

Working with iGEM projects of potentially high risk

Guideline for a good safety concept

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1 Introduction

Working with toxins or projects which contain highly potent toxins demands special safety measures and adherence to strict safety rules during the whole project. There are various parties you have to consult about your plans. First of all you have to be well informed about the potential risks your project carries at all times. Then you have to contact the iGEM Safety Committee to make sure iGEM will accept your project or to know which tasks you may have to focus on in order for them to do so. Therefore constantly follow the iGEM rules. The person in charge of the safety at your institute or university will also be monitoring you. There is a variety of people you will have to persuade with broad research, planning and detailed knowledge about the safety of your project. Moreover working with potentially dangerous toxins demands a special mindset. Everyone of your team members working in the lab has to be mindful of what they are working with and fulfill all the required safety standards.

2 Overview

To sum up the three most important points you have to keep in mind when working with toxic substances are the following:

1. First, stay in contact with iGEM so you can consider their advice and guidelines.
2. Second, clarify everything with your university so that your work takes place under the right circumstances.
3. Last but not least make sure that all members of the team work with the right mindset and carry out their tasks carefully, taking the potentially high risks into consideration.

3 Identifying risk factors

The first step of every good safety concept and the most necessary one for all the conversations and interviews you'll have is good preparation. If you have chosen one project idea you have to look for every important paper referring to your topic. Inform yourself thoroughly about the details and traits of the organisms you plan to work with. If you would like to engineer E.coli with properties of other organisms you have to make sure that you know everything about it, what it can and can't do.

It's highly recommended to find an expert for the system (organism/protein/or whatever) you are working with. Contact him or her and pierce them with questions. Questions about their safety requirements as well as their experiences with certain organisms or methods. Present them your plan (or the parts referring to their special field) and ask them if they think it's sensible. Even if it's a prestigious professor don't hesitate to contact them. In general every scientist is very happy and open towards people who are interested in their work. If you can't reach the authors of the paper it helps to reach out for scientists near you who are working in the same field. For example: Our topic of interest was a protein of the family of AB-Toxins. We knew that there is a working group specialised on AB-Toxins in a town close to ours. So we contacted the group who referred us to an expert who worked his whole life on this topic. You should always check the data and conclusions of papers you'd like to rely on with other scientists of the field. Because even publications and peer reviews can not guarantee a one hundred percent reliability. If you have the power and knowledge of bioinformatics you can start a first subproject where for example you model special mutations your construct has or test their influence. With the power of bioinformatics you can already provide a lot of useful informations before even starting your project.

4 The iGEM safety committee

One of iGEMs highest priorities is the safety of their contestants and their projects so you have to ask the committee whether you are allowed to continue with your project or not. For preparations you can check the iGEM safety requirements where you can find the safety form. There you will get all the information you need. Take into consideration if you need a check in form before you start to work. After you collected all the information you can and you are sure that this will be the project your putting all your motivation, blood and energy in for a year, you have to make sure that the iGEM safety committee will approve this project. Therefore, you have to contact the iGEM safety committee early on. Once your project is accepted you have to put a special focus on the careful complementation of safety sheets and check in sheets. In addition you should be prepared to send them special documents like a clearance certificate. To convince iGEM and or any other person there are some quite simple rules to follow:

1. for every protein or every part you want to use, quote every paper or other source providing relevant information concerning your working methods or any related safety issues
2. research or design assays to proof certain characteristics and convince the committee that they are safe
Our example: We wanted to detoxify a very toxic protein. So first of all we had to design and test a so called "toxicity assay". We compared the toxic wild type with our atoxic mutant to proof, that our mutant lost the properties making the wild type toxic
3. look for every other source (e.g.: the bioweapon list of america, australian list, iGEMs White List) and check whether your organism or substance is listed there or if there is an exception for a special subtype you can use
4. collect every documentation you can get from any kind of safety officer of your university, institute or working group

Bear in mind that it's possible your part will not be included in the next years distribution kit or will be marked with a special flag. Be aware of that you need to make informed and well considered decisions regarding the safety of your work and your environment. Whenever you're confronted with difficulties don't hesitate to reach out for assistance. Even professors or researcher of high rank will be happy if you contact them because of their work. Never resort to compromises regarding work safety.

5 University and Institutes

Now you probably think your done: You have every important document, found out your project will be safe, you can work in S1 laboratories and iGEM approved your project. And after you talked to various experts you are optimistic your project will work.

But as soon as you start your work in your university, institute or working group you will face new obstacles. Every institution has its own biosafety office or officer. Every person in charge of the safety of the laboratories has to be convinced separately about your work and you. The first person you have to talk to is the official biosafety officer of your university. You have to present your project plans and he or she has to confirm that you can work in S1 laboratories. You will receive requirements your team has to fulfill such as documentation forms, safety clothing etc.. If your project requires more than a S1 laboratory the work eventually has to be registered. This process is coupled with a bunch of bureaucracy for your team, your PIs and additional people who are responsible for the lab safety. Due to their high standards iGEM requires even more documents. If possible, avoid a project where you have to work in a S2 laboratory. If you have no choice it's possible to ask someone to do the required S2 work for you whereas you go on in S1 surrounding. In our case we were allowed to work with anything that had to do with DNA but had to refrain from work with actual bacteria. We

had to separate the DNA-sequence of our protein into the heavy chain and the light chain. To make sure that we separated it correctly, the light chain was cloned in E.coli and sequenced. This work was done by our PIs in an S2 Laboratory. We could continue our project after ensuring that everything we're working with was safe.

Every country has a governmental authority which is responsible for safety issues in universities and general research. Ask your biosafety officer for further information. Always discuss the plans for your work with these authorities. If you gained their approval every professor or lab responsible will be reassured.

Now it's time to talk with every important person in the institutes you are working in. The best method is to invite them all (the director of the institute, the professor of the working group together with his biosafety officer of the group and eventually every other important professor like the dean of studies) to a presentation. There you have to present your initiative idea, a first version of a working plan (who, when, where, what, for how long) and most important: show them every information you have. From early research of potential risks over your arrangements with the iGEM Safety Committee to your consultation with biosafety officers and governmental authorities. Your presentation shouldn't take more than 15 minutes. Present a plan on how you'll keep them updated. Write a mail to every interested or important person with ongoing updates whenever you make major process in your project. Keep the professors and advisors updated with data like sequencing results, gel images or every other kind of important data you produce. And make sure to convince them that you fully understood your project and its risks. Gaining the trust of your professors and advisors is one of the most important tasks you will face during your project. Not only do you need their trust during your current work but it will also ensure a well-functioning work relationship in the future. Therefore you need to make sure you never handle this task halfheartedly. Always take into consideration how your words and actions will be received by your working partners.

6 The team members

The most important part in guaranteeing work safety are your team members as they will execute most of the work. You have to ensure that every team member working in the lab fully understood the guidelines for safety. Before starting any work in the lab you will have to organise general lab safety seminars and courses with a special focus on the methods you need. Any lab work should be supervised by at least one more experienced team member. No team member should work alone in the laboratory especially if you are working with a potentially very toxic or at least riskful organism or substance. Always work according to the highest safety standards and with special caution and prudence.