

BREAKERS

The logo for 'BREAKERS' features the word in a large, sans-serif font. The letters 'B', 'R', 'E', 'A', and 'S' are black, while 'K', 'E', and 'R' are a teal color. A thick black diagonal line slashes through the word from the bottom-left to the top-right. Below the slash, several small, colorful geometric shapes (triangles and squares) in shades of blue, orange, and black are scattered, suggesting a break or explosion.

The following contains an ethical review for the 2016 Lethbridge High School iGEM Team. This was developed by the 2016 OLS_Canmore team, as part of a collaboration project. It includes an analysis of four main ethical points (sepsis, bacteria in wound sites, the doctrine of double effect, and “do no harm”) as well as an analysis from a religious perspective.

Table of Contents:

1. Lethbridge Project Summary
2. The Ethics and Risk of Sepsis
3. The Ethics of Bacteria Entering a Wound Site
4. The Doctrine of Double Effect
5. Do No Harm
6. Religious (Roman Catholic) Perspective

Lethbridge High School Project Summary:

(written by the Lethbridge HS Team)

We recognized that in most emergency situations, excessive blood loss is a threat that could result in hypovolemic shock, anemia or even death. Preventing or reducing blood loss would greatly increase the chances of survival as well as speeding up the healing process. After discussing different wound sizes and how our project could be applied to each, we decided we would focus mainly on treating medium to large sized wounds. Then, we started designing a construct based around snake venom. Some snake venoms are very effective at inducing blood clotting by skipping many steps of the clotting pathway and thereby greatly increasing the rate of blood clotting. The Cerastes snake venom acts similar to thrombin in the blood-clotting cascade, causing inactive fibrinogen to be converted into active fibrin monomers. Along with Factor XVIII, the fibrin monomers form a crosslink structure that traps red blood cells, resulting in a blood clot.

After that, we hope to develop a fast-acting and effective prototype that will be able to clot pressurized blood being pumped through a simulated wound. If this is accomplished, we'll attempt to design a tool or delivery system to make sure that we apply the right amount of our system to the wound in order to get the best clot. In addition, we want to test whether or not the clotting factors can move through the body causing an embolism elsewhere. This is something we want to prevent and need to test if our system can remain local in the wound. Our team hopes that our inexpensive and effective technology will be able to help military personnel, disaster victims, and other people affected with severe bleeding survive their ordeals, and have a better quality of life afterwards. In doing so, we will reduce strain on healthcare systems, simplify treatment of major bleeding for EMTs and doctors, and keep families together.

Sepsis and the ethics behind this, relating directly to the consequences of using the product on a human:

(written by the OLS_Canmore Team)

There are already some possible ethical concerns around the use of snake venom as a clotting agent. Though the topical application of venom has benefits, there is a chance for sepsis to occur, especially if the bacteria are being applied to an open wound. We also know the consequences of snake venom being injected directly into the bloodstream. These would pose similar risks to those of sepsis. The idea around this project is fascinating, but in this aspect, it would be negligent and unethical not to recognize and work to prevent the possible dangers that accompany the chances of sepsis. The specifics of intended procedures would have to be further elaborated beyond the intent that is listed above in the summary to determine whether the risks are mitigated, and whether they outweigh the rewards.

The ethics behind bacteria entering a wound site:

(written by the OLS_Canmore Team)

Ethically speaking this project asks many questions the team would need to answer. These questions are centered primarily on implementation of the project. However, two main questions developed on the basis of this project description are:

1. Clotting: As the Lethbridge team has chosen to use snake blood for their construct, the possibility that clotting could occur elsewhere in the body other than at the wound site is assumed to be relatively high. Ethically speaking this problem could be evaluated many ways. If one were a follower of Kant's beliefs (deontological ethics) for example, they would be bound by their duty. Their duty would be to save the life of the person or prevent them from further harm, regardless of the possible consequences. Meaning that one could justify the potential use of snake's venom even if there was a high possibility hypercoagulation as the intent when committing the act is good. They focus on the potential that we could save a life. Based off that, the use of snake venom could be an ethical approach while keeping in mind that the Lethbridge team also intends on investigating the consequences of their procedures before any possible application to humans as not everyone believe that the intent is the most important part of an action.
2. Bacteria: The second ethical dilemma surrounds the direct contact of bacteria with a vulnerable wound site. Currently this project uses the chassis *E. coli* K-12. This presents a problem as the directly contact of the *E. coli* K-12 could lead to infection or septic shock.

Most laboratory strains such as k-12 have very rarely if ever been directly implicated in disease (1). This means that the likelihood of someone getting sick from contact with the construct is very unlikely. However, one could be concerned about the patient going into septic shock, also known as sepsis. Sepsis can take place as a result of an infection and cause very drastic changes in the body. Often times the inflammation caused as a result of sepsis can lead to tiny blood clots. This can block oxygen and nutrients from reaching vital organs (2). This in combination with the potential clotting of blood due to snake venom could have drastic, and life threatening effects on the patient. The ethical approach of Plato which focuses on Eudemonia or well-being could justify this action, as it is intended to heal, but again further research must be conducted to justify or oppose the use of the product (3).

(1) <https://ic.ucsc.edu/~saltikov/bio119l/BIOSAFETY/COLIHAZ.HTM>

(2) <http://www.healthline.com/health/septic-shock#Overview1>

(3) <http://peopleof.oureverydaylife.com/platos-beliefs-ethics-4672.html>

The Doctrine of Double Effect:

(written by the OLS_Canmore Team)

The “Doctrine of Double Effect” is mostly used in the medical community, it essentially says that anything done for a positive end result, but which may cause serious harm, is ethical (1). Though this is in direct conflict with the oath to “Do No Harm” it is an accepted practice in the medical community. There are misinterpretations though; and this situation can be a misinterpretation of that practice. The “Doctrine of Double Effect” stands in cases such as: a military sniper killing a terror bomber or a catholic doctor performing an abortion in a case where pregnancy would kill the mother. What these have in common is that they are last efforts to save lives. The purpose of this project is for the topical application not to be a last ditch effort, but for it to be a go-to in the case of an emergency. In this case, because the possible chance of harm may outweigh the possible good, it may still be considered unethical, despite possible double effect. Development of procedures to minimize risk and further research on the project will be essential to make the solution ethical in this sense.

(1) McIntyre, A. (2004). Doctrine of Double Effect. Retrieved October 14, 2016, from <http://plato.stanford.edu/entries/double-effect/>

"First do no Harm" as it relates to a potentially harmful biological product:

(written by the OLS_Canmore Team)

The saying “first do no harm” is one that is heavily related to bioethics and medicine. It refers to the way that both in the medical and scientific community we are meant to make choices. This was developed as a basic way to evaluate all choices as they can sometimes be fairly tricky and need to be made quickly. The basis of this viewpoint is to do what you think is right first in high stress situations, but also to maintain respect. This means that though you know your treatment or project could be helpful if the people most directly affected do not agree with what you are doing you are not free to do so, and to do so would be wrong (1). The “Do No Harm” viewpoint also emphasizes that one should not place people in a hierarchical order. Meaning that when considering the effects of one's project you should not place on viewpoint or person in preference but rather all as equal (2).

This applies to the project because when considering the effects of the project one must consider the true effects it could have on those directly affected (the patients). First of all let's look at application. With the current implementation method there is still a possibility, though limited that a patient could experience sepsis, or another effect from the biological system that the snake venom could cause the blood in the patient to clot somewhere other than the wound site. Applying the “First do no harm” principle in a high stress situation if this could save the patient's life then they should do so. However if the patient is able to consent they must provide this consent. The second issue is surrounding that of the use of a GMO on a person. Many people are against GMOs or have religious beliefs against the use of GMOs. The same as above applies when applying the “First do no harm” principle. If in a high stress situation it is up to the doctor to do what they think is best for their patient. But if the patient is conscious they must understand that it is a GMO and consent. The third consideration is the very basic ethical approval of the project. If a number of professionals both within the medical field and synthetic biology feel as though this project or any other part of its testing, construction and etc., have negative impacts which outweigh the benefits, it is not ethical (nor in accordance with the “Do No Harm” perspective). If this were the case, and understanding the scope and limitations of the project it certainly is not at this point, the project or that part of the project must be abandoned by the team.

(1) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2528718/>

(2) <https://depts.washington.edu/bioethx/tools/princpl.html>

Catholic Ethics

(written by the OLS_Canmore Team)

From the Catholic perception man is created in the image and likeness of God, and this must include a profound amount of respect for creation and its miracle. Synthetic biology can be a valuable resource to human progress, when used properly. However, Catholicism has established that within the Church our central moral and unethical complication is the manipulation of life (1). As a result, science and technology should never alone be the meaning of existence and human progress; we still must find a balance of what 'manipulation of life' really is (2). Genetic manipulation is a growing domain within biology, which has brought up vital questions and concerns. The current rapid development within synthetic biology ensures we must be quick to follow and respect the standards within the field, and develop these standards if none exist.

Before deciding the ethical accountability of a project you must first develop a perspective on what is and what is not the manipulation of life. There are many views and opinions describing the sinfulness of tinkering with human life, such as stem cell and embryonic alterations, which has been clearly outlined as unethical by the catechism (1). The Vatican says that "applied biology and medicine work together for the integral good of human life when they come to the aid of a person stricken by illness and infirmity and when they respect his or her dignity as a creature of God" (2). There are many views and opinions describing the sinfulness of tinkering with human life, such as stem cell and embryonic alterations, which have been clearly outlined as unethical by the catechism (1). Alternatively, is putting a plasmid into a bacterium the same concept, or does that belong to a separate classification? Whether or not significant changes are made is an important factor because we are not adjusting the organism's genome but instead simply placing a plasmid inside, much like an organ transplant, which receives no criticism within the church. We asked Father Wilbert, the Canmore parish priest, what he thought about our area of work and his main concern was the involvement of human life and how critical the idea of working to better society is.

A person's contribution to the evolvment of mankind is important when participating in work that is not always deemed right. A historic philosopher named Kant theorized that right or wrong is based off of one's intentions to fulfil an action, and that good will is the ultimate virtue because it cannot be turned to selfish reasoning (3). The Catholic belief coincides with Kant's ideas on good will. This also includes the importance of bettering mankind when participating in synthetic biology, rather than using it to accomplish immoral ends.

A similar topic related to ethics is a person's conscience for the Vatican says, "science without conscience can only lead to a man's ruin" (2). We must be aware of the complications that can arise and know personally what is right from wrong. "That everyone might see clearly

that the Church and her Pastors are not opposed to true and solid science, whether human or divine, but embrace it, encourage it, and promote it with the fullest possible devotion” said Pope Leo XIII. Understanding that the Catholic Church completely supports scientific advancements for the improvement of our race is important, but to do it properly and ethically is vital.

The line between religion and science is not black and white, allowing room for varying perspectives. Therefore, outlining the rights and wrongs within a project is difficult to do without including bias. The position of this and any other project on the spectrum of right and wrong should rely on the well-considered and fully informed decisions of many diverse perspectives if any conscientious progress is to be made.

- (1) http://www.vatican.va/archive/ENG0015/_INDEX.HTM
- (2) http://www.vatican.va/roman_curia/congregations/cfaith/documents/rc_con_cfaith_doc_19870222_respect-for-human-life_en.html
- (3) <http://www.csus.edu/indiv/g/gaskilld/ethics/kantian%20ethics.htm>