BIORISK MANAGEMENT CASE STUDY: INTERNATIONAL GENETICALLY ENGINEERED MACHINE FOUNDATION

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SUMMARY

The Internationally Genetically Engineered Machine (iGEM) Foundation is an international organization that coordinates an annual, world-wide synthetic biology competition. Its risk management process includes multiple reviews during the competition cycle. iGEM's practices have evolved over time but have focused on enabling individuals from all levels of the synthetic biology community to participate in risk management. iGEM openly shares information about its practices, including publishing policies and risk assessments online and sharing lessons with the life science community. iGEM:

- considers an **extensive scope of risks,** including laboratory biosafety, dual-use research, environmental release, antimicrobial resistance, human experimentation, human subjects research, and animal use.
- **supports teams** through online resources, tools, online workshops, and tailored video content in the iGEM Academy.
- uses **standardized forms** to collect information about the safety and security practices of each team.
- draws on **in-house expertise and external consultants** for risk assessment, including both volunteers and paid professionals.
- **conducts annual reviews and updates** of its programs, including safety and security risk management processes.
- **rewards innovation** through safety-related grants and prizes.

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THE VISIBILITY INITIATIVE FOR RESPONSIBLE SCIENCE (VIRS)

The goal of the Visibility Initiative for Responsible Science (VIRS) is to share information about the value of biorisk management and how life science stakeholder organizations approach the issue. VIRS was conceived by a multi-stakeholder group during an April 2019 working group meeting of the Biosecurity Innovation and Risk Reduction Initiative (BIRRI) program of NTI Global Biological Policy & Programs. With support from NTI, Stanford University Bio Policy & Leadership in Society VIRS produced a set of Case Studies in biorisk management, and The Biorisk Management Casebook that provides cross-cutting insights into contemporary practices.

THE BIORISK MANAGEMENT CASE STUDIES

The Biorisk Management Case Studies describes biorisk management processes for a diverse set of life science research stakeholders. The collection serves to evaluate the feasibility and value of knowledge sharing among both organizations that have similar roles and those that have different roles in managing research. Case studies were developed in consultation with organizations through a combination of research based on public sources, interviews, and providing a template with guiding questions for organizations to complete directly. Additional analysis can be found in The Biorisk Management Casebook: Insights into Contemporary Practices[1] in this collection. Project Directors: Megan Palmer, Stanford University; Sam Weiss Evans, Harvard University.

DISCLAIMER

Biosafety and biosecurity risk management practices can change over time. This case study represents one point in time and is a sample of an evolving set of risk management practices. For additional information on current practices please contact the organization directly.

CONTRIBUTORS

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ORGANIZATION BACKGROUND

The iGEM Foundation is "an independent, non-profit organization **dedicated to the advancement of synthetic biology, education and competition, and the development of an open community and collaboration."**[1] In pursuit of these goals, the iGEM Foundation hosts the iGEM Competition, "an annual, worldwide synthetic biology event that gives students the opportunity to push the boundaries of synthetic biology by tackling everyday issues facing the world."[2]

iGEM's main program is the iGEM Competition, an annual, worldwide synthetic biology event aimed at undergraduate university students, as well as high school and graduate students. [...] Multidisciplinary teams work together to design, build, test, and measure a system of their own design using interchangeable biological parts and standard molecular biology techniques. iGEM teams work inside and outside the lab, creating sophisticated projects that strive to create a positive contribution to their communities and the world. —iGEM Competition website[3]

The culmination of the iGEM Competition is the Grand Jamboree, "an annual event that showcases work from the iGEM season."[3] At the Grand Jamboree, teams present their work through a promotional video, presentation, and website (referred to as a "wiki"). The projects are judged by a group of volunteers and awards are granted, including both non-competitive gold, silver, and bronze medals and competitive special awards (including one to reward excellence in applied biosafety and biosecurity and another to reward thinking broadly about the impact of the team's work).

The first iGEM competition was held in 2004 with 5 teams. Since then, iGEM has expanded to include more than 350 teams from around the world.[4] From the inception of the competition, iGEM projects have had the potential to raise safety and security concerns. In 2007, iGEM received financial support to attend to issues "beyond the lab" from Synberc, a multi-university research center in synthetic biology funded by the United States National Science Foundation (NSF) to advance the field of synthetic biology and promote its responsible development.[5] This dedicated funding stream sparked deeper consideration of safety and security concerns within the competition. The Safety and Security Committee (SSC) was formed in 2007 with full support from the four staff members at iGEM headquarters.

Initially, safety and security reviews were performed by the SSC and were somewhat informal in nature. However, in the early 2010s, iGEM encountered some particularly concerning projects that helped to spark improvements to iGEM safety screening processes. While there had been discussions about safety before then, iGEM implemented its first formalized safety screenings in 2011 and scaled up its screening processes soon after.[6] This scale-up process included outsourcing some aspects of project review that previously had been conducted by SSC volunteers to paid consultants.

iGEM understands that the way it deals with risks affects the broader synthetic biology community. If an iGEM participant were seriously hurt, or if there were a lab leak, there could be serious consequences for the competition. For example, teams or volunteers might choose not to participate and venues or funders could pull support. A high-profile incident could also damage public support for using synthetic biology to solve important local and global challenges. It could result in much greater scrutiny of, and the imposition of unnecessarily draconian restrictions on, synthetic biology research and development in academia and industry. These considerations helped guide the evolution of iGEM safety and security policies throughout the development of the competition.

iGEM has two concurrent threads of biorisk management, both managed by the Vice President for Respect and Responsibility: the **Safety and Security Committee** and the Human Practices Committee. The Safety and Security Committee considers biosafety and biosecurity risks that could occur over the course of a team's project, including dual-use information hazards. The **Human Practices Committee** invites iGEM participants (referred to as iGEMers) to think broadly about the impact of their work. A third committee, the **Responsible Conduct Committee,** can be brought in to adjudicate consequences for issues raised by the Safety and Security or Human Practices Committees as needed.

PROCESS

Scope of risks considered

iGEM considers a broad range of safety and security risks that encompass and extend beyond laboratory biosafety and work with pathogens. These include considerations related to dual use, environmental release, gene drives, antimicrobial resistance, animal use, human subjects research, and human experimentation. iGEM places strict prohibitions on certain types of research as outlined in their safety policies (Appendix A)[7]:

- Release of genetically modified organisms outside the lab
- Human experimentation
- Work with Risk Group 3 organisms
- Use of any biological materials from Risk Group 4 organisms

iGEM also maintains a "white list" of activities, organisms, and parts (e.g., genetic elements) that teams are explicitly allowed to use (Appendix B).[8] Teams must request explicit permission from iGEM to perform activities and to work with biological materials that are not covered by the white list. iGEM has made several modifications to the white list over time. For example, while the white list originally only included work with specific biological materials (organisms and parts), it was expanded in 2019 to include research activities. This change was intended to move toward more functional rather than taxonomic descriptions of risk, which enabled iGEM to better capture risks arising from technologies like gene drives. iGEM also added certain antimicrobial resistance-related work in 2017 in response to calls from the UN and WHO[9-11].

Examples of **activities that require advance permission** from iGEM include:

- Use of human samples
- Development of gene drives
- Increasing or conferring new resistance to antimicrobials
- Making hazardous biological agents more hazardous, enabling them to avoid diagnosis or detection, or creating novel hazardous biological agents
- Use of animals

Examples of **biological materials that require advance permission** from iGEM to use include:

- Organisms that require enhanced containment, including human, animal, and plant pathogens
- Organisms obtained outside the lab or from non-traditional suppliers
- Parts associated with virulence, pathogenicity, toxicity, or immunomodulation
- Parts derived from organisms in Risk Group 3 or listed by export control regimes, such as Australia Group[12]
- Parts that are likely to increase the potential for horizontal gene transfer
- Primary cells from multicellular organisms
- All multicellular organisms (except for C. elegans and several plant model species)
- CRISPR guide RNAs and other regulatory RNAs that target human genes

Overall sequence of steps

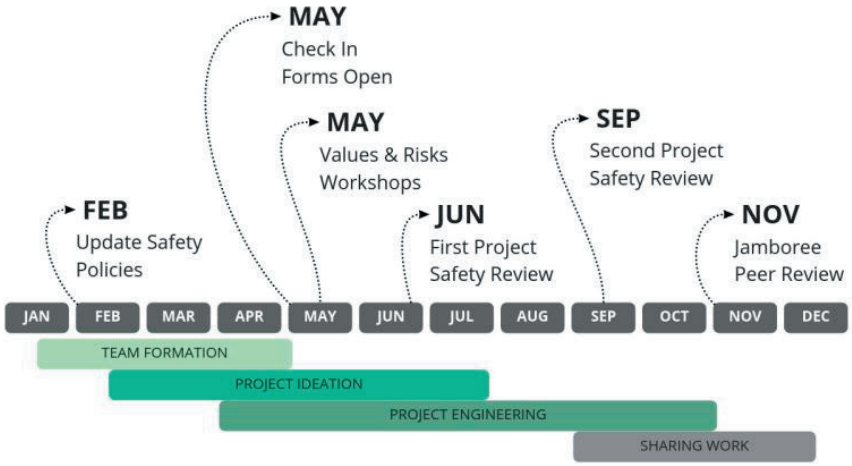

Figure 1: iGEM safety review timeline.

iGEM publishes safety rules and policies at the beginning of every competition cycle (see Appendix A).[7] These outline iGEM's expectations and positions with respect to a variety of safety and security issues. The rules apply to all teams. The policies are dependent on the project chosen by the team (e.g., not all teams will use animals but if they do, there is a policy they must follow). Adhering to the rules and policies is a requirement for participation.

FORMS

iGEM **uses three types of forms** that enable safety and security evaluations at various points in each project's lifecycle:

- All teams are required to submit a **Project Safety Form** (Appendix C).[13] Safety form submissions are reviewed twice over the course of an iGEM project: an initial review in June when many teams are finishing planning their work and entering the lab, and a final review in September when many teams are finishing in the lab and beginning to work on communicating their results. The September submission is formally submitted by the team's PI. It occurs late enough in the competition stage to capture new risks that may have emerged over the project's development, but it is early enough that it allows the Safety and Security Committee sufficient time to respond to any concerns before judging commences in November.
- **Check-In Forms** (Appendix D)[14] are required for teams pursuing projects that pose an elevated risk, as determined by iGEM (see iGEM Safety Policies, Appendix A6 and iGEM White List, Appendix B7). Teams may not start work on risky aspects of their projects until receiving approval from iGEM. Along with the white list (Appendix B7), Check-In Forms were introduced in 2014 in response to projects in 2011–2013 "in which teams worked with dangerous components before the safety screeners had an opportunity to act."[6] Check-In Forms can be submitted starting in May and remain open until judging is concluded as iGEM projects continue to evolve and new risks arise.
- **Animal Use Forms** are similar to Check-In Forms but allow teams to make a case to be allowed to use animals in their projects.[15]

For more information about these forms, see the Risk assessment section.

SAFETY AND SECURITY JUDGING

In addition to reviewing safety-related forms throughout the competition cycle, safety and security evaluations take place at the iGEM jamboree, where projects are evaluated for a Safety and Security award. Originally, judges nominated teams for this award based on their attention to safety and security in their projects and winners were selected by the Safety and Security Committee. However, iGEM is now transitioning to a system that more closely resembles that used for other iGEM awards where teams can self-nominate and the award is now intended to celebrate applied biosafety and biosecurity work. In a related effort, iGEM has started a grant program to provide funds for teams pursuing applied safety and security projects.[16] This change in emphasis underscores iGEM's stance that meeting safety and security standards should be mandatory and strives to elevate the importance of applied safety and security work.

At the jamboree, judges (and sometimes other iGEM participants) also proactively reach out to the Safety and Security Committee if they identify safety or security concerns that are not addressed by a team in their poster, talk, or website ("wiki"). iGEM employees on the Safety and Security Committee set up meetings with these teams and impose mitigation measures, which can range from requiring edits to the team's wiki to disqualification.

HUMAN PRACTICES JUDGING

Unlike Safety and Security, where teams are assessed at intermediate stages of their projects, Human Practices are evaluated at the end of the iGEM competition. iGEM defines Human Practices as "thinking deeply and creatively about whether a synthetic biology project is responsible and good for the world."[17] Teams are required to meet certain Human Practices standards to qualify for non-competitive medal awards (every team can obtain a medal if they meet the requirements). A key requirement is that teams' Human Practices work should impact how the team approaches other aspects of their project. The Human Practices Committee can be brought in by a judge to evaluate a team's wiki regarding the broader impacts of the team's work, which can touch on safety and security concerns.

RISK ASSESSMENT

All iGEM form templates and completed team forms are publicly available for all years of the competition. Forms are made public in part so that teams can understand how to fill them in well.

SAFETY FORMS

Safety Forms are initially submitted in June to identify risks early in the project. They are expected to take approximately 1–5 hours for the team to complete. This large time window derives from the fact that some fields of the form can often be copied from previous years (e.g., description of laboratory environment), whereas other fields may require more intensive research (e.g., identifying the risk group of the organisms from which each genetic part originated).

The form collects information about biosafety and biosecurity hazards associated with each team's project as well as the procedures and practices being used to manage risks identified. It also asks teams to consider risks associated with the project were it to be expanded upon or carried to real world application. These questions are designed to encourage teams to develop projects that are "safe by design" and to encourage them to consider the feasibility and safety of their projects in the real world. While these latter questions are primarily intended to promote critical reflection, if a team's future work could raise dual use concerns, iGEM may advise the team on how to communicate about their work given its potential for misuse.

Safety Forms are resubmitted in September. They are intended to capture what actually happened (rather than what the team thought they would do). These forms are identical in format but require the signature of the Principal Investigator.

Both initial and final Safety Form submissions are evaluated by external screeners that are biorisk management professionals certified by the International Federation of Biosafety Association (IFBA). These screeners categorize projects in one of three ways based on their level of risk: Proceed, Caution, Halt. Projects in the "caution" and "halt" categories are reviewed by iGEM Safety and Security employees, who work with the team directly to resolve simple issues and forward more substantive cases to the Safety and Security Committee.

For an example safety form, see Appendix C[13]

CHECK-IN FORMS

The majority of teams pursue projects covered by the white list of explicitly allowed experiments and materials. Teams that pursue projects where aspects of their work are not covered by the white list must submit Check-In Forms so that the iGEM Safety and Security Committee can review their proposed research activities. Examples of common activities requiring a Check-In Form include work with organisms requiring Biosafety Level 2 containment, virulence factors, toxin-encoding genes, plants, or animals. These forms are expected to take approximately 1–3 hours for the team to complete. For proposed activities that are unlikely to be approved (for example, those explicitly banned by the competition) or where a form covers an activity, organism or part covered by the competition white list, iGEM employees contact the team directly and request they make changes. For activities that do require prior approval, iGEM employees provide a summary of each form to the Safety and Security Committee, who can also access the full form. The Safety and Security Committee has 5-7 days to respond if it objects to the team's proposal, otherwise teams are allowed to proceed with the work detailed in the form (silence procedure).

For an example Check-In Form, see Appendix D[14]

RISK MITIGATION

Safety policies are explicitly described on the iGEM website (Appendix A),[7] **and adherence to these policies is required for participation in the competition.** Misunderstandings between the iGEM Safety and Security Committee and an iGEM team are usually resolved through discussion. If a team feels the Safety and Security Committee made an incorrect decision, it can appeal to the Responsible Conduct Committee, which can overturn decisions made by the Safety and Security Committee. The Responsible Conduct Committee also reviews any major punishments (such as disqualifications) recommended by the Safety and Security Committee.

During the early stages of the project, risks are predominantly identified through Check-In Forms, initial Safety Forms, and risk-related workshops. In most cases the following types of mitigations are recommended:

- Complete safety training
- Address issues that can be fixed without radical changes to the project design (e.g., use different personal protective equipment, outline procedural risks)

- Fill out a Check-In Form or Animal Use Form (if required based on iGEM policies)
- Fill out a Safety Form (if this form is incomplete or missing)
- For examples of how iGEM has approached risk mitigation for a selection of projects, see Appendix E.

Screeners of Safety Forms can also flag concerns around proposed environmental release, which is currently prohibited by iGEM, and dual-use research of concern, including recommending that teams attend a dual-use research of concern workshop. Finally, iGEM can prohibit teams from conducting research that violates iGEM policies within the context of the competition. Teams that do not follow iGEM policies can be subject to sanctions as described below.

If a team carries out work inconsistent with iGEM's rules and policies, this work can be excluded from judging and removed from its wiki. In more serious cases, iGEM can also disqualify teams for failing to comply with its policies; disqualification decisions typically involve both the Safety and Security Committee and Responsible Conduct Committee. If warranted, iGEM can also report the team to its institution, national regulators, or in extreme cases, to law enforcement.

EXPERTISE REQUIRED

iGEM uses a combination of paid, external screeners, in-house experts, and volunteer consultants to evaluate projects for safety and security concerns.

iGEM Safety Forms are reviewed by screeners certified by the International Federation of Biosafety Association (IFBA). Originally these forms were reviewed by iGEM staff and volunteers, but iGEM changed to an external model after the review process became too burdensome to be completed on an all-volunteer basis and when a funder provided resources to enable paid external evaluations. There are approximately six screeners who each review 50–60 projects. iGEM estimates each form takes 30 minutes to review. Teams are matched to screeners from their own regions to account for regional differences in norms and rules. For example, different organisms can belong to different risk groups in different countries depending on whether the pathogens are endemic. In addition to lessening the workload of the iGEM Safety and Security Committee, these screeners provide external validation for iGEM review processes.

The iGEM Safety and Security Committee consists of individuals with a wide range of expertise, including biosafety officers, former weapons inspectors, practicing researchers, public health officials, and science, technology, and society studies scholars. Membership on the committee is by invitation only. When recruiting new members, iGEM prioritizes individuals who can provide complementary technical and geographic expertise.

FEEDBACK & IMPACT

iGEM screens hundreds of projects every year, which is likely more than what a typical Institutional Biosafety Committee would review. **This large sample size of projects, coupled with the small size and flexibility of the iGEM Foundation, enables iGEM to identify security concerns and modify its processes year-by-year.**

iGEM tracks data related to safety and security through an end-of-year report, which includes information about how many teams were flagged for further review, the reasons given for safety and security reviews, and overall trends in different areas of concern. To facilitate this analysis going forward, iGEM seeks to develop more quantitative and categorical metrics (e.g., severity rating for Check-In Forms, categories of hazards) rather than relying on qualitative data alone. In the future, iGEM would also like to develop metrics to assess the quality of "safety thinking" of teams in the competition. This could include comparing the number of high-quality applications submitted for the safety grant program to the total number of participating teams.[16]

iGEM reviews its procedures in January and February of every year, including updating the white list and all forms. These forms are updated based on issues raised during the prior year. For example, past updates have addressed unnecessary Check-In Forms and teams pursuing projects in ambiguous policy areas (e.g., gene drives). iGEM evaluates the success of these updates by determining whether similar concerns are raised year-over-year or whether past issues appear to have been resolved.

iGEM employees draft a list of recommended policy changes, which are provided to the rest of the Safety and Security Committee for comments. The committee reviews any edge cases and discusses them as a group. For example, in 2017, iGEM added antimicrobial resistance-related parts to the list of biological materials requiring pre-approval (see iGEM White List, Appendix B[8]). This addition was prompted by WHO and UN initiatives related to antimicrobial resistance.[9-11] However, this change in policies sparked a debate. Through discussions, the committee refined iGEM

policies to enable iGEM to identify projects that could contribute to the spread of antimicrobial resistance without requiring every team working with common antibiotic resistance markers to submit its project for review.

Given the large number of projects iGEM reviews, iGEM has experienced difficulties with turnaround times for Check-In Forms, which are designed to be reviewed quickly (less than three weeks) so teams know whether they can proceed with their proposed work. While the check-in process is designed to be fast and lightweight, these forms tend to be submitted in batches near other safety-related deadlines, which can create backlogs.

SHARING

To help teams succeed in the competition, iGEM provides extensive information about Safety and Security policies and steps required for receiving (non-competitive) medals and (competitive) awards on their website. All of iGEM's form templates and completed team forms are also publicly available for all years so that teams have examples to work from while completing the forms themselves.

iGEM also shares their work in international fora, including international working groups, side events at the Biological Weapons Convention, and academic publications. These publications include:

- McNamara J, Lightfoot SB, Drinkwater K, Appleton E, Oye K. Designing Safety Policies to Meet Evolving Needs: iGEM as a Testbed for Proactive and Adaptive Risk Management. *ACS Synthetic Biology.* 2014;3(12):983-985. doi:10.1021/sb500058e[6]
- Millett P, Binz T, Evans SW, Kuiken T, Oye K, Palmer MJ, van der Vlugt C, Yambao K, Yu S. Developing a Comprehensive, Adaptive, and International Biosafety and Biosecurity Program for Advanced Biotechnology: The iGEM Experience. *Applied Biosafety.* 2019; 24:2:64-71. doi:10.1177/1535676019838075[18]
- Millett P, Isaac CR, Rais I, Rutten P. The synthetic-biology challenges for biosecurity: examples from iGEM. *The Nonproliferation Review.* 2021. doi:10.1080/10736700.2020.1866884[19]
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iGEM has also started to develop a set of lessons learned and statistics at the conclusion of each competition year. This information is distributed to others upon request. iGEM hopes to serve as a convening space for discussions related to responsibility and safety, including through events that iGEM hosts as part of its annual Jamboree.

REFLECTIONS

iGEM's approach has been to collect large amounts of information to identify a maximum number of safety and security concerns. By having a simple (and mandatory) process, iGEM may be able to more easily identify and engage with safety and security edge cases than other organizations. In other organizations, the process of obtaining permission to do some types of research can be quite burdensome (e.g., dual-use research of concern). In these cases, the approval process itself acts as a barrier, leading fewer researchers to seek approval for edge-case work and thus fewer opportunities for these organizations to address ambiguous policy areas. **Organizations interested in engaging with edge cases could benefit from adopting simple review processes where most research projects are approved.** However, organizations would also need to carefully consider any resulting liability.

Given the large amounts of information collected, iGEM also devotes considerable time to screening projects. Other competitions could consider limiting the scope of work for the projects that they consider to limit the number of risks that might arise. For example, other competitions could focus exclusively on cell-free systems, which would eliminate certain risks associated with working with living organisms.

Finally, **iGEM benefits from embracing flexibility.** Synthetic biology evolves every year; so do iGEM policies.

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APPENDIX A:
IGEM SAFETY POLICIES INTRODUCTION (2022)

Reprinted from https://responsibility.igem.org/safety-policies/introduction

Safety Policies provide further clarification on the use of specific technologies in the iGEM Competition.

- **Release Beyond Containment:** You cannot release or deploy any genetically modified organisms outside the lab. You must check in before bringing any product of synthetic biology outside of the lab. Review this policy
- **White List:** You must check in before beginning experiments with any organism, part, or activity that is not on the White List. Review this policy
- **Human Experimentation:** Testing your project on humans (including yourselves) is strictly prohibited. You must check in before beginning any laboratory experiments involving humans or human samples (including but not limited to blood, DNA, other bodily specimens, and health or psychological outcomes). Review this policy
- **Animal Use:** You must check in and submit an Animal Use Form before beginning any experiments involving animals or animal samples. This includes vertebrates (e.g. rats, mice, guinea pigs, hamsters, amphibians, and fishes) and higher order invertebrates (e.g. cuttlefish, octopus, squid, lobster, bees, or American or German cockroaches). Review this policy
- **Human Subjects Research:** All human subjects research (e.g. surveys, interviews, public engagement) you carry out must be done in accordance with relevant laws and regulations, as well as any institutional rules or guidance. Review this policy
- **Gene Drives:** Gene drives are not allowed in iGEM projects without a special exception from the Safety & Security Committee. Review this policy
- **Antimicrobial Resistance:** You must check in before beginning experiments likely to increase the risk posed by antimicrobial resistance (e.g. by using novel resistance factors, adding known factors into new organisms, or using resistance factors not previously used in your facility). Review this policy
- **SARS-CoV-2:** Any work using live SARS-CoV-2 virus (the causative agent of COVID-19) must follow World Health Organization (WHO) guidance, in addition to all local and institutional rules. WHO guidance may be stricter than local safety rules. You must check in before beginning experiments with live SARS-CoV-2 or parts from SARS-CoV-2 . Review this policy
- **Environmental Samples:** As long as parts or organisms are not isolated from them, samples from the environment, the food industry, or other non-traditional suppliers may be used in your experiments. You must check in before using any parts organisms obtained from outside the lab or from non-traditional suppliers. Review this policy

APPENDIX B: IGEM WHITE LIST (2022)

Reprinted from https://responsibility.igem.org/guidance/white-list

This page provides the details of organisms, parts, and activities teams can use in iGEM, along with those which require approval from the Safety and Security Committee before they can be used. You must check in before beginning experiments with any organism, part, or activity that is not on the White List.

Organisms

Organisms on the White List can be used without being checked-in. Teams require permission in advance from the Safety and Security Committee to use all other organisms, such as the examples provided below (right column). Permission should be requested by completing a Check In Form before using an organism not on the White List.

WHITE LIST	NOT ON WHITE LIST—CHECK IN REQUIRED
• Risk Group 1 microorganisms, other than spore-forming fungi (For example: *E. coli* K-12, S. *cerevisiae, B. subtilis, Lactobacillus* spp.) (see guidance on risk groups)	• Spore-forming fungi (including from Risk Group 1) • All organisms that require enhanced containment (e.g. BSL2), such as those from Risk Group 2 or plant pathogens, or that otherwise pose a risk should they be released (see guidance on risk groups) • Any organisms obtained from outside the lab or from non-traditional / non-institutional suppliers
• Commercially available disarmed strains of plant pathogens commonly used to transfect plants (such as *Agrobacterium tumefaciens)*	• Wildtype strains of plant pathogens commonly used to transfect plants (such as *Agrobacterium tumefaciens*) • Other disarmed strains of plant pathogens intended to be used to transfect plants, including those prepared by an iGEM team
• Bacteriophages T2, T4, T7, M13, P1, ΦX174 (Phi X 174), and λ (Lambda), unless containing a virulence factor (see below) • Phagemids	• Other viruses and bacteriophages, **including SARS-CoV-2 virus**
• Human and primate cell lines that have been tested and certified free of known pathogens (such as MCF-7; consult your vendor about certification!) • Cell lines from plants, fungi, or animals that are not primates (such as CHO cells or plant cells)	• All primary isolated cells (that is, cells taken directly from the body of a multicellular organism) • All organisms isolated from an environmental sample
• *C. elegans* (nematodes) • *Physcomitrella patens, Arabidopsis* spp., *Nicotiana* spp.	• Other multicellular organisms (animals, plants, insects, etc.)
• Teams are responsible for ensuring that any use of a model organism is consistent with their local, institutional and national rules and regulations	• Additional permission is required from the Safety and Security Committee for the use of any vertebrates (e.g. rats, mice, guinea pigs, hamsters), or higher order invertebrates (e.g. cuttlefish, octopus, squid, lobster) in iGEM projects – see the Animal Use Policy page for more details.
	• Any organism not explicitly white listed

Parts

Parts on the White List can be used without being checked-in. Teams require permission in advance from the Safety and Security Committee to use all other parts, such as the examples provided below (right column). Permission should be requested by completing a Check In Form **before** using a part not on the White List.

WHITE LIST	NOT ON WHITE LIST—CHECK IN REQUIRED
• All Registry parts, except those with a Red Flag placed by the Safety Committee	• Registry parts that have a Red Flag. A complete list of parts with Red Flags can be found here.
• *Proteins or protein-coding genes from animals, plants, or Risk Group 1 / Risk Group 2 microorganisms, EXCEPT those in the list of dangerous categories*	• Proteins or protein-coding genes in the following dangerous categories: • Virulence factors (see FAQ below) • Factors that help pathogens evade or shut down the immune system • Factors that help pathogens halt the host's DNA/RNA replication, transcription, or translation • Factors that regulate the immune system, such as cytokines and interferons • Proteins that are toxic to humans, animals, or plants • Enzymes that produce a molecule that is toxic to humans, animals, or plants • Parts likely to increase potential for horizontal gene transfer, such as transferase
• Non-protein-coding parts in the following categories: • Promoters, RBSes, Terminators • Binding sites for transcriptional regulators, endonucleases, and other proteins that bind to DNA • Aptamers and catalytic RNAs • CRISPR guide RNAs, microRNAs, small interfering RNAs, and short hairpin RNAs that do not target human genes	• All other non-protein-coding parts or genes, including: • CRISPR guide RNAs, microRNAs, small interfering RNAs, and short hairpin RNAs that target human genes • Parts that encode non-proteinaceous toxins, such as bioactive peptides, non-protein amino acids, and other non-proteinaceous components harmful to humans, animals, or plants • Parts likely to increase potential for horizontal gene transfer, such as origin-of-transfer sequences
• Prions from non-mammalian organisms, such as yeast	• Prions from mammals, such as human PrP
	• Any part from a Risk Group 3 organism, regardless of its function
	• Any fragment of the SARS-CoV-2 virus
	• Any part containing any gene which could endow or enhance pathogenicity, or in itself or through its transcribed or translated products, represent a significant hazard to health from a human or animal bacterial or fungal pathogen or a plant pathogen listed by the Australia Group • Any part containing any gene from a human or animal viral pathogen listed by the Australia Group • Any part containing any gene which codes for a toxin listed by the Australia Group
	Any part not explicitly white listed

Activities

Activities on the White List can be carried out without being checked-in. Teams require permission in advance from the Safety and Security Committee some activities. Permission should be requested by completing a Check In Form before carrying out these experiments.

WHITE LIST	NOT ON WHITE LIST—CHECK IN REQUIRED
All activity, except those explicitly listed as requiring a check in	Conducting laboratory experiments using human samples, such as blood, DNA, other bodily specimens, and health or psychological outcomes, including from members of the team (Human experimentation policy)
	Working with animals or samples from animals (in iGEM, "animals" are vertebrates, like rats or fish, and higher-order invertebrates, like octopus and bees) (Animal use policy)
	• Experiments likely to increase the antimicrobial resistance of any human, animal, or plant pathogen. • Experiments making use of antimicrobial resistance factors not in common use in the host institution • Experiments intended to confer resistance for an antimicrobial not previously conferred to that organism (e.g., conferring vancomycin resistance to a bacteria that has never been made resistant in the past)
	Bringing a product of a genetically modified organism outside the lab (Release beyond containment policy)
	Experiments likely to bias the inheritance frequency of a genetic marker in an organism's progeny, such as through the creation of a gene drive.
	Experiments covered by the Antimicrobial resistance policy, such as: • Increasing the antimicrobial resistance of any human, animal, or plant pathogen • Creating novel antimicrobial resistance factors • Conferring a resistance to an antimicrobial not previously conferred to that organism (e.g., conferring vancomycin resistance to a bacteria that has never been made resistant in the past) • Making use of antimicrobial resistance factors not in common use in the host institution
	• Making a hazardous biological agent more hazardous, such as enhancing the virulence or transmissibility of a human, plant, or animal pathogen, or altering its host-range • Creating a novel hazardous biological agent, such as by rendering a non-pathogen virulent, or conferring the ability to damage or degrade important materials (such as electronics, plastics, etc.) • Making a biological agent or toxin more suitable for use as a weapon
	• Potentially disrupting immunity or immune function • Potentially rendering a vaccine ineffective • Potentially enabling a hazardous biological agent to evade common diagnostic or detection tools

APPENDIX C: IGEM SAFETY FORM (2022)

Reprinted from https://responsibility.igem.org/safety-forms/project-safety

WHO FROM YOUR TEAM SHOULD BE CONTACTED ABOUT THIS FORM?

Team Member Name

Contact Email

Following iGEM's rules and policies

1. **Are you planning to do any of the following activities, which are prohibited in the competition? Check all that apply.**

   If yes, STOP. Contact the Safety and Security Committee for advice by at safety [AT] igem [DOT] org.

   - Using organisms from Risk Group 3 or 4
   - Using parts from an organism in Risk Group 4
   - Releasing or deploying a genetically modified organism outside the lab
   - Testing your product on humans (including yourselves)
   - No, we are not planning to do any prohibited activities

2. **Please read over iGEM's White List. Will your team use any organisms or parts not on the whitelist, or do any activities not on the whitelist? Check all that apply.**

   BEFORE you begin any work not covered by the white list, your team must submit a Check In Form to the iGEM Safety and Security Committee.

   - Yes, we are using organisms not on the White List
   - Yes, we are using parts not on the White List
   - Yes, we are doing any activities not on the White List
   - No, all our work is covered by the White List

3. **Are you planning to do any of the following activities that require advance permission from iGEM? Check all that apply.**

   According to iGEM's safety policies, certain kinds of work require your team to obtain advance permission from iGEM. Please submit a Check In Form (and, if applicable, an Animal Use Form) to gain permission before starting work.

   - Working with animals or samples from animals (in iGEM, "animals" are vertebrates, like rats or fish, and higher-order invertebrates, like octopus and bees) (Animal use policy)
   - Bringing a product of a genetically modified organism outside the lab (Release beyond containment policy)
   - Conducting laboratory experiments using human samples, such as blood, DNA, other bodily specimens, and health or psychological outcomes (Human experimentation policy)
   - Using parts or organisms obtained from anywhere other than a trusted commercial or institutional supplier (Environmental samples policy)
   - Biasing the inheritance frequency of a genetic marker in an organism's progeny, i.e. creating a gene drive (Gene drives policy)
   - Increasing risks from antimicrobial resistance, such as by using novel resistance factors (Antimicrobial resistance policy)
   - No, we are not doing any of the kinds of work outlined above

4. **Are you collecting any data about people, such as their opinions, quotations, medical history, gender, behavior, attitudes, or concerns?**

   For good reasons, many countries require formal approval for Human Subjects Research, as well as consent procedures for participants. You may need formal permission from a Research Ethics Committee, Institutional Research Board, or equivalent. Remember compliance with relevant laws and regulations is a requirement for participation in iGEM.

   - Yes, and we have obtained formal / institutional approval for our work (or will obtain it before starting data collection)
   - Yes, and we have confirmed that relevant laws, regulations, and institutional rules do not require us to get formal approval
   - Yes, but we're unsure if we need formal approval (please read the human subjects research policy)
   - No, we are not doing surveys, interviews, or other human subjects research

5. **Please upload a photo or two of your lab showing the relevant safety features.**

   Files can be uploaded at uploads.igem.org. If your project does not involve lab work and thus your team has no plans to access lab space, please note this.

6. **What is the biosafety level of your work space?**

   If you are working in a biosafety cabinet it may be a biosafety level 2 space (then select Level 2), but biosafety cabinets are sometimes also used in a biosafety level 1 laboratory to provide a sterile work space (then select Level 1). If in any doubt, please discuss this with a biosafety professional or your instructors, supervisors or lab techs to make sure you understand how the equipment you use helps to manage risks. See also the guidance on risk groups.

   ○ Not applicable as we have no lab component
   ○ Level 1 – standard microbiological lab
   ○ Level 2 – moderate containment
   ○ Level 3 – high containment
   ○ Level 4 – **extremely high containment**
   ○ We have several different lab spaces with different biosafety Levels. Please describe:
   Please describe your different lab spaces
   ○ Other
   Please describe your other biosafety level

7. **Which work areas will you use / are you using to handle biological materials? Check all that apply.**

   Please check all the containment provisions you are using.

   ○ No lab work (e.g. software project)
   ○ Open bench
   ○ Biosafety cabinet *(Note: there are important differences between biosafety cabinets and laminar flow hoods / clean benches. iGEM encourages the use of biosafety cabinets but discourages the use of laminar flow hoods or clean benches. This Factsheet from the University of Michigan helps explain the differences.)*
   ○ Specialist greenhouse
   ○ Specialist animal house
   ○ Specialist insect facility
   ○ Chemical fume hood (Note: this is designed to manage risks from hazardous chemicals. It is different from a biological safety cabinet designed to manage risks from hazardous biological agents and a clean bench or laminar flow hood designed to prevent contamination.)
   ○ Unknown
   Please describe why your work areas are unknown
   ○ Other
   Please describe your other work areas

About your project

8. **Describe the goal of your project: what is your engineered organism (or other synthetic biology product, system, or tool) supposed to do?**

   Even though your project might change, please describe the main project idea you are working on right now, including specific technical details. See the example answers for help.

   Bad example answers: (not enough detail)

   - We are engineering E. coli to cure liver cancer.
   - Climate change is a very important problem. Our algae will reduce CO2 emissions and fight climate change.

   Good example answers:

   - Our bacteria will be engineered to interact with human cells. They will detect tumor cells that express biomarkers for liver cancer. They will use invasin to enter the tumor cells, and then secrete apoptin to kill the tumor cells.
   - Our algae will receive gases high in CO2. We will increase their expression of Photosystem II proteins to make them absorb more CO2 from the gas.

9. **Which whole organisms, including viruses and cell lines, will you engineer in your project? Check all that apply.**

   These would be the organism(s) in which you are planning to put your parts or which you are modifying in your project.

   - Escherichia coli *(give all strains you are using, e.g. "DH5-alpha, BL21")*
     Please list strains
   - Saccharomyces cerevisiae (Yeast)
   - Lactobacillus spp.
   - Bacillus subtilis
   - Others *(give genus, species, and strain, e.g. "Vibrio natriegens ATCC14048", "Adeno-Associated dependoparvovirus B (AAV 5)")*
     Please list other organisms
   - Not engineering any organisms *(please comment)*
     Please comment on not engineering organisms

10. **Will you use any other organisms in your project?**
    For example, without engineering an organism directly, you might plan to extract RNA or DNA from the organism, or test your product on it.
    List organisms, including genus, species, and strain

11. **As part of your project, are you planning to make / have made new parts or substantively changed existing parts in the Registry?**

    ○ Yes

    ○ No, our project will only use genetic parts that are already in the registry

12. **Could any of your parts be hazardous on their own and/or in the context of your project?**

    - Parts that are hazardous on their own (e.g. a protein toxin, an enzyme that synthesizes a dangerous chemical)
    - Parts that have a hazardous function in their parent organism, but that might not be hazardous when used in your project (e.g. a virulence factor that helps a virus get into cells)
    - Parts with no hazardous function in their parent organism, but that might be hazardous when used in your project (e.g. quorum-sensing circuit that triggers release of an insecticide)
    - Other hazards
    - None of our parts could be hazardous

    If you identified any hazards above, describe them here. It may also be helpful to identify how you will acquire a part (e.g. PCR isolation, gene synthesis company).

13. What experiments will you do with your organisms and parts?

Please explain briefly. We are particularly keen to understand the boundaries or scope of your project. You should include the names of species / cell lines / strains. You should include experiments involving parts taken from other organisms, even if they are being synthesized rather than isolated from nature – you need not include any parts already in the registry.

Example answers

- Our bacteria is meant to live on plant leaves, so we will test them on tobacco *(Nicotiana benthamiana)* in a lab greenhouse.
- We want to use a protein from ants, but its sequence is unknown. So we will capture ants *(Camponotus spp.)* to extract DNA and RNA to find the sequence of the protein we want.
- Our bacteria need to interact with human cells for a medical application. We will test them in human cell culture using the HEK293 cell line.
- We are interested in a RNA-binding protein expressed in *Kluyveromyces lactis.* We have found the sequence in a paper and will have it synthesized by a commercial provider.
- Our project will not involve experiments with organisms or parts. We will run digital directed evolution experiments to identify a candidate receptor binding protein for our fungicide.

14. What kinds of chemicals are you using in your project?

- Heavy metals
- Carcinogens
- Mutagens
- Highly flammable chemicals
- Acids and corrosive chemicals
- Other controlled chemicals (e.g. explosives, psychoactives)
- Other hazardous chemicals
- Not using any hazardous chemicals

If you selected any of the hazardous kinds of chemicals above, please list the specific chemicals you are using.

Identifying project risks

15. What hazards are presented by the organisms, parts, chemicals, or experiments you described in Part 2? Check all that apply.

This question is about possible hazards present during the iGEM competition and/or while you are working in your lab space. We know you will likely be taking actions to minimize the risk that any of these hazards result in harm to your team, your colleagues, or your community.

- Human health or safety hazards *(e.g. from pathogens, hazardous chemicals)*
- Environmental hazards *(e.g. from organisms that get out the lab, such as potentially invasive species)*
- Dual-use hazards *(e.g. from misuse of knowledge you create)*
- Other hazards to team members or colleagues in the laboratory
- Other hazards beyond the laboratory
- No hazards

Please list the of specific hazards that caused you to check off the categories above. Describe in detail what aspect of your project presents each hazard.

16. **For each of the hazards you identified in the previous question, please give 1-3 sentences describing how harm could occur.**

For most hazards, this will involve accidental exposure to a biological or chemical agent or accidental release of an agent, but we invite you to be creative and comprehensive in your answers.

Example answers

- Our team is using needles to transfer our *S. epidermidis* culture, and a team member could accidentally stick themselves with a needle through their gloves and become infected. *(exposure)*
- When preparing large amounts of culture, it's possible that spores could be inhaled, which could lead to irritation or allergies. *(exposure)*
- We need to mail samples between two labs in different cities. If we fail to package our samples properly, our bacteria, which is resistant to vancomycin, could leak out of the package. *(release)*
- Because we are making its cell wall more stable, our engineered bacteria may be resistant to standard disinfection protocols. *(release)*
- The plants we will test are not indigenous to the region, and could be invasive if we accidentally carry seeds out of the lab. *(release)*
- Our non-canonical amino acids might be used for genetic recoding by someone trying to subvert DNA synthesis screening algorithms *(dual-use)*

Anticipating future risks

17. **Imagine that, in the future, your project was fully developed into a real product that real people could use. How would people use it? Check all that apply.**

Note: we understand that a real world use of your project might require doing experiments that would not be allowed during the competition, like releasing modified organisms into the environment.

- Our project is foundational / we do not have a specific real-world application in mind *(e.g. library of standardized promoters, system for communication between cells)*
- Only digital or non-biological products *(e.g. software to model directed evolution experiments, ethical and policy recommendations)*
- Only in the lab *(e.g. reporter strain for measuring the strength of promoters)*
- In a factory or other industrial manufacturing context *(e.g. cells that make a flavor chemical for food, cells that make biofuel)*
- In a consumer product that ordinary people buy *(e.g. cells that clean your clothes, bread made with engineered yeast)*
- In agriculture / on a farm *(e.g. cells that guard against pests, engineered rice plants, cells that promote growth of crop plants)*
- In a small enclosed device *(e.g. a bio-sensing strip with cells that detect arsenic, a paper-based cell-free diagnostic)*
- In the natural environment *(e.g. cells that remove pollution from lakes, engineered forest trees that can resist drought)*
- To be used in the human body, or in food *(e.g. anti-cancer bacteria, bread made with engineered yeast, engineered rice plants)*
- Other *(e.g. bacteria that live on Mars)*

Please describe the other future use

Please describe how your project would be used in the real world.

18. **If you were permitted, would the continued development of your project require release beyond containment?**

A definition of release beyond containment may be found in the relevant safety policy.

- ○ Yes, open release in the environment *(e.g. environmental bioremediation)*
- ○ Yes, release into a human or animal body *(e.g. living therapeutic)*
- ○ Yes, semi-contained release *(e.g. cell-based biosensor in a small device)*
- ○ Yes, release to a non-laboratory contained environment *(e.g.e.g. wastewater treatment plant)*
- ○ Yes, release of a product of synthetic biology, but not any living organisms *(e.g. biosynthetic fragrance, cell-free diagnostic)*
- ○ No, the future development of my project would not require release beyond containment

If yes, please briefly (1–3 sentences) describe what experiments, tests, or final uses would need to take place outside of laboratory containment. Include any institutional approval processes or national regulations that you are aware you would need to comply with.

19. **Have people on your team had a conversation (within your team or with someone outside the team) about how any of the bad outcomes below might relate to your project? Check all that apply.**

- Harm to human health and safety *(e.g. from pathogens, altered immune function)*
- Harm to agricultural animals, crops, or domesticated animals *(e.g., from pathogens, ecological disturbances)*
- Harm to materials, equipment, and infrastructure *(e.g. from degrading important materials)*
- Harm to the environment, including wild plants and animals *(e.g. from horizontal gene transfer, out-competing non-engineered organisms)*
- Reducing global, national or health security *(e.g. from disabling medical countermeasures, making it easier to do harm with biology)*
- Creating or reinforcing of social inequities *(e.g. from engineering a technology that disproportionately benefits an already-advantaged group)*
- Breaking norms about engineering biology *(e.g. from engineering an organism that is considered unethical to engineer)*

20. **Considering the future use(s) and conversations from the previous questions, do you think your project could potentially lead to any of the bad outcomes listed below? Check all the appropriate boxes and expand in the comments section.**

The possibility of a bad outcome does not mean your project is bad; virtually all modern biotechnology presents some risk. Being a responsible synthetic biologist requires you to think about how to manage risks to ensure your project has a positive impact as it enters the real world.

- Harm to human health and safety *(e.g. from pathogens, altered immune function)*
- Harm to agricultural animals, crops, or domesticated animals *(e.g., from pathogens, ecological disturbances)*
- Harm to materials, equipment, and infrastructure *(e.g. from degrading important materials)*
- Harm to the environment, including wild plants and animals *(e.g. from horizontal gene transfer, out-competing non-engineered organisms)*
- Reducing global, national or health security *(e.g. from disabling medical countermeasures, making it easier to do harm with biology)*
- Creating or reinforcing of social inequities *(e.g. from engineering a technology that disproportionately benefits an already-advantaged group)*
- Breaking norms about engineering biology *(e.g. from engineering an organism that is considered unethical to engineer)*
- Other
  If other, please describe
- Project could not lead to any bad outcomes

21. **How might the bad outcomes that you identified in the previous question come to pass? Check all that apply.**

- Accidental exposure to a hazardous organism or chemical
- Accidental release of an engineered organism or part into the environment
- Combining the results of the project with other technologies
- Deliberate misuse by someone intending to cause harm
- Other unintended consequences
  If other, please describe
- No bad outcomes identified

22. **If your project were fully developed, could any of your engineered organisms or parts spread autonomously in the environment?**
Organisms or parts might enter the environment intentionally (e.g. in field trials) or accidentally.

- ○ Yes, autonomous environmental spread of one or more of our organisms or parts is possible
  Describe how this could happen
- ○ No, our engineered organisms or parts are unable to spread in the environment
  Describe why they are unable to spread
- ○ No, we use biocontainment strategies (e.g. kill switches, auxotrophy) to prevent spread (please briefly note these strategies and why you chose them)
  Describe these strategies and why you chose them
- ○ No, our project does not involve engineered organisms or parts
- ○ Other
  If other, please describe

Managing risks

23. **Who are the experts, other than your supervisor(s), supporting you in managing risks? If you discover a hazard or risk in your project, who would you go to for help?**

You might plan to seek help from institutional biosafety officers or others that have expertise with the experimental techniques, organisms, or parts involved in your project.

24. **What safety and security rules or guidance cover your work?**

In your country / region, what are the laws and regulations that govern biosafety or biosecurity in research laboratories? At your institution, what are the guidelines for laboratory biosafety and biosecurity? Please provide a link to these resources, or briefly describe them if you cannot find a link.

25. **Will your project need extra support or review to manage the risks you have identified above?**

By "extra", we mean support or review beyond what happens for every life sciences project at your institution.

- ○ Yes, at the iGEM project stage (e.g. from the iGEM safety and safety committee, bioethics advisors, institutional biosafety officers)
- ○ Yes, if our project were to be developed further for a real-world use after the iGEM project stage (e.g. regulatory review, assistance designing field trials)
- ○ No, the project does not need additional support or review.

26. Have your team members received any safety and/or security training?

For the purposes of iGEM, safety and security training covers the procedures and practices used to manage risks from accidents or deliberate misuse of your projects.

- ○ Yes, we have already received safety and/or security training.
- ○ We plan to receive safety and/or security training in the future.
  Please specify approximately when
- ○ We will not have safety or security training. *(Please explain in detail how team members will become aware of and learn how to manage risks in the absence of training. If training is not relevant because there is no lab component to your project, please note this.)*
  Please explain how you will learn to manage risks

27. Please select the topics that you learned about (or will learn about) in your safety and security training.

- Lab access and rules (e.g. appropriate clothing, eating and drinking)
- Responsible individuals (e.g. lab or departmental specialist or institutional biosafety officer)
- Differences between biosafety levels
- Biosafety equipment (e.g. biosafety cabinets)
- Good microbial technique
- Disinfection and sterilization
- Emergency procedures
- Rules for transporting samples between labs or shipping between institutions
- Physical biosecurity (e.g. tracking materials, access controls)
- Personnel biosecurity (e.g. watching for unusual behaviour)
- Data biosecurity / cyberbiosecurity (e.g. managing database access)
- Dual-use research and/or experiments of concern
- Chemical, fire and electrical safety
- We will not have safety and security training

†28. What laboratory biosafety and biosecurity measures are you using to manage the risks in your project?

This could include actions your team decided on or actions required by your advisors or institution. Select as many as are relevant.

- Accident reporting *(system to record any lab accidents)*
- Personal Protective Equipment / PPE *(wearing lab coats, gloves, eye protection, etc.)*
- Inventory controls *(tracking who has what physical materials and where the materials are)*
- Physical access controls *(controlling who can access your lab or storage spaces)*
- Data access controls *(controlling who can access computers or databases)*
- Lone Worker or Out of Hours policy *(procedures for working alone or at times when normal support is unavailable)*
- Medical surveillance *(finding out if you get sick because of an organism or chemical you used)*
- Waste management system *(such as decontaminating waste before it leaves your institution)*
- Additional containment *(such as working at a higher biosafety level)*
- Other risk management tools
  If other, please describe your measures

29. **What other actions have you taken to manage the risks in your project?**

This could include voluntary actions or actions required by your advisors or institution.

- Project-specific safety or security training *(e.g. training on handling certain organisms)*
- Participating in a safety workshop hosted by iGEM *(e.g. the Values and Risks workshop)*
- Other consulting with iGEM about managing risks *(e.g. submitting a check-in form, emailing a committee)*
- Consulting with other experts about managing risks *(e.g. an institutional biosafety officer)*
- Consulting with stakeholders about managing risks
- Evaluating countermeasures against your organism, parts, or other products *(e.g. efficacy of therapeutics, detection in case of environmental release)*
- Crafting a responsible communication plan *(e.g. redacting specific information, highlighting the biosafety measures used)*
- Modifying your experimental design or methodology *(e.g. using an attenuated strain, employing biocontainment measures)*
- Deciding not to do an activity *(e.g. deciding against animal use experiments, avoiding infection experiments with a plant native to your country)*
- Other risk management action

Please briefly describe how the risk management actions you checked above apply to your project.

30. **Overall, how will the actions you've taken, expert support, rules, training, and other procedures and practices you described help you to manage the risks in your project?**

Please provide a detailed answer. You might include more information on:

- The rules and guidance you identified
- The training you have had
- The equipment and spaces you had or will have access to
- Waste treatment / inactivation procedures
- Other procedures and protocols you will follow
- Please give details of how these will help you to manage the risks you have identified.

Sign-Off

31. **Is there anything else you would like us to know?**

This might be about risks associated with your project, how you are managing them, or your compliance with iGEM's safety and security rules and policies; above improvements you would like to see to our safety and security efforts; about anything that has not been sufficiently clear, or where additional guidance would be useful; and anything else you think would be relevant.

APPENDIX D: IGEM CHECK-IN FORM (2022)

Reprinted from https://responsibility.igem.org/safety-forms/check-in

Who from your team should be contacted about this form?

Team Member Name

Contact Email

Check In Description

What kind of Check In are you submitting?

- ○ Whole Organism
- ○ Part
- ○ Activity

How does this organism, part, or activity fit into your project goals?
In 1-3 sentences, please briefly describe how this organism, part, or activity fits into your overall project plan.

Why are you checking in this organism, part, or activity?
Choose the main reason you are submitting this form.

- ○ We saw that it's not on the White List
- ○ We saw it's required by one of the safety policies
- ○ We wanted extra guidance on biosafety and/or biosecurity
- ○ We were told to submit a Check In by the iGEM safety team
- ○ We were told to submit a Check In by one of our supervisors
- ○ Other (please comment)

  If other, please comment

Organism Description

What is the name of the organism you are checking in?
If possible, provide strain, e.g. "SARS-CoV-2, heat inactivated USA/GA-EHC-2811C/2021" or "laboratory mice (C57B6/J)". You may check in multiple organisms using a single form if your plans for managing the risks in your work with them are identical.

Organism name

What kind of organism are you checking in?
These categories are based on the White List guidance on organisms. Choose the main reason you are checking in this organism.

- ○ Human pathogen
- ○ Plant pathogen
- ○ Spore-forming fungi
- ○ Virus or bacteriophage
- ○ Primary isolated cells *(i.e. cells taken directly from the body of a multicellular organism)*
- ○ Other organism requiring enhanced containment *(e.g. other Risk Group 2 bacteria)*
- ○ Organism obtained from the environment / non-traditional supplier
- ○ Other organism (please describe)

  If other, please comment

What Risk Group is this organism?
See the guidance on risk groups.

- ○ Risk Group 1
- ○ Risk Group 2
- ○ Risk Group 3 – not allowed in iGEM!
- ○ Risk Group 4 – not allowed in iGEM!
- ○ This organism is not a microbe. It does not have a Risk Group.
- ○ Other
  If other, please comment
- ○ Unknown
  If unknown, please comment

Is the organism on the Australia Group List, the U.S. Select Agents and Toxins List, or national equivalents?

If Yes, please email safety [AT] igem [DOT] org. These organisms and their parts are restricted for international shipment.

- ○ Yes
- ○ No

How will you acquire this organism?

- ○ My institution *(e.g. supervisor, another lab, central store)*
- ○ Isolating from an environmental medium (e.g. soil, water)
- ○ Ordered from a commercial source (e.g. a culture collection, repository, or organism design company)
  If commercial source, please indicate which company
- ○ Other (please comment)
  If other, please comment

Part Description

What kind of part are you checking in?

These categories are based on the White List guidance on parts. Choose the main reason you are checking in this part.

- ○ Virulence factor
- ○ Part that encodes a toxin
- ○ Part from a human or animal pathogen listed by the Australia group
- ○ Registry part with a red flag
- ○ Part from a Risk Group 3 organism
- ○ Part obtained from the environment / non-traditional supplier
- ○ Other protein-coding gene not on the White List
  If other, please note why gene is not covered by White List
- ○ Other non-protein-coding gene not on the White List
  If other, please note why non-protein-coding gene is not covered by White List
- ○ Other part (please describe)
  If other, please comment

Is the part very similar to any parts already in the iGEM registry?

Please search the registry of standard biological parts and share links to any closely-related parts that you find. An example of a very similar part would be one that codes for the same protein but has been codon-optimized for a different organism.

What is the parent organism for this part?

- ○ Organism name *(give genus, species, and strain, e.g. "Vibrio natriegens ATCC14048")*
  Enter parent organism name
- ○ No parent organism *(e.g. part was designed in silico)*

What Risk Group is the parent organism?

See the guidance on risk groups.

- ○ Risk Group 1
- ○ Risk Group 2
- ○ Risk Group 3
- ○ Risk Group 4 – **not allowed in iGEM!**
- ○ The organism is not a microbe. It does not have a Risk Group.
- ○ Part has no parent organism
- ○ Other (please comment)
  If other, please comment
- ○ Unknown (please comment)
  If unknown, please comment

What is the natural function of this part in its parent organism?

If this is not a part taken from nature, please note this.

In what organism or cell-free system will you use this part?

For organisms, give genus, species, and strain, e.g. "E coli DH5-alpha".

Have you altered the part from its natural sequence, structure or function?

- ○ Yes *(please provide details, including intended changes to structure or function)*
  Describe how the part is altered
- ○ No

Could this part be hazardous on its own and/or in the context of your project?

- ○ Part is hazardous on its own *(e.g. a protein toxin, an enzyme that synthesizes a dangerous chemical)*
- ○ Part has a hazardous function in parent organism, but might not be hazardous when used in your project *(e.g. a virulence factor that helps a virus get into cells)*
- ○ Part has no hazardous function in parent organism, but might be hazardous when used in your project *(e.g. quorum-sensing circuit that triggers release of an insecticide)*
- ○ Other hazards
- ○ No hazards

  Please comment on any hazards you've identified. If you identified any hazards above, describe them here

Activity Description

What kind of activity are you checking in?

These categories are based on the White List guidance on activities. Choose the main reason you are checking in this activity.

- ○ Bringing a product of a genetically modified organism outside the lab (policy)
- ○ Conducting laboratory experiments using human samples, such as blood, DNA, other bodily specimens, and health or psychological outcomes (policy)
- ○ Increasing risks from antimicrobial resistance (policy)
- ○ Biasing the inheritance frequency of a genetic marker in an organism's progeny, e.g. creating a gene drive (policy)
- ○ Creating a novel hazardous biological agent
- ○ Making a hazardous biological agent more hazardous or more suitable for use as a weapon
- ○ Enabling a hazardous biological agent to evade common diagnostic or detection tools
- ○ Rendering a a vaccine ineffective
- ○ Other activity (please describe)
  If other, please comment

Please give a step-by-step description of the planned activity, such a detailed experimental protocol.

Identifying and managing risks

What risks have you identified from this organism, part, or activity?

Please discuss both the hazards you have identified and how they might be realized. For example, is the risk due to the potential accidental exposure or due to potential release? You should provide links to relevant supporting information, such as culture collection data sheets.

What measures have you put in place to manage the risks you have identified?

Please provide detail on how you are managing the risks identified in the question above.

Are there alternative ways to achieve your project goals that would present less risk?

Please discuss your rationale for needing to work with this organism, part, or activity. If you do not believe it poses elevated risks, you may note that here as your rationale.

Is there anything else you want to tell us?

You can use this space to provide more details about risks from your project and how you are managing them. We also welcome your ideas on how we might improve how we manage risks covered by this form, or your feedback on the form itself.

APPENDIX E: IGEM RISK MITIGATION EXAMPLES

- **Changed experimental design:** One iGEM team wanted to test their engineered melanin-producing yeast in a stratospheric probe. However, the Safety and Security Committee had concerns about the potential environmental release of genetically modified organisms and the legal ambiguity surrounding activities in the stratosphere. After consultation with the Safety and Security Committee, the team changed their experimental design and instead ran an experiment where they launched wild-type yeast in a probe, with different melanin added to the media.
- **Changed project design:** One iGEM team was working on a project to recycle electronics, but they realized that their system had the potential to be used offensively to digest working electronics. The team decided instead to refocus on extracting metal ions from pit water rather than dissolving electronics directly, and later engaged in discussions with the Safety and Security Committee about their project.
- **Changed containment plans:** One team wished to conduct experiments with mosquitoes and submitted a Check-In Form for these experiments. iGEM required the team to adhere to NIH arthropod containment guidelines in order for their experimental plan to be approved. Ultimately the team did not carry out any mosquito experiments during the competition.
- **Requiring expert supervision:** One team planned to culture various fungi from their environment, which could have included pathogens that are not permitted within iGEM. Through Check-In Forms, iGEM confirmed that the team was supervised by trained mycologists and had plans to identify the fungi before culturing them in significant volumes.
- **Delegating experiments to more highly trained researchers:** Some iGEM teams have proposed to conduct research that poses an elevated level of risk, such as work with toxins or other hazardous materials. In some cases, an iGEM team will ask other more experienced researchers to perform these experiments on their behalf.
- **Forbidding some work:** The team described above who cultured fungi from their environment isolated a species of fungus that posed biosafety risks. In many countries, this fungus is classified as Risk Group (RG) 2, and the team's supervisors believed that it was safe to work with this fungus under Biosafety Level (BSL) 2 conditions. However, this fungus was classified as RG3 according to the biosafety laws of the country where the team was based. Even though modifications had been proposed to the law to downgrade the fungus to RG2, iGEM prohibited the team from working with the fungus given its local classification as RG3 and iGEM policies that forbid working with organisms classified as RG3 or above.