE: If using the autoclaves to sterilize cultures, ensure that the autoclave is functioning properly (i.e., getting to the proper temperature and pressure). Verification of proper function should be done with a commercially available *Bacillus subtilus* spore test kit.

13. Work benches, surfaces and equipment where procedures involving GMOs have taken place must be decontaminated when the procedures are completed. NOTE: This is to minimize any persistence of GMOs inside the laboratory and minimize cross-contamination with any other work.

14. Any equipment that is, or may be, contaminated with GMOs must be decontaminated prior to being removed from the laboratory. Travel to another laboratory for decontamination can only happen if items are in redundant containers (e.g., double bagged, or double boxed) and the outermost containers is verified to be non-contaminated.

15. Decontamination can be achieved by any method effective in rendering the GMO non-viable, including autoclaving or other heat treatment; chemical treatment (bleach); UV light sterilization; or incineration.

16. A supply of disinfectant(s) effective against the GMOs used in the laboratory must be available in the laboratory for decontamination purposes. Containers of disinfectant(s), including any solutions for decontaminating hands, must be clearly labeled with the contents and, where necessary, the expiry date. Solutions must not be used after the expiry date.

17. All cultures of GMOs being stored inside the laboratory must be sealed during storage to prevent dissemination of the GMOs. Non-exempt GMOs may not be stored outside the laboratory in which they are being used. NOTE: The type of containment necessary to prevent the GMOs from escaping will vary depending on the type of GMO being stored and must receiver prior approval.

18. Persons who have been performing procedures with GMOs in the laboratory must decontaminate their hands before leaving the laboratory. NOTE: This may include the use of soap and water, if appropriate.

19. If any spills of GMOs occur inside the laboratory, the contaminated surfaces must be decontaminated as soon as reasonably possible, and notified to the Laboratory Safety Manager, the chair of the Institutional Biosafety Committee, and the Executive Director.

Bigelow | Laboratory for Ocean Sciences

Institutional Biosafety Committee (IBC)
GMO Registration Document
(Completion of all sections required)

Bigelow Laboratory's policy is that all proposed research that will use recombinant and/or synthetic DNA methods must first be reported to the IBC committee via this registration document. Based upon NIH Guidelines there are several classifications of experiments defined by risk group and activity. Based upon Bigelow Laboratory's Policy on Genetic Modification, there are two relevant classifications, Exempt and Limited non-exempt.

Section 1. Statement of Exempt/non-exempt Status.
Exempt Experiments (please check the descriptor that best relates to your experiment)

- ❏ Those synthetic nucleic acids that: (1) can neither replicate nor generate nucleic acids that can replicate in any living cell (e.g., oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and (2) are not designed to integrate into DNA, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight. If a synthetic nucleic acid is deliberately transferred into one or more human research participants and meets the criteria of Section III-C, it is not exempt under this Section.
- ❏ Those that are not in organisms, cells, or viruses and that have not been modified or manipulated (e.g., encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes.
- ❏ Those that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.
- ❏ Those that consist entirely of nucleic acids from a prokaryotic host, including its indigenous plasmids or viruses when propagated only in that host (or a closely related strain of the same species), or when transferred to another host by well-established physiological means.
- ❏ Those that consist entirely of nucleic acids from a eukaryotic host including its chloroplasts, mitochondria, or plasmids (but excluding viruses) when propagated only in that host (or a closely related strain of the same species).
- ❏ Those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent. A list of such exchangers will be prepared and periodically revised by the NIH Director with advice of the RAC after appropriate notice and opportunity for public comment (see

Section IV-C-1-b-(1)-(c), *Major Actions*). See Appendices A-I through A-VI, *Exemptions under Section III-F-6--Sublists of Natural Exchangers*, for a list of natural exchangers that are exempt from the *NIH Guidelines*.

- ❏ Those genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA.

Non-exempt Experiments (please check the descriptor that best relates to your experiment). This list of descriptors is a subset of those presented in the NIH guidelines, based upon certain areas of research not believed to be relevant to Bigelow Laboratory at the time this document was last edited.

- ❏ Experiments in Which DNA From Risk Group 2, is Cloned into Nonpathogenic Prokaryotic or Lower Eukaryotic Host-Vector Systems
- ❏ Experiments Involving the Use of Infectious DNA or RNA Viruses or Defective DNA or RNA Viruses in the Presence of Helper Virus in Tissue Culture Systems
- ❏ Experiments Involving the Formation of Recombinant or Synthetic Nucleic Acid Molecules Containing No More than Two-Thirds of the Genome of any Eukaryotic Virus
- ❏ Experiments Involving Whole Plants. Experiments to selectively breed traits in plant lineages, genetically modify plants by recombinant or synthetic nucleic acid molecule methods, to use such plants for other experimental purposes (e.g., response to stress), to propagate such plants, or to use plants together with microorganisms or insects containing recombinant or synthetic nucleic acid molecules.
- ❏ Experiments Involving More than 10 Liters of Culture. The appropriate containment will be decided by the Institutional Biosafety Committee. Where appropriate, NIH Guidelines Appendix K, *Physical Containment for Large Scale Uses of Organisms Containing Recombinant or Synthetic Recombinant or synthetic nucleic acid Molecules*, shall be used.
- ❏ Any experiment using DNA from Risk Group 3 or 4, or restricted organisms or cells known to be infected with these agents. Risk Group 3 is defined as agents associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available. Risk Group is defined as agents likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available.

Section 2. Information on DNA and agent(s) to be used.

(1) the source(s) of DNA:_____

(2) the nature of the inserted DNA sequences: _____

(3) the host(s) and vector(s) to be used: _____

(4) whether an attempt will be made to obtain expression of one or more foreign genes, and if so, the proteins that will be produced:

_____

_____

Section 3. Experimental Methods for both Exempt and Limited non-exempt.
Describe in detail the experimental methods and bench top protocols that you will employ in your proposed research. Include any other information you think would be beneficial for the IBC to know in evaluating your request. If you have classified your research experiments as non-exempt, please also provide additional background information on the context of the experiments, the agents and DNA to be used, and why they are being conducted. *Use as much space as needed.*

Section 4. Experimental Containment and Waste Disposal Plan.
Describe in detail your plans for containment of your experimental agents, and disposal of any and all waste or byproducts (e.g., seawater used in growing your experimental organism) derived from your experiments. Bigelow Laboratory's Policy on Genetic Manipulation identifies a minimum set of procedures to follow for both exempt (Appendix C) and limited non-exempt (Appendix D) experiments. Please use these procedures as a starting point, i.e., cut and paste relevant procedures below, and add additional detail as needed.

Section 5. Signatures

This form is applicable to experiments proposed by both Bigelow SRSs and those external to the Institution. Please obtain the appropriate signatures before submitting the proposal or conducting the experiment.

Sign here if a Bigelow PI	Sign Here if an External PI
_____	_____
PI Name (Print):	PI Name (Print):
_____	_____
PI Name (Signature):	PI Name (Signature):
_____	_____
IBC Chair (Print):	Executive Director (Print):
_____	_____
IBC Chair (Signature):	Executive Director (Signature):

Bigelow | Laboratory for Ocean Sciences

Internal Biosafety Committee (IBC)
Approval Procedures

Responsibilities of the Internal Biosafety Committee (IBC).

1. The primary responsibilities of the IBC are two-fold: 1) to oversee the evaluation and approval process for proposals using recombinant DNA technologies, and 2) to ensure that researchers using such methods are following through with compliance with the Bigelow Laboratory Policy on Genetic Manipulation and the NIH guidelines on this topic, in particular those related to the health and safety of the environment and surrounding community.
2. The approval process has two paths, one for exempt experiments and one for non-exempt/external experiments, as detailed below in the "Proposal Approval Process" section. The IBC is responsible for shepherding the submitted applications through the process as detailed below.
3. The current version of the full NIH guidelines and FAQs can be found on the Bigelow storage drive \\storage.bigelow.org\Safety\forms\IBC\ and all SRS's are STRONGLY encouraged to read and be familiar with the documents contents.

Proposal Approval Process.

1. If your proposal will use recombinant or synthetic DNA techniques, regardless if it's a proposal or a letter of intent for a proposal, the lead SRS must complete a GMO Registration form \\storage.bigelow.org\Safety\forms\IBC\ and turn it in with their Bigelow PTS form to their respective Grants person. NOTE: PTS forms and thus the GMO Registration form are due **4 weeks before the proposal due date if the experimental work is considered exempt and 8 weeks before the proposal due date if the experimental work is considered non-exempt.** After SRO approval of the PTS, the Grants person will forward the GMO registration form to the IBC committee chair to mediate the approval process.
2. A properly completed GMO Registration form requires complete answers to all sections of the form. Providing detailed information at the outset will facilitate the processing of the request and prevent delays while additional information is gathered.
3. GMO Registration forms marked as exempt and submitted by a Bigelow SRS will be read and evaluated by the IBC. If there are questions about the type of the research or the methods to be used, the first course of

action in these instances will be to seek clarification from the lead SRS, but if questions or concerns remain, particularly if there are questions about the exempt/non-exempt status, then the application will be discussed with the Executive Director for evaluation and final approval.

4. All GMO registration forms originally marked as non-exempt or any GMO registration form that includes work with/or is led by a scientist external to Bigelow or GMO work to be done off the Bigelow Laboratory campus will be read and evaluated by the IBC committee. The IBC will provide a written recommendation to the Executive Director who will make the final decision based upon criteria as set out in the Bigelow Laboratory Policy on GMO work document. Note, that if the experiment is non-exempt, additional detail, beyond the 500-word brief description, will be required particularly on containment and incident response procedures as well as more detailed background information on the experimental design.
5. Upon approval of the IBC proposal form, the lead SRS will be notified and the form returned to the relevant SRO for additional handling/signatures that may be required.
6. As we all recognize the speed with which this research field advances, the onus is on the PI to report to the IBC any and all changes to the methodology previous approved before that work is to be conducted. This updated information must be conveyed in written form and will be appended to the original application. The updated methodology will go through the same procedural steps as defined above for approval.