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Developing a Comprehensive, Adaptive, and International Biosafety and Biosecurity Program for Advanced Biotechnology: The iGEM Experience

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Abstract

Introduction: The international synthetic biology competition iGEM (formally known as the international Genetically Engineered Machines competition) has a dedicated biosafety and biosecurity program.

Method: A review of specific elements of the program and a series of concrete examples illustrate how experiences in implementing the program have helped improved policy, including an increasing diversity of sources for genetic parts and organisms, keeping pace with technical developments, considering pathways toward future environmental release, addressing antimicrobial resistance, and testing the efficacy of current biosecurity arrangements.

Results: iGEM's program is forward-leaning, in that it addresses both traditional (pathogen-based) and emerging risks both in terms of new technologies and new risks. It is integrated into the technical work of the competition—with clearly described roles and responsibilities for all members of the community. It operates throughout the life cycle of projects—from project design to future application. It makes use of specific tools to gather and review biosafety and biosecurity information, making it easier for those planning and conducting science and engineering to recognize potential risks and match them with appropriate risk management approaches, as well as for specialists to review this information to identify gaps and strengthen plans.

Discussion: Integrating an increasingly adaptive risk management approach has allowed iGEM's biosafety and biosecurity program to become comprehensive, be cross-cutting, and cover the competition's life cycle.

Keywords

synthetic biology, biological engineering, biotechnology, adaptive biosafety, iGEM, genetic engineering

Each year, around 6000 students and community lab members form over 300 teams from over 40 countries to compete against each other for medals and prizes based on their advances in synthetic biology design, implementation, and integration into society. This is the world's largest international synthetic biology competition, known as iGEM (the international Genetically Engineered Machines competition), and it has a dedicated Biosafety and Biosecurity Program.[1] Integrating an increasingly adaptive risk management approach has allowed iGEM's program to become comprehensive, be cross-cutting, and cover activities throughout the competition life cycle.

iGEM's program is forward-leaning, in that it addresses both traditional (pathogen-based) and emerging risks both in terms of new technologies and new risks. It is integrated into the technical work of the competition—with clearly described roles and responsibilities for all members of the community. It operates throughout the life cycle of

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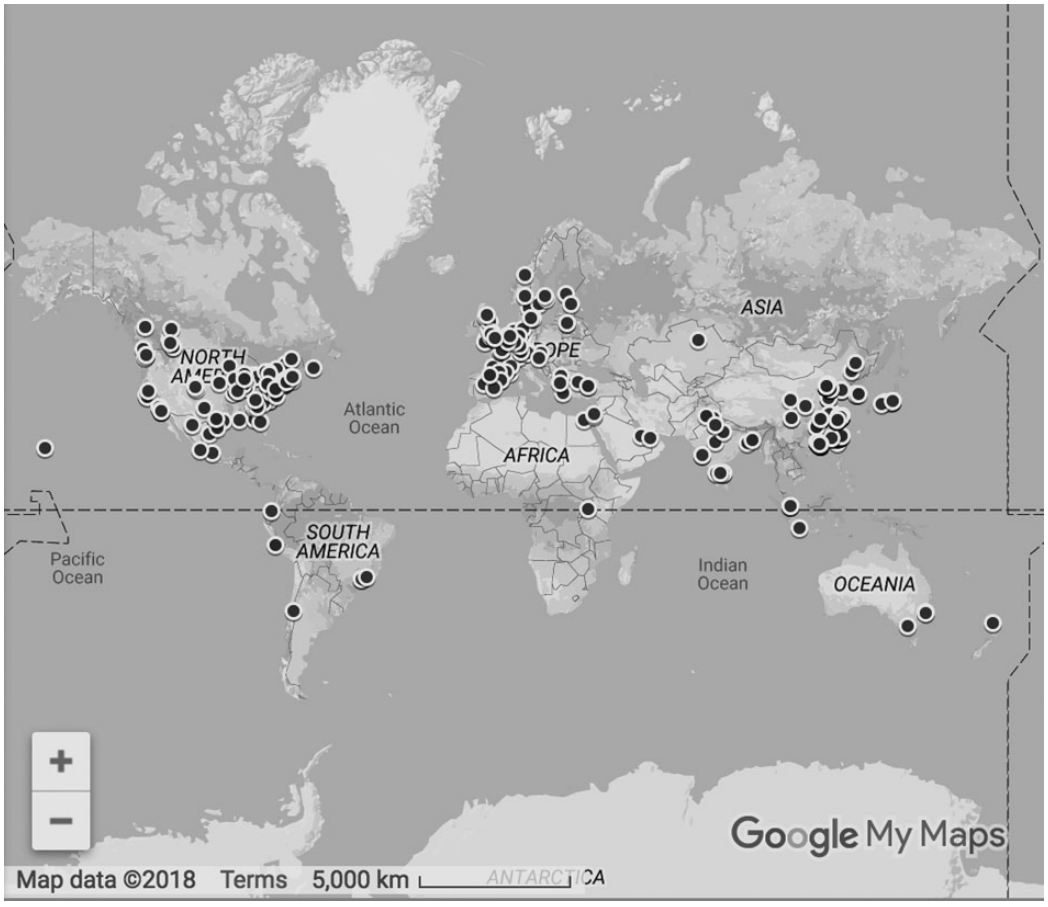

Figure 1. Teams competing in the 2018 iGEM (international Genetically Engineered Machines) competition (see http://2018.igem.org/Teams).

projects—from project design to future application. It makes use of specific tools to gather and review biosafety and biosecurity information, making it easier for those planning and conducting science and engineering to recognize potential risks and match them with appropriate risk management approaches, as well as for specialists to review this information to identify gaps and strengthen plans. The program makes use of both incentives (such as through a Safety and Security Award for excellence and human practices components of its medals) and penalties for noncompliance (up to and including disqualification).[2]

iGEM has an inherently adaptive approach to safety and security, integrating the engineering design-build-test cycle into its own program, as well as the teams that compete.[3] This has yielded a series of concrete examples of how experiences in implementation have helped improve policy, including an increasing diversity of sources for genetic parts and organisms, keeping pace with technical developments, considering pathways toward future environmental release, addressing antimicrobial resistance, and testing the efficacy of current biosecurity arrangements. We review each of these aspects of iGEM's safety and security program below.

A Forward-Leaning Approach

Teams are routinely at the forefront of what is technologically possible. Emerging biosafety and biosecurity issues are common during the yearly competition. These issues can undercut traditional approaches to risk assessment and management, such as focusing primarily on which organisms are being used.[4] Even when using genetic parts, risk assessment has often drawn on what is known about the donor organism. Comparative assessments based on the wild-type organism vs the engineered organism are getting more and more complicated due to increasingly advanced biotechnologies, including synthetic biology and biological engineering. For example, the same genetic parts are not necessarily being used in a similar system, are being combined with many different parts (including from a much wider range of organisms than with which they interact in nature), and increasingly differ from and may ultimately have no natural origin. As advances in biotechnology become more complex and sophisticated and move further away from natural comparators, these challenges to traditional biosafety and biosecurity are unlikely to go away.

iGEM both develops and tests new biosafety and biosecurity measures. It has had to address challenges from (a) the pace of

diffusion of technologies across hundreds of teams and thousands of students and (b) uncertainty over what norms, rules, and procedures on biosafety, biosecurity, and the environment will govern behavior across an extraordinary range of countries and institutions. Since its creation in 2004, there have been over 2000 teams from almost 60 countries, producing over 30 000 synthetic biologists. On occasion, iGEM has needed to create its own policies. These complement national or institutional rules and can help bridge differences between national approaches. For example, in 2018, the program included policies on not releasing projects or their products from the laboratory, human experimentation, gene drives, antimicrobial resistance, use of animals, use of parts from risk group 4 organisms, and deletion as modification.[2] iGEM has shared its experiences across its biosafety and biosecurity efforts with a variety of regional and international initiatives, including the UN Convention on Biological Diversity, the Biological Weapons Convention, the Australia Group, the International Expert Group on Biosafety and Biosecurity Regulation, and regional biosafety associations in Europe and the Asia-Pacific regions.

Integration Into Technical Work

iGEM believes safety and security is everyone's responsibility, from team members, through instructors, advisers, and principal investigators, to the iGEM Foundation itself.

Team members—who can be high school students, undergraduates, and "overgraduates" such as graduate students and community labs—are responsible for working safely in the laboratory, including carefully considering biosafety and biosecurity issues in their projects, as well as consulting instructors and the iGEM Safety and Security Committee (SSC) as needed. They are also responsible for supplying iGEM with detailed information about their project, potential risks, how they will manage them, and striving to be conscientious members of the synthetic biology community.

Instructors, who oversee individual teams at their home institutions, are responsible for ensuring participants will work safely and securely in the laboratory. They are expected to be actively involved in the development of a project and oversee its implementation. They review and certify the safety and security information provided by the team and ensure their work is in good standing with the biosafety authorities of the host institution and the country.

iGEM, through its program, is responsible for approving projects and ensuring compliance with the competition's safety and security rules and policies, as well as for working with participants and instructors to strengthen safe and secure work in synthetic biology. The program relies heavily on its SSC, with members from North America, South America, Europe, and Asia and specialists in biosafety, biosecurity, contained use, and bioethics. It currently has over 30 members, with around a quarter being synthetic biologists, another quarter being current or former regulators, and many of the remainder being a mix of current and former technical experts from intergovernmental organizations or members of national and regional biosafety associations, including the American Biological Safety Association, the Asia Pacific Biosafety Association, the Brazilian National Biosafety Association (ANBio), the Canadian Association for Biological Safety, and the European Biological Safety Association. All of the SSC members, apart from iGEM's vice president for safety and security, serve on a voluntary basis. They use a variety of project management tools and approaches to facilitate remote work across so many time zones. Outside of the competition timeframe, the SCC meets around once a month; this becomes more frequent as teams begin to provide information, up to about once a week toward its conclusion. Members typically serve for several years and are able to engage as actively as other commitments allow. There are ongoing efforts to expand geographic representation (with Africa notably underrepresented at present) and to add additional expertise (such as in bioethics, animal use, and human subjects research). The SSC provides an important resource in creating biosafety and biosecurity tools. For example, they were key in developing the safety forms used in the competition. Having such a diverse membership (in terms of expertise and geography) has helped ensure that the information being gathered meets both best practice and is appropriate across different regulatory and oversight regimes.

Most teams competing within iGEM are affiliated with a university. Teams are required to follow all relevant institutional and national rules and regulations, including those on biosafety and biosecurity. Through the Safety and Security Form, teams have to demonstrate a familiarity with relevant rules and regulations and institutional bodies that oversee them. iGEM works with any team unable to do this to ensure that appropriate oversight measures are in place. For example, 1 team in Southeast Asia was unable to interact with their institutional biosafety professionals. The SSC was able to connect them with appropriate national expertise through the regional biosafety association.

Some projects are reviewed specifically by institutional bodies, and others are covered by existing permissions. To ensure that all projects undergo a basic review, additional requirements are placed on teams from other types of institutions such as high schools or community labs. In many cases, these teams borrow lab space from a university (and thereby fall under their oversight arrangements). In others, they have their own arrangements, such as established biosafety committees or equivalent.

From Project Design to Future Application

Teams are required to think about biosafety and biosecurity issues throughout the competition and beyond, with specific actions required during project design, during work in the lab, and how they transfer both tangible and intangible results outside the lab and into society.

Safe and Secure Project Design

As part of being responsible scientists and engineers, all teams are required to identify and manage risks associated with their

project. This starts during the project design phase. All teams must share what risks they have identified and the procedures, practices, and other measures they have taken to mitigate them. When thinking about these possible risks, teams need to consider potential harm to themselves and their colleagues, communities, and the environment. They are encouraged to think about both "what is being done" (such as the techniques being used) and "what is being used" (including both organisms and genetic parts).

To strengthen both risk assessment and risk management approaches:

- In 2018, iGEM began working with regulators and experts around the world to develop a risk assessment tool for its teams. Teams have also worked on this issue—for example, the 2016 Arizona State team won an award for developing a white paper on context-specific risks.[5] This white paper is highlighted to other teams on iGEM's Safety and Security Hub and has been a core component of outreach to teams and broader communities.
- Teams have to identify and describe the procedures, practices, or containment measures they will use to manage the risks they identify. Some teams also focus their technical work on improving how this can be accomplished. For example, the 2012 Paris Bettencourt team won an award for developing a 3-level biocontainment system.[5] iGEM continues to seek novel containment approaches to make projects even more safe and secure.
- Teams are encouraged to reflect on the risks they identify and consider how they can redesign their projects to avoid them. For example, the 2014 Aachen team won an award for designing safety into their project and demonstrating that their precautions worked.[5] iGEM's SSC continues to work with teams to help them identify ways to accomplish their technical ends via safe and secure means.

Safe and Secure Laboratory Work

iGEM encourages teams to pursue ambitious projects but requires them to work in suitably equipped facilities and use their national or institutional biosafety standards or, in the absence of such standards, the World Health Organization (WHO) Laboratory Biosafety Manual. Due consideration must be given to the characteristics of organisms and parts they will work with and what potential hazards they may pose by themselves or in combination. The competition makes use of a white list, which details organisms and parts deemed safe to work with in a standard laboratory. Teams are encouraged to reduce risks by using safer substitutes for more hazardous organisms or parts. Whenever a team wants to use an organism or part not on the competition's white list, they have to seek approval from the SSC via a check-in form. This provides additional details as to what they want to use, what the biological characteristics are, how they will obtain it, what they will do with it, what risks this might involve, and how they are managing these risks.[2]

As all biological lab work, even simple experiments, carries some risk, teams must follow a set of safety and security rules:

- Teams must be in full compliance with iGEM's safety and security policies.
- Teams must use the competition's forms to provide information on any risks from their project and steps taken to manage them.
- The SSC must have approved (a) check-in forms before a team uses parts and organisms not on the white list and (b) animal use forms before teams use vertebrates and some invertebrates.
- Instructors must sign off relevant forms.
- All deadlines for providing safety and security information must be met.
- Teams must follow all relevant international, regional, national, local, or institutional laws, rules, regulations, or policies, including national or institutional biosafety and biosecurity rules. If conducting any experiment with human subjects (including noninvasive experiments, such as surveys), teams must comply with all rules governing experiments with human subjects.
- Teams must work in the biosafety level appropriate for their project.
- Teams cannot conduct work with risk group 3 or 4 organisms, parts from a risk group 4 organism, or work in a safety level 3 or 4 laboratory.
- Teams must follow iGEM shipment requirements when submitting samples.
- Teams cannot release or deploy their project outside of the laboratory (including putting them in people) at any time during the competition or at the Giant Jamboree.

The iGEM SSC can (and has) disqualify any team found to be in noncompliance with these rules. If teams satisfy the SSC that they have modified their project to be in compliance, they may be requalified. As disqualification from the competition is the largest penalty iGEM can impose, this sends a clear message to the teams on the importance of thinking seriously about safety and security in their projects.

Working with Parts

Because they are working with biological parts, teams need to consider the function of each part to determine whether and how it can be used safely. When assessing the potential hazard posed by parts they want to use, teams need to think about the part's origin, how they will obtain it, its function, and how it may interact with other parts in their project. Teams are encouraged to avoid the use of harmful parts and to seek safer alternatives.

Even if the individual parts in a project are safe, they may have a harmful function when combined with other parts or placed in specific systems. Teams are also required to think about how their parts will work together. For example, could they be used as a virulence factor in another system? Could they be harmful to humans or the environment in some other way?

To help teams identify potentially hazardous parts, "Red Flags" are put on any part that might pose a risk when combined in certain systems or with certain other part. Harmful parts (such as those that encode human toxins) are not accepted. If a team wants to work with any part with a "Red Flag," they require permission from the SSC before the parts are shipped to a team.

On a regular basis, all parts in the Registry (which houses and maintains the competition's parts) are screened for hazardous potential by a commercial partner.[6] The screening process looks at the likely origin and function of the part (by conducting BLAST searches against sequence databases) and approximate hazardous function using control lists and internal databases maintained by the partner firm. Any part shown to pose a risk is identified and can result in the part receiving a "Red Flag."

Safe and Secure Transfers

Transfers can take different forms. Once a team has completed its project, they will need to transfer physical results back to iGEM (such as submitting parts to the Registry). They might also share their organisms or parts with other teams. They will certainly transfer the results of their work to the synthetic biology community through their wiki, poster, and presentation (all required to compete). Throughout their project, teams might also transfer data, information, or knowledge on both biological engineering and their project more broadly, including through outreach, engagement, and publication activities. Teams are required to think about safety and security whenever transferring materials or information.

iGEM teams and the Registry frequently exchange samples of DNA through the mail. Although these shipments are generally not hazardous, they are still governed by national and international laws. iGEM teams must learn how to ship DNA samples safely and legally, as well as learn which samples require specific permission to be shipped.

Thinking about risks due to accidental or deliberate release helps make participants responsible biological engineers:

- Some teams have included details on how they addressed safety and security concerns in their talks, posters, and wikis. For example, the 2017 Wageningen UR team won an award for how they addressed these issues in their presentation and poster.[5]
- Other teams have put safety or security at the core of their project. For example, the 2011 IIT Madras team won an award for experimental work to develop selection markers other than antibiotic resistance.[5]
- Some teams have developed specific outreach materials or resources for the iGEM community on safety and security issues. For example, the 2015 Bielefeld-CeBiTec team won an award for their report on the dual-use nature of advanced biotechnology.[5]

Gathering and Reviewing Biosafety and Biosecurity Information

All teams use forms to provide details of their project's risk assessment and management plan. An initial draft, detailing what they intend to do in their project, is required at the time of the year when most teams begin to move from the planning to laboratory phases of their projects. They are then expected to update their draft whenever their plans change. A final version becomes due as teams wrap up their lab work and begin to focus on how to communicate about their project. A second commercial partner screens the information provided by teams. They use a network of internationally certified biosafety and biosecurity professionals to review the details provided. They look for potentials risks the team has not identified and how well the risk management measures match those they have. The external partner highlights potential issues to the SSC, with a recommendation as to whether each team should proceed, proceed but provide more information or take certain steps, or, in the most serious cases, halt their work pending further risk assessment and management.[2] In 2018, 39 of the 317 (12%) teams participating were referred to the SSC, indicating a need for more substantive consideration of safety and security issues. There were comparable referral rates in recent years (42 of 312 teams, or 13% in 2017, and 26 of 299 teams, or 9% in 2016). Most of these referrals required additional action by the SSC, but around a quarter needed the greatest levels of support, in some cases requiring 5 or 6 rounds of additional information being requested from the team.

Teams have to provide additional details if they want to carry out work with an elevated risk—based both on that they would like to use and what they plan to do with it. All such submissions are reviewed directly by the SSC. Teams wanting to use parts or organisms or carry out activities not on the competition white list have to complete a check-in form, which allows them to set out their plans in more detail, explore specific risks, and outline their risk management approach. Check-in forms are also required for almost all work with insects, plants, or animals and are used to ensure adequate containment measures are in place.

Any team wanting to use vertebrates (eg, rats, mice, guinea pigs, hamsters) or higher order invertebrates (eg, cuttlefish, octopus, squid, lobster) must seek approval from the SSC via an animal use form. To get approval, a team must be able to provide evidence of a thorough institutional animal review (or

equivalent) and to provide a thorough justification of why they want to use the animals based on the 3 Rs:

- **Replace**—whenever possible, alternatives to animal models should be used. Teams must explain why no alternative approaches are possible.
- **Reduce**—if animals are to be used, the fewest possible needed to accomplish the goal of the research should be used. Teams must show they are using the appropriate number of animals to power their study.
- **Refine**—animal research must use methods that minimize or alleviate pain, suffering, or distress and enhance animal welfare. This includes appropriate housing, environment, stimulation, and feeding of animals.[2]

Important feedback on the efficacy of the program is obtained at the Giant Jamboree, where teams present details of what they did, what they accomplished, and what they have done with their new insights. All teams share this information in a variety of formats (presentation, poster, and wiki or mini-website). All teams are judged (ie, reviewed) by experts from multiple fields and peer reviewed by hundreds and, in the case of finalists, thousands of other participants. Every year, biosafety or biosecurity concerns not previously identified come to light. To date, almost all such cases have been the result of teams describing activities not detailed in any of the information provided earlier in the competition life cycle. Any omissions by the commercial partner screening the projects would likely come to light with such a comprehensive peer review process.

Discussion

A number of practical challenges and opportunities have been identified through the program, including an increasing diversity of the source of materials being used in projects, keeping pace with technical developments, considering pathways toward environmental release, addressing antimicrobial resistance, and testing the efficacy of biosecurity arrangements. On an annual basis, key insights are shared with relevant technical communities through a short summary of key safety and security lessons learned.

Increasing Diversity of the Origins of Parts and Organisms

During the 2017 competition, the SSC became aware of an increase in teams wanting to work with samples from the environment (such as soil or water samples), the food industry (such as meat or blood from butchers), or other nontraditional suppliers (including human samples from team members). The SSC gathered guidance, good practice, and other resources to support teams and made them available on a case-by-case basis. These resources were summarized, integrated into the communities Safety and Security Hub, and linked to relevant rules and policies prior to the 2018 competition.[2]

Teams need to think carefully about potential pathogens in these samples:

- There could be safety risks—for example, samples from animals, including those from butchers, might contain zoonotic pathogens.
- There could also be security risks—environmental samples might contain pathogens controlled because of their potential for misuse (such as those on Australia Group export control lists, Select Agents in the United States, or Schedule 5 agents in the United Kingdom).

Unless they can take steps to ensure otherwise, teams are asked to assume samples from the environment, food industry, or other nontraditional suppliers could include pathogens or toxins. As a result, they are not on iGEM's white list, and teams planning to use them need permission from the SSC.

Keeping Pace with Technical Developments

In 2016, a team attempted to make a gene drive.[7] They did not make a functional drive but did manage to get components to work. As gene drives do not include any pathogens or parts connected with virulence or transmissibility, they do not appear on common control lists. None of their components were specifically captured by the competition's safety and security rules and policies at that time. As soon as the nature of the project was identified, the SSC began working with the team, noting that they were eloquent and engaged in considering broader implications of their project but had not anticipated the amount of scrutiny their project would receive. This project was reported in the wider press, noting that (a) international gene drive experts reported that the project was "not dangerous" and (b) the team had designed in specific safety precautions.[8]

This project demonstrated the speed at which groundbreaking research can be adopted and used by a much wider technical community, including an undergraduate team in an international science competition. There was less than a year between the publication of key technical information and the project being presented. This makes it very difficult for oversight and regulatory bodies to keep pace.

In the months following the 2016 competition, iGEM constructed a specific policy on gene drives.[2] This has subsequently been shared with regulators around the world and fed into a number of national policy development processes, for example, into technical discussions among European Union regulators. iGEM's policy requires that any research on gene drives is dependent on special permission from the SSC. This requires a team to convince the SSC that the project is safe, based on the host organism, parts, and containment measures. Best practices in containment, developed by leading gene drive researchers, must be implemented. The planned project has to be discussed on a conference call with recognized international experts on gene drives and biosafety and biosecurity. Any commercially acquired parts must be obtained from companies that screen against regulated sequences. Teams have to self-declare their intent to use gene drives—helping to address the challenge of identifying relevant work. A functional description of gene drives (rather

than a list of specific parts) was developed to help teams do that. Gene drive–specific language and examples were inserted into the white list, embedding them into iGEM's routine safety and security activities. A ban on gene drives as parts in the competition Registry also helps to mitigate risks of accidental release.

Considering Pathways Toward Future Environmental Release

iGEM has a strict no release policy. Projects have to stay inside the laboratory. Some projects, however, would envisage environmental release should they ever be sufficiently developed. Past examples have included the creation of engineered systems to clean up environmental contaminants, or the use of biosensors to detect the presence of compounds of interest. Through their human practices work, teams often explore what it might take to get regulatory approvals for such a product. Teams are also required to consider both immediate risks to the environment as well as potential risks should their project be fully realized.

In 2018, one team worked with iGEM's SSC to develop a protocol and experimental approach to demonstrate the absence of engineered organisms and to allow them to take dyes produced by their engineered system out of the laboratory.[9] iGEM remains interested in finding better ways to showcase projects safely and security and is keen to work on approaches that allow them to be taken outside of the laboratory.

Addressing Antimicrobial Resistance

Resistance to important drugs is an increasing challenge to human and animal health. It has led to high-level discussions at the United Nations General Assembly, a commitment to address this issue by world leaders, and an action plan from the WHO. Some parts encoding antimicrobial resistance (AMR) are also common research tools, including some antimicrobials of great public health importance. For example, several of the WHO's Critically Important Antimicrobials are also common research tools. Responsible scientific or engineering activities must avoid contributing to increased resistance to these important medical countermeasures. Although no project is permitted to leave the lab, in 2017, iGEM developed its own policy to help minimize the use of resistance factors for antimicrobials of critical importance to public health.[2] Where possible, alternative markers are encouraged. iGEM is also reviewing the use of resistance factors in parts used in the competition. AMR-related parts are accepted into the Registry, but any part containing sequences connected to WHO's list receives a safety flag. Such parts will not be included in the distribution kit and explicit permission for their use is needed from the SSC.

Testing the Efficacy of Biosecurity Arrangements

Some teams focus all or part of their project on safety and security issues, including testing the efficacy of current biosecurity arrangements. For example, some of the companies that supply genetic material screen their orders. They use software tools to assess whether the parts are hazardous and controlled by laws and regulations. In 2013, the Lethbridge iGEM team working with several commercial gene synthesis companies tested the efficacy of screening procedures. The main Lethbridge project was on RNA pseudoknots and ribosomal frameshifting. They noted a potential application that might allow a nefarious actor to conceal a hazardous sequence within an apparently benign sequence. They developed 17 sequences that included hidden components from controlled pathogens and toxins, and they submitted these to the companies (who knew they were coming). The companies treated these sequences as they would any other order and screened them. In all cases, concealed sequences relying on pseudoknots were detected and all-but-one frameshifted sequence were also detected. Throughout the project the team had also been liaising with relevant security authorities.[5]

Conclusion

The expansion of our understanding of how biological systems function has resulted in a more nuanced understanding of risk. The emergence of new biotechnology techniques is resulting in new types of hazard. As risks rely on hazards, then a biohazard should no longer be confined to pathogens or toxins but should be understood as any biological component that manipulates the function of a biological system into an unsafe state. This framing helps scale concepts of risk assessment and management—as it does not matter whether the system being disrupted is an individual (plant, animal, or human) or an ecosystem. There have been calls to evolve risk assessment and management approaches to better fit this worldview, particularly through an adaptive risk management approach.[4]

iGEM has integrated the 6 core components of adaptive risk management into its program, namely to

1. Go beyond traditional agent-based risk assessment—for several years, biosafety and biosecurity efforts have moved beyond agent-based risk assessment and management to a more functional, parts-based approach.
2. Evaluate risk on "a case-by-case basis" as opposed to "in a broad and generic manner"—with every project being reviewed separately and assessments specifically considering in-context use of parts and organisms.
3. Embrace a more project life-cycle approach with the "aim to review the research before it begins and then periodically assess and evaluate the project concerning changes in the research that may present additional elements of importance for risk management," as well as considering potential risks should the project ever make it to market.
4. Use multiple risk management approaches, including both biological tools and human solutions—the program includes both technical solutions (such as

appropriate containment) and human components (with a heavy focus on both training and responsible conduct).

5. Embed consideration of certain bioethics elements into biological risk assessment and management process. For example, "What trade-off between the chance of benefit and the risk of harm is justifiable and acceptable and for whom?" For many years, "human practices" has been a core component of the competition, and successful teams universally consider "how their project affects the world and how the world affects their project."[10] Furthermore, iGEM has added a number of bioethicists to its SSC to help tackle the growing number of requests to use animals and other bioethics-related questions.
6. Involve a wider set of stakeholders, including "scientists, biosafety officers, institutional leadership, and ethics consultants, with the aim of maximizing safety as well as scientific progress"—the program is built on a belief that safety and security are the responsibility of all. This promotes the involvement of the widest possible group of stakeholders.

iGEM has used this adaptive approach to address a number of practical, real-world challenges and opportunities for biosafety and biosecurity, including an increasing diversity of sources for genetic parts and organisms, keeping pace with technical developments, considering pathways toward future environmental release, addressing antimicrobial resistance, and testing the efficacy of current biosecurity arrangements.

Ethical Approval statement

This paper does not contain any studies requiring specific ethical approvals. All procedures performed were in accordance with the ethical standards of the relevant institutional and/or national rules and regulations, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Statement of Human and Animal Rights

This paper does not contain any studies with human participants or animals performed by any of the authors.

Statement of Informed Consent

This paper does not contain any studies with human participants requiring informed consent.

Declaration of Conflicting Interests

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