

# Value sensitive design for iGEM

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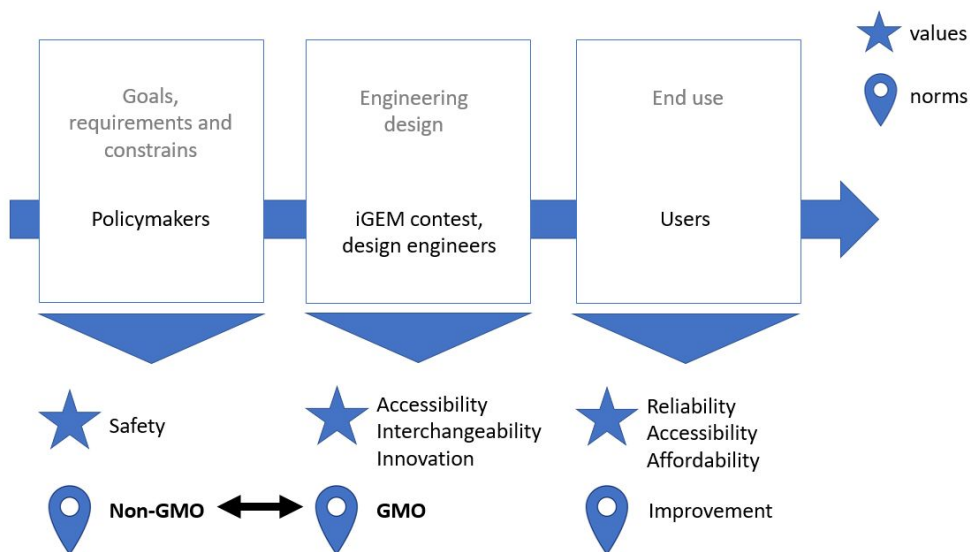
## Introduction

In the previous assignment we have identified the important stakeholders in this project and interviewed a couple of them. Based on the information and the insights the interviews gave us, we decided to specify our niche market to the farming industry. To get a more complete overview of the values of the important stakeholders in this field, additional interviews with farmers and veterinarians were conducted (appendix). For translating values into design requirements, it was important to clarify these values. In this paper, we will elaborate on the choices we made and did not make as influenced by the values of our stakeholders, which is called value sensitive design (VSD). VSD is based on continuously indicating stakeholders and their values, hopes and concerns related to the project and the way in which the technical features of the design can meet these values and help prevent undesired project outputs (Palmeros, 2017). We aimed to reach successful VSD by integrating the values of our stakeholders in the design requirements for our tool. According to van de Poel (2010), this is an effectual way to do VSD.

In order to conduct the value sensitive design correctly, it was necessary to know what values we were working with. The public authorities emphasized that genetically modified organisms should not leave the lab, but should only be used as cell factories, which guarantees environmental safety. This was probably the most restraining value and therefore extremely important to take into account. Farmers indicated mostly that the tool should be easy to use, reliable and quick. Above that, its price should be low. These same values were indicated by veterinarians as being the most important, with reliability, ease of use and speed taking primary focus and pricing being less important though still very valuable.

Eventually it turned out that we took three main values into account based on the insights we gained while talking to different stakeholders. In figure 1, the main norms and values are shown related to the different actors. Note that, according to the policymakers, the design should be GMO-free to ensure safety. However, this contradicts the norm that in order to ensure innovativity, interchangeability and accessibility, iGEM requires the use of genetically modified organisms. For the final users (we are not yet sure if these users are also our direct customers) the tool should be more accurate, faster and cheaper than the already existing techniques.

This report describes how we came up with these norms and on which values our design is based. Furthermore, the second part of the report describes how we want to achieve user acceptance and how we would like to optimize the industrial design while continuously gaining feedback from users. Thereby, we would like to stress the unused potential of synthetic biology for a healthy and sustainable economy. Legislation is still not stimulating enough, and therefore we argue that policy makers should be pioneering to create an environment that stimulates synthetic biology innovations.



**Figure 1. Summary of values and norms (based on concerns and potentials different actors see) in the design process. Model inspired by *Investigating Ethical Issues in Engineering Design* (van de Poel, 2001).**

## The design process according to current norms and values

During the iGEM project, we adjusted our design recipe continuously based on the insights we gathered, not only based on literature and other technical information, but also based on the people we have spoken to and their opinions and the values underlying those. Below, we discuss several different design options we have considered during the project. However, as our design keeps changing according to the knowledge we gather, none of those options were as good as the current design. This is not only based on technical constraints, but also on ethical constraints. The options below therefore are not satisfactory when taking into account all the societal concerns we deal with in this project, but we believe that our current design is.

As participation in the iGEM contest requires the tool to be GMO-based, GMOs were physically present on the device in the first draft of the design of the tool. This design option was rejected based on the values of the different actors that are of importance for our technology. The Risk Assessor of the RIVM did not show much concern about the current design of our technology, because the microorganisms do not leave the laboratory environment and are only used as cell factories to produce proteins. The value that underlies this, is that GMOs entering the natural environment is unwanted and considered unsafe. The general public is also likely to fear the technology when it involves uncontained genetically modified organisms. This statement is supported by the interview with the general practitioner, who expressed many doubts about using GMOs in general as it might threaten our environment. This is why the final design specifications were adjusted and the device does not contain any GMOs anymore. To join the iGEM contest the “bricks” of the tool are produced with GMOs in the laboratory.

Besides the adaption described above, another option inevitably was to design a tool to be used in the lab only by specialists. It is important to compare our technology to current methods used for antibiotic resistance detection. For that we spoke with an antibiotic resistance specialist currently working at RIVM. He indicated that currently either plating or PCR is used to detect antibiotic

resistance. With the proper instructions and equipment, the former method might be something that can be done outside of the lab. Also, the sample preparation is rather straight-forward as the sample can be used directly on the plate. However, its major drawback is that the detection is not based on genetics but on gene expression, making it unreliable. Above that, detection takes at least 2-3 days. PCR on the other hand, is a method based on genetics, which can be seen as a more reliable method. Nonetheless, this cannot be performed outside the lab and the equipment needed is rather expensive. Besides that, the sample preparation is more of a challenge, as DNA or RNA needs to be isolated from the sample.

Above that, doctors, veterinarians and farmers indicated that it is very important to them that our innovation makes the detection of antibiotic resistance quick and easy (accessible). In general, sending samples to specialists in the lab takes a lot of valuable time which can easily be reduced using our technology. This is why farmers see value in a *home detection kit* to use in the field.

On top of that, farmers indicated that a home detection kit should not only save time, but also save money. This does not mean that the direct usage of the tool should be cheaper than the current diagnostic methods. However, the return on investment (the break even point) is an important value for every business. Eventually we assume that the design of a home kit will be less expensive, because lab work done by specialists is the most expensive way of diagnostics. It still is important to keep the production costs as low as possible, so the costs for the materials used for the design should be kept to a minimum. This is why a simple piece of paper is the basis of our technology: this is not only cheap, but also easy to dispose which makes it even more user-friendly.

To compare the current methods to our tool, we will first focus on the exact use of the tool and then the sample preparation. For each of the aspects of our design, we can indicate the associated values. As reliability of the result has the highest priority, we chose a genetic detection method, using CRISPR-Cas. This is a highly sensitive and accurate method. As the result should be easy to interpret we used a special variant of CRISPR-Cas, called Cas13a or C2-C2. In this way, a direct readout can be achieved so it is clear which antibiotic not to use straightaway, rather than using the Cas9-family which was most straightforward in the beginning of our project. Cas9 was not able to give direct readout and therefore was not useful for fast home detection tool. To reduce the costs of the tool, we aim to engineer our detector in such a way (with tardigrade proteins) that it can be stored on a simple piece of paper. In this way no special treatment is needed to store the kit and no expensive materials will be used. This is already a great improvement compared to the current methods. Still, the sample preparation is a huge challenge, as the isolation required is comparable to the PCR method. DNA needs to be isolated from the sample, which cannot be achieved without the proper instructions. Our next step for the design will be to work out a protocol that comes with the kit, to ensure the ease for the use of the tool.

Compared to the current methods, using GMOs might be slightly more hazardous. As mentioned above, the risk has been minimized by keeping the microorganisms contained. Clearly, not using GMOs at all would have been even more (ethically) safe, but as this project is conducted for the iGEM competition, we could not choose to work without them. Therefore, one of the most important values that we took into account when deciding the design specifications for this tool were keeping the GMOs contained and, partly as a result of that, making the technology safe, not only for its direct users but for the complete population. When we chose to keep the microbes in the lab and only put proteins they produced out there, we minimized the negative impacts of our

technology as much as possible. Currently, a different method is already available to determine the kind of antibiotic that should be applied, which does not involve any GMOs. However, this method is not as reliable as our method, and cannot be applied outside the lab in a home detection kit.

However, we should consider whether the home detection makes our tool less reliable. Home detection indicates that the farmer or another user can use the tool in the field or at home themselves. The value accessibility might be in contrast with the reliability and accuracy. To make the tool both accessible and reliable, we were thinking about both a clear protocol and a foolproof sample preparation method. The ideal option for sample preparation is a pre-fab tube containing all enzymes needed for DNA-extraction to which a sample (such as saliva or urine) only has to be added. We also want to incorporate a ‘control drop’, which indicates whether DNA-extraction was successful. When the control is negative (so no output), the sample can be added to the actual device. In this way, the chance of obtaining false results is minimized.

Michelfelder *et al.* (2013) described the hierarchical nature of values. Values are linked to norms, which in its turn determine the exact design requirements. We set up such a pyramid to visualise this, in order to have a clearer idea of the design requirements (figure 2). Concluding, these values, norms and requirements are taken into account during our design process to make sure that our design will be socially accepted by the public and users, and can be implemented under current legislation.

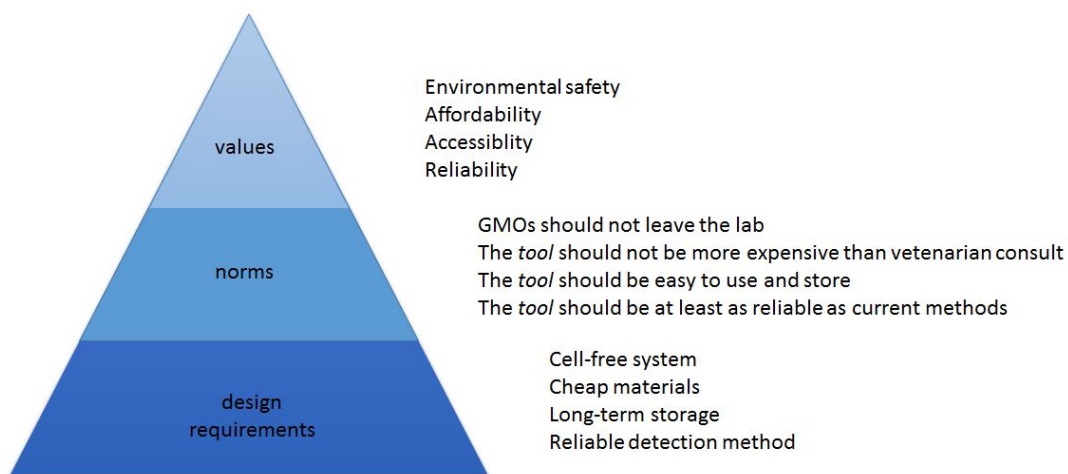


Figure 2. Hierarchical nature of values filled in for our *home detection kit*. Michelfelder *et al.* (2013).

## Influencing current norms and values in future prospects

### *Public engagement*

The growing threat of antibiotic resistance to public health makes it important to spread awareness about the issues that farmers face considering cattle diseases. Also, awareness on international scale can help to get support from the policy makers and general public to develop more accurate, easy to use and cheap devices to fight antibiotic resistance. One way to do this is through the use of workshops. These workshops can be used as a platform for making the public aware of the severity of the problem that antibiotic resistance represents and as an instructional instrument to familiarize the end-user with the use of our tool. In this way, the workshops cover two challenges; they help

make the tool as easy to use as possible (thus taking into account the ease of use value) and they teach the end-user how to use the tool, which requires face-to-face interaction with an instructor. Also, we can adapt our device design based on the insights we get when doing public engagement. This way, we are able to optimize our industrial design.

### *Legislation and policy makers*

Even though a GMO- based technology might be harder to implement into society, it is not impossible. We state that the perception of the general public is important to accept synthetic biology innovations. Currently, the broader public is not familiar with the opportunities and possibilities of synthetic biology, and a lot of synthetic biology innovations are kept secret to avoid a negative public perception. This is not favourable to stimulate innovations nor public acceptance when products are implemented in society. Policy makers can take the lead to inform the public better about the opportunities of synthetic biology. They can facilitate better communication by investing in science communication and campaigns. Unused potentials, such as microbes that form degradable bio-based products and convert waste streams into resource streams in our economy, should be used for the sake of our healthy society and sustainable economy. If our design works, we have proof that these kinds of synthetic biology design developments have great potential and should be stimulated more, both by the public and the policies. We argue that the current perception of the public and the current legislation is not stimulating for thinking in terms of synthetic biology innovation. This way, we might be able to persuade policymakers to help change perceptions.

## **References**

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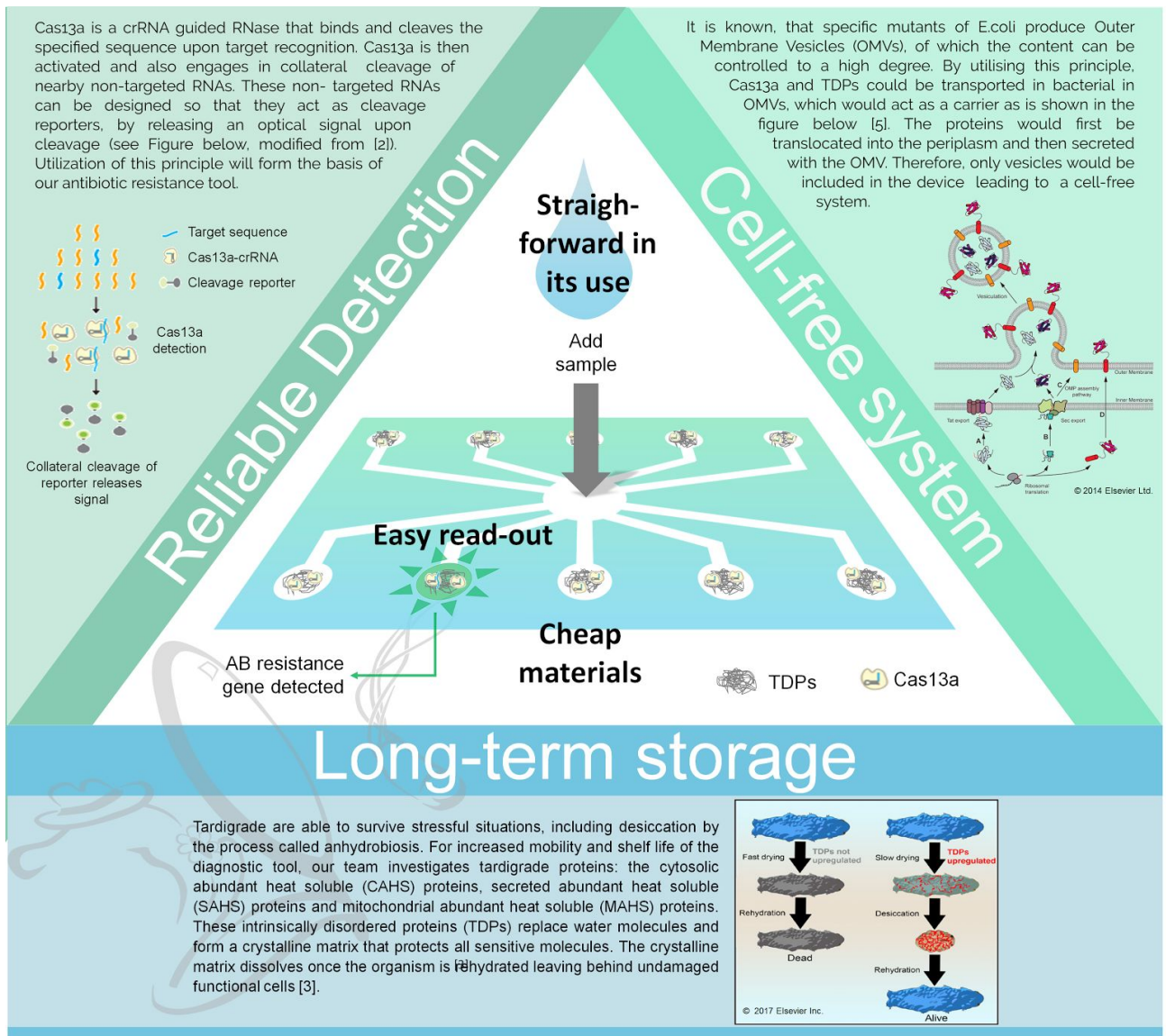
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# Appendix

## 1.Details design



**Figure 3. Schematic representation of the key features important in the design of a home detection kit for antibiotic resistance.** These features are based on the values, hopes and concerns of actors playing a role in the niche market the tool will be implemented in.

## 2.Interview

### Questions to ask

- who are you and what do you do as a farmer?
  - what kind of animals do you have?

### Bacteria and disease, how does it work

- What is the biggest challenge you face on your farm?
- What kind of diseases are the biggest challenges on your farm?

- What are the biggest challenges as a farmer in The Netherlands?
  - How about international ?
- Which animal is the most prone to catch a disease (cow, chicken etc.)?
- Which is the most difficult to treat?
- How do you treat these diseases? (Same recipe for everything or do you treat for sth specific?/ who decides the treatment?)
- Do you know what kind of bacteria causes these diseases?
- How do you prevent diseases
  - Do you use antibiotics, how much? (1 high dose/ many small doses?, on daily or yearly basis?)
  - What other stakeholders are there involved? (vets, diagnose centres, doctors, bio research groups...)

### **Diagnostics**

- When animals get sick, do you make use of diagnosis?
- Are there third parties involved? (vets/diagnostic centres... involved?)
- How is the process now?
  - How fast?
  - How expensive?
  - How reliable?
  - Worth the bothering?
  - What are the biggest challenges during diagnostics?
  - What do you get back?
  - What are the next steps after you got the results?
- Does your cattle use antibiotics?
  - When do they use it?
- How do you know that the cattle needs antibiotics?
  - always on

### **Device**

- Would you find it interesting to be able to determine which bug is making your cattle sick, and which is the best antibiotic to kill it?
- Would you prefer a user-friendly disposable test so that you can perform the diagnose yourself? Or rather have the test and send it to a laboratory so that they can quickly confirm you what the results are?
- What would you find most convenient to sample?