

Like
Buying a
Pig in a Poke
or

*Why
animal
testing could
compromise the whole
competition.
Submitted
by*

Marcus Podewski



24 October, 2010

Content

1	Introduction	3
2	Wetlab: Aim and Methods	4
2.1	Experiments with Mice	4
3	Thoughts on Animal Rights and Freedom of Research	6
3.1	Animal Welfare Act	7
3.2	Freedom of Research	8
3.3	Ethically justified?	9
4	iGEM and Animal Testing	10
4.1	An »Unusual« Research Group	10
4.1.1	A Variety of Differences	11
4.1.2	Differences with Significance	12
4.2	Endangerments	12
5	Conclusion and Catalog of Measures	14
	References	16

1 Introduction

Animal testing addresses to us fundamental questions of the treating non-human creatures. The use of other creatures for the benefit of mankind rises not only ethical questions in a huge variety but burdens us also with the responsibility of our acts. This is and has to be the basis of all considerations except somebody argued that animals did not have any ethic-relevant state.¹ Mostly all people in the western hemisphere would say that it is wrong to kill or hurt an animal for fun or, if one has a god reason, with unsatisfied cruelty. This seems to be a widely shared view, but which position do we represent in the progression of creatures? Where do the borders of our authority lie? How far could we go? Which experiments are ethically justified, which are not? Such questions are already hard to answer for normal research projects, but the problem tightens once again, when young students are up to do animal experimentation.

This year's Heidelberg iGEM team has an ambitious project: designing a genetherapeutical regulator and proving its functionality within *in vivo* experiments. Heidelberg is not the first team that wants to work *in vivo*. In 2008, a Slovenian team from the University of Ljubljana executed the first animal testing within the iGEM competition. Their aim was to design a vaccine against *Helicobacter pylori* and they got the grand prize for their efforts. The team did not have an Human Practise part, but entered into the question of biosafety extensively.² Furthermore they verified their animal experimentation through the national legislation and achieved legal standards for Slovenia:

"All procedures were approved by the Veterinary Administration of the Republic Slovenia and the Ethical committee for the laboratory animals following all the current Slovenian legislation that has been harmonized with the EU legislation on the use of laboratory animals in research."³

However, a reflection of the *meaning* or the defensibility of their animal testing did not take place. They did not get beyond the most basic considerations. In such a far reaching project, this is insufficient. According to the missing reflections of the Slovenian team in 2008 about the meaning of their research for the iGEM competition, this paper is aiming on to deal with that issue. After all, the risk exists that those teams working *in vivo* could set new standards within the competition, which may emulate other teams in the following years. A number of possible problematic questions and endangerments rise from such an animal based research, which all lead to the question: Should it be allowed that a few young (bachelor-)students conduct animal experiments after just three months of research?

To deal with this issue, I will, firstly, sketch the kind of animal testing that will be conducted by the Heidelberg iGEM team. Secondly, I will introduce the current *status quo* in Germany concerning animal testings, freedom of research and the animal protection movement. Moreover, I will examine if the tests match the German regulations for animal experimentation. If not, any further analysis is invalid. Thirdly, it will be my aim to analyse animal testing within

¹Descartes was an important exponent of such a view. In his opinion animals were just automats without relevant feelings.

²See <http://2008.igem.org/Team:Slovenia/Notebook/Safety>.

³<http://2008.igem.org/Team:Slovenia/Notebook/Methods>.

the special character of the iGEM competition. What kind of particular problems may arise from the fact that the research will not be done from a normal research group but from an iGEM team?

To solve these diverse occurring problems, I will outline a catalog of possible approaches, which could moderate the difficulties with animal testing during the competition. Certainly, it will not be my aim to deal with the ethically justification of animal experimentation in general.

2 *Wetlab: Aim and Methods*

The aim of the Heidelberg iGEM team is to design a regulator for gene therapy . To reach this aim, the team uses miRNAs, which is a promising way to intervene in internal cellular processes. Such a regulator could be a great gift for therapeutical measures in clinical application. In this sense, it could be a first-rate tool with an important meaning for the health and welfare of humans. Of course, this is at this point just a possibility and it is up to the effort and ambition of the team if the regulator will be useful.

To put the regulator into practice, animal testing is of great relevancy. The tests are conducted to analyse the elaborated construct within a metabolism and to find out if the in theory confirmed data works. They are thus the first serious step to a clinical application because with them it could be proved that the construct really operates.

Indeed, it is possible to test constructs on several cell cultures for certain tissues and organs, but certainly the results gained from this approach are limited. Moreover, one could not draw conclusions from cell cultures to the »factual« effect within an organism in a broader sense. The results are limited because cell cultures do not encounter the regulations within a metabolism or circulation and could not, thus, reproduce the diversity of an organism. They are simplified and constructed only for specific treatments. They miss the complexity and unpredictability of closed systems. The missing junction to a metabolism is also related to the second disadvantage of cell cultures. While they are not able to reflect the plurality *within* an organism, they are also not able to mirror the variety *between* organisms. Even after the succesful application of a construct in a cell culture, everything could differ by transferring it into an organism. Tiniest modifications within the hormonal balance or the composition of the blood or other usually appearing differences could have, for the tested construct, far-reaching consequences, which might be totally unknown and not anticipated.⁴

2.1 *Experiments with Mice*

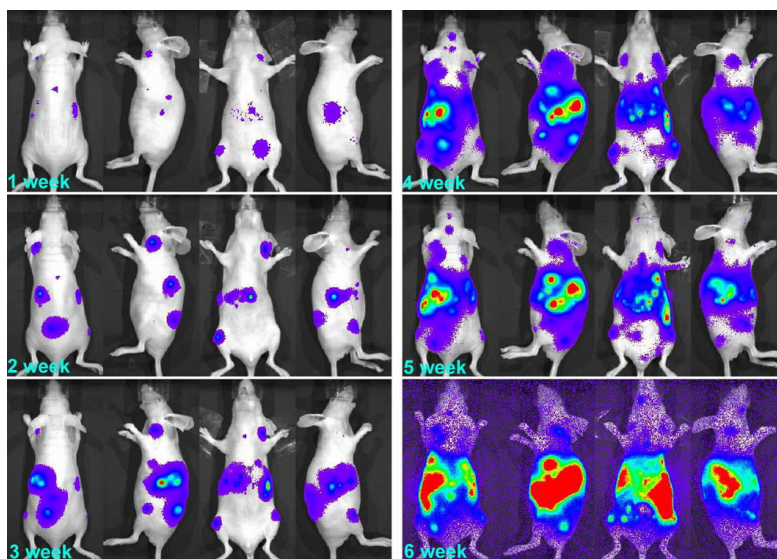
The experiment will be conducted by five groups with respectively three mice per group. The experiments will take place twice because the team wants to test different versions of the constructs. The constructs to be tested will be injected in the first 21 mice on Friday (22 Oct) and in the second 18 on Friday (29 Oct). The team will be able to present the data of the first round at the wiki, data of the second round only on the jamboree.

The experiments will be conducted by the research group of Dr. Oliver Müller, who works

⁴This is also one of the primal arguments for animal testing, although the construct, or whatever else, was testified on cell cultures succesfully.

on cardiovascular gene transfer via viral vectors. He cooperates with the Heidelberg iGEM team because legal restrictions make demands on animal testing which could not be fulfilled by the team alone.⁵ The cooperation allows the iGEM team Heidelberg to use mice of the research group of Dr. Müller. Such a cooperation can only take place if the cooperation parties research on the same tasks and use nearly the same constructs. So, the application for a license for animal testing, which has to be gained, listed exactly the constructs and matters that are allowed to get into contact with the mice (e. g. luciferase).

The mice will be injected into the tail-vein. In the following days, nearly all cells of the body will be infected by the virus »carrying« the construct. According to the construct packaged in the virus, different cells of the mice should be expressing luciferase. The off target should only lead to luciferase expression in all cells but the liver. The on targeting construct leads to an expression of luciferase solely in liver cells. The tuning construct should reveal that synthetic shRNAs in a miRNA context with randomized binding sites can lead to a tuned read-out of strong median and weak expression level of luciferase in all mouse cells. Within the positive control the virus infects all cells resulting in the highest luciferase expression all together.⁶ This would allow a comparison to indicate how far the virus generally infests the body. Not until this reference has been cleared, it is meaningful to compare several procentual data concerning how the construct operates within the body and between the different groups. The virus itself (an adenoassociated virus) will not harm the mice because it is harmless in general.



After the injection on Friday (22 Oct), the virus "carrying" the construct began to infest the body of the mouse. Here we could see the luciferase expression after six days. The elaborated construct functioned well and as expected. (© Heidelberg iGEM team)

Figure 1: Luciferase expression

After six days, the first group of mice will be narcotized and injected with a substrate (d-luciferin) that activates the luciferase. Afterwards, they will be analysed on a bioluminescence imager (see also figure 1). This treatment will not cause any pain for the mice. The light rays which emerge on a subcellular level will be quantified and released by the measurement device. A comparison between the groups could thus show us if the constructs are working

⁵For the legal restrictions see Chapter 3.1.

⁶The negative control is executed through the off target with perfect binding sites.

fine and whether if they lead to different expression levels or not.

After this examination the mice will be used by the research group of Dr. Müller for further experiments on a similar task. All experiments to be accomplished have to be done or supervised by members of the research group of Dr. Müller as they are listed on the license for animal testing. Concerning the treatment (supervision and care), conducting of the experiments and the anesthetization, such persons have to verify their qualifications with e. g. certain advanced training or an apprenticeship.

3 *Thoughts on Animal Rights and Freedom of Research*

After this first sketch concerning the conducted experiments, the *status quo* of animal testing in Germany shall be considered. It is, thereby, not my aim to discuss the theory of animal rights or to make an ethical report in a narrower sense at this point. Here, I just want to outline the current situation in Germany, which is influenced strongly by the distinction between freedom of research and the Animal Welfare Act (AWA) or rather the animal protection movement. The current AWA passed in 2006 and elevated animal rights on a constitutional level, on which it comes into conflict with the freedom of research that is based in the German Basic Constitutional Law.⁷ This conflict shall be sketched out and viewed under our specific aim: to solve the problem concerning animal testing within the iGEM competition.

German scientists execute animal testing in a broad variety of institutions and in 2009 on 2 786 435 animals - most of them were mice (1 876 563) and rats (514 722).⁸ The German society sees the millionfold use of animals as a necessary "evil", which one tries at best to replace with alternative methods. The German government is also dedicated to this aim. The ecological movement is - in international comparison - relatively strong which is demonstrated by the impressive multitude of nature conservation and animal protection organisations, which get involved against animal testing,⁹ and in the political party DIE GRÜNEN, which gained 10,7% of the votes at the last federal elections (see e. g. figure 2). All of these associations advocate for a stricter implementation of the existing laws or rather an increase of the laws concerning animal testing. On the opposite, a multitude of research institutes exist who disapprove the increase and who mention that the scientific practice is at risk. The DFG, for instance, the primary German research institute, is afraid (1) that the freedom of research is endangered,¹⁰ (2) that the basic research is enchained and (3) that the capacity for international competition is constricted.¹¹ They predict a cessation of gaining scientific knowledge by putting the existing laws into practice or even increasing them.

⁷§5 section 3: "Art and science, research and teaching are free."

⁸The Federal Ministry for Food, Agriculture and Consumer Protection (BMLE) publishes the number of animal experimentations every year. This number contains all animal testing - from those animals which were only taken a blood sample to those which were extensively examined until death. The data increased in 2009 marginal for 3,5%, which is owing the intensified research with transgenic animals. The dates for the years 2007, 2008 and 2009 can be found at BMLE: *Versuchstierzahlen*.

⁹For example: Bund für Umwelt und Naturschutz (477 279 members), Naturschutzbund Deutschland (460 000 members) or the umbrella organization Deutscher Naturschutzring with approximately 5 000 000 members or the umbrella organization Deutscher Tierschutzbund (800 000 members). This data includes not the members of the German offices of WWF (358 000 members) and Greenpeace (550 000 members).

¹⁰See DFG: *Staatsziel*.

¹¹See DFG: *Stellungnahme*.



Here we can see a demonstration ending at a rally in front of the Ulm cathedral lead by the GRÜNE, which are highly dedicated in their campaign against genetic engineering for agriculture. They had called the population of Ulm up to move against the establishment of GMO's in Germany. On the banner in front of the church is the slogan written: "Stop the gene pressure group". (© GRÜNE Baden-Württemberg, flickr.de)

Figure 2: Demonstration and rally in Ulm, 2003

3.1 Animal Welfare Act

The basis of most Protection of Animals Acts - as in Europe and the USA - are the principles of the 3Rs, which were established by RUSSELL and BURCH in 1956.¹² The main ideas of the 3Rs are the following: (1) To *replace* animal testing by methods which do not involve animal experimentation. (2) To *reduce* them to the lowest possible level. (3) To *refine* the methods in a way, that the burden on the animals would be minimized.

The German as well as the European legislation go far beyond the restrictions of the 3Rs, whereupon the German Animal Welfare Act is one of the strictest Protection of Animals Acts in Europe.¹³ The fundamental aim of the AWA is recorded in §1:

"No one may cause an animal pain, suffering or harm without *good reason*."¹⁴

In the following 22 articles, it is explained what is meant by "good reason". Nonetheless, the law remains in many points vague and unprecise. The treatment of vertebrates demonstrates this vaguity impressingly. The AWA responds to vertebrates like mice in §7 section 3:

"Experiments may be carried out on vertebrates only if the pain, suffering or harm they can be expected to inflict on the laboratory animals is *ethically justifiable* in view of the purpose of the experiment. Experiments causing lasting or repeated severe pain or suffering to vertebrates may be carried out only if the results are expected to be of *outstanding importance* for the fundamental needs of human beings or animals, including the solution of scientific problems."

What is meant with "ethically justifiable", stays unprecise. Because of this, animal welfare activists and animal ethicists as well as applicants bemoan that the phrase is hard to handle

¹²See RUSSELL/BURCH: *Principles*.

¹³In 2010 the European legislation was tightened, so that it coincide more with the German; see WEDDERBURN: *Experiments*, passim.

¹⁴A German version of the law can be found at <http://www.gesetze-im-internet.de/tierschg/> and the English version at <http://www.animallaw.info/nonus/statutes/stdeawa1998.htm>.

without a concrete catalog of ethical tools. Such an ethical tool is by now not established in a satisfying way. Nonetheless, both points - the “good reason” and “ethical justification” - must be explained in detail in the research application.

In any case, for our aim the following points are crucial: The German legislation grants great importance to animal testings. Experiments may take place, only if a) there is a *good reason*; b) the testing is *ethically justifiable*; c) the experimentation is from *outstanding importance* and d) they do not violate fundamental conditions. Such conditions are, for instance: it is not allowed to conduct animal testing to produce munition, weapons or cleaning agents;¹⁵ or to conduct testings on animals listed by the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES)¹⁶ or the German Order in Protection of Feral Fauna and Flora.¹⁷ However, all in all animal testings have to be »indispensable«.

The conflict between freedom of research and AWA rises several problems, especially because people want to preserve their interests on both sides. The applicant sometimes tends to understate the burden of animals and to overstate the expected advantage. This is impressive manifested in the standard phrases for the ethical justification of animal testing, which resemble more form letters than well-thought-out explanations. The assessor on the other hand is sometimes overstrained by lack of time, by lack of knowledge in the specific scientific field and by lack of the awareness that he himself is sometimes lead by intuitions concerning the judgement of the ethical justification which are subjective and not free of mistakes.¹⁸

3.2 Freedom of Research

The freedom of research is founded in the Basic Constitutional Law and is of great importance for the German legal tradition. In general, it avouches that every scientific interest should be feasible, which does not breach against other constitutional laws. In addition, it awards fundamental attributes which are central for our political and social way of life. The Declaration of the World Congress for Freedom of Scientific Research, that took place in Rome in Feb 2006, shows this impressively: “Freedom of Scientific research is required by democracy, is a basic civil and political right and is one of the main guarantors of human health and welfare.”¹⁹ German institutions like the DFG argue in the same way:²⁰

“Freedom of scientific research is one of the main guarantors of human health and welfare for three main reasons. The first is because scientific freedom has produced some of the principal discoveries that have lead to increases in healthy longevity worldwide. Secondly we have all benefited directly and indirectly from scientific discovery. [...] Finally, in the domain of human health, medical needs are seldom simply that. They are often also opportunities to go on living or to be free; free of pain, free or more free in the sense of being mobile or more mobile, more able effectively to operate in the world. Health is important not simply because we all value health and all want long and healthy lives. It is

¹⁵See AWA, §7 section 4 and 5.

¹⁶See checklist at <http://www.cites.org/eng/resources/pub/checklist08/Checklist.pdf>.

¹⁷German Order in Protection of Feral Fauna and Flora (Verordnung zum Schutz wild lebender Tier- und Pflanzenarten) - see checklist at http://bundesrecht.juris.de/bartschv_2005/anlage_1_26.html.

¹⁸See KOLAR: *Abwägung*, 230f. for examples in both cases.

¹⁹See DECLARATION.

²⁰See DFG: *Forschungsfreiheit*, 1.

important also because poor health is confining and good health is liberating.”²¹

The first two arguments by the Declaration are intuitively clear. They were cited in nearly all apologies for freedom of research. Research has brought mankind a longer endurance on earth and an enhanced medical care. In order that this development does not end but rather could be advanced, one has to grant research a wider scope for development.²² Such a development would be in the interest for ourselves as well as our children and descendants.²³ The thereby argument implies that it is better to have slack regulations, so that the scientific development can be pushed further more quickly and more extensive. The third item is unusual but arguing in the same direction. It states that it is better to be healthy than to be diseased and implies that it is ethically bidden to prevent diseases. This can be possible, if and only if research will be pushed ahead, wherefore one needs freedom of research reaching as far as possible.

The University of Heidelberg has also taken a stand in this issue and published two papers, which justifies animal testing within the university institutions. Both are probably written by the animal protection officer of the university of Heidelberg.²⁴ He defends animal testing as follows: Firstly, he refers to the Declaration of Helsinki²⁵, that considers animal testing to be necessary as a basis for scientific knowledge. Secondly, he mentions that animal experimentation would often be a necessary assumption for the experimental treatment of humans. Thirdly, he emphasizes the importance of animal testing in respect to the research of metabolism, immune system or the entire organism. Fourthly, he points to scientific development, that enables many patients to gain improved medical care and what could just be achieved by animal testing. Fifthly, he mentions that it will not be possible to reduce animal testing even further, because of the limits of the focused alternatives.

3.3 *Ethically justified?*

Besides the reasons for or against animal testing mentioned above, the AWA constitutes a catalog of reasons, who legitimates animal testing in principle. In addition, the “ethically justification”, such as the §7 section 3 of the AWA instructs, must be ensured. If the animal experimentation a) grounds on a “good reason”; b) covers at least one of the below mentioned subject areas; c) does not involve excluded species and d) is “ethically justified”, than it may be executed. Possible reasons for ethically justifiable animal testing according to AWA are:

1. To prevent, detect and medicate diseases.
2. To detect ecological endangerments.
3. To prove materials and products on their harmlessness.

²¹See DECLARATION. The following citations correspond to the same source.

²²“We all also benefit from the knowledge that research is ongoing into diseases or conditions from which we do not currently suffer but to which we may succumb.”

²³“It makes us feel more secure and gives us hope for the future, for ourselves and our descendants, and others for whom we care.”

²⁴Prof. Dr. Rainer Nobiling, staffmember at the Departement for Experimental Surgery, is a physiologist. It seems questionable, that a member of the surgery and somebody, who has a positive attitude concerning animal testings, is also an animal protection officer. See at <http://www.uni-heidelberg.de/presse/ruca/ruca03-2/mein.html>. For the second paper see http://www.uni-heidelberg.de/tierschutz/Wozu_Forts.html.

²⁵That is a set of principles concerning human experimentations and research ethics developed by the World Medical Association.

4. To conduct fundamental research.

Designing a genetherapeutical regulator covers two of the named reasons: the first, which consists in mediating diseases, and the fourth, which consists in doing fundamental research in order to solve basic scientific problems or to gain new and important knowledge. The fourth point was mentioned, because the iGEM based research is evidently not part of a clinical application or part of the concrete development of regulators for clinical applications. For now it does not result in practical advantage. The team can just show that such a regulator is possible.

However, the first (a) and second (b) demanded points are fulfilled. Harming animals will be done for scientific research, that fits two (1 & 4) of the four required subject areas. The third point (c) can be neglected. The used animals are mice and do not fit with one of the listed animals in the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) or the Order in Protection of Feral Fauna and Flora.

The aim of the research is clearly elaborated, so that it is comprehensible, why the animal testing is indispensable within the research approach. Moreover, the approach is ethically justified (d). The mice do not suffer pain, are treated well and get drugged before the injections. To have well feeling laboratory animals is also in the concern of the scientists because the data of stressed animals is more or less useless. All requirements are fulfilled and, in this sense, the tests are ethically justified. This is, of course, not an unexpected result, especially because Dr. Müller's research group was permitted an animal testing licence and this group works on the same task as the iGEM team. If this was different the Heidelberg team would not be able to cooperate with them. But at this point a doubt occurs. Our considerations were based on the assumption that the Heidelberg iGEM team is a normal research group like the work group of Dr. Müller. Certainly, this is not the case. They differ in essential points from each other. But do they differ in a way relevant for ethical appraisals and relevant for the iGEM competition itself?

4 *iGEM and Animal Testing*

In the last chapter we could see that the practiced research has to have a certain level of relevance and necessity so that the *in vivo* experiment is justified. This applies especially to the iGEM team.

4.1 *An »Unusual« Research Group*

Although the tests will not be executed by student members,²⁶ there remain several problems. The team members, who plan the tests, are - for students - in an exceptional situation, that is normally reserved for investigators. They decide on their own about the content, method and aim of the animal testing. Even if they do not touch the mice, they act like investigators and therefore they have the same responsibility.

Treated as an ordinary research group, the research of the iGEM team leads to no moral

²⁶As we could see in Chapter 2.1 at page 4.

problems: it is ethical²⁷ – but the Heidelberg iGEM team is not »normal«. They are young (bachelor) students with no experience in animal testing and who conduct their research in just three or four months. As we could see, the team has to take the same responsibility like an investigator for animal testing. But obviously the planning members differ from »normal« investigators and the iGEM team differs from »normal« research teams. The crucial questions are: (1) In which points do they differ exactly? (2) What is different between a student's decision leading to animal testing and an investigator's? (3) Which influence does this differences have on the quality of the decision?

4.1.1 A Variety of Differences

There are four criterias which outline the special character of the iGEM team in contrast to a »normal« research team. *First*, team members lack experience with *in vivo* experiments. In general, animal testing is no object for the university education of biologists. It takes first place in so called Praktika (periods of practical training), which are obligatory, but it is unusual that undergraduate students execute the required animal testing. For anybody who accomplishes animal testing, the University of Heidelberg requires an obligatory one week course. Without such a course it is not allowed to execute animal experimentation.

Second, the briefness of the project is unusual. Usually, research leading to animal testing takes more than just three or four months. At first, it is difficult to do sufficient research in such short time that would justify animal testing. Furthermore, it requires a certain preliminary lead time for submitting applications, for conferring of ethic commissions, or in simple words: for keeping the legal and bureaucratic guidelines.²⁸

Third, the results will not be presented and provided to the community of scientists enduringly. The Heidelberg iGEM team presents their results just at the jamboree in Boston. It is improbable that other students pick up the project and continue the work. They may be an intrigued audience but not a community who can use the results.²⁹

Fourth, they differ in their basic claim. Of course it is the aim of iGEM to put the teams in a position for doing scientific research and working as scientists. However, this will not be done with the final earnestness with which normal research groups normally do work (or, at least, should work). iGEM is after all a competition of bachelor students who are obligate to "have lots of fun".³⁰ But to execute animal testing within the competition would give the whole idea of iGEM a serious and grave touch. Animal testing are the first serious step to do clinical applications. This is an aim which has to be persued with a lot of responsibility and care. Even more important, such projects would not be about creative and "funny" ideas, they would concern the decision about the life of animals, which are after all sentient beings. Accordingly, this is a decision, which should be done with awe.

²⁷See Chapter 3.3.

²⁸The Heidelberg iGEM team could relinquish such a preliminary lead time for animal testings because of the cooperation with the research group of Dr. Müller; see Chapter 2.1 at page 4.

²⁹Certainly, the mice shall be used by the research group of Dr. Müller in which they could be helpful to obtain relevant data.

³⁰This point is so important that it is one of the requirements. See §12 at <http://2010.igem.org/Requirements>.

4.1.2 Differences with Significance

In this subsection, I will focus on the second question: How does a student's decision differ from an investigator's decision, when it comes to animal testing?

The *normal scientist* has a broader knowledge and a better understanding of the questionable subject. Thus, his ideas may rather lead to his aim and he may rather estimate the relevance and importance. Furthermore, he makes his decisions during a well invested, promoted and elaborated project. Hence, his work will be published in the most cases.

The *student* must not warrant the used research grant. He is able to deal with them in a more sensible way. Furthermore, the student based research at iGEM focused on interesting and unusual ideas, which other research groups could not implement. In this way, the standard on the meaningfulness and necessity of the project is lower in contrast to normal research. So, the iGEM based research has a broader scope and less responsibility than others - not in an ethical way, but in a financial one, which could quickly become an ethical one. The unbureaucratic and uncomplicated access can invite to do more than necessarily or ethically bidden.

Another main difference applies in the publication of gained results. This year's project of the Heidelberg iGEM team is settled between basic research and the development of instruments for the concrete therapeutic appliance. Therefore, it is subjected to the conditions of applicability. An audience that is restricted to the jamboree may be in contrast to this claim. The iGEM community may find the ideas behind the project interesting, but it will not have the resources or the ambition to continue the work; but just the chance of continuance can justify animal testing. The special iGEM character raises the risk that the results trail away unheard. A broader publicity could be ensured by making the results public - according to the case of the Heidelberg iGEM team in a gene therapeutic journal.

4.2 Endangerments

Not only the specific character of the iGEM team leads to several problems, but also the character of the iGEM competition itself. A competition lives of the ambition of the participants. Besides the creativity, the friendly get together, the exchange of thoughts and arguments, it is rivalry. The incentive is to be better than the others. This could lead to an ethical questionable trend concerning animal testing.

The successful execution of animal testings - as planned by the Heidelberg team -, would be an impact on the standards of the competition. To work *in vivo* is a considerable step for a research group because it proves that the construct works not only in theory but also within a metabolic system. Supposedly, the judges will see this point in a similar way and the effect could lead to a prize. To be scored well could animate other teams to do animal testing as well ... or even worse: It could become a kind of tacit qualification to work *in vivo* for getting a prize or for being a finalist. It could set new boundaries which others will or have to fulfill.

Moreover, another problem may occur. Animal testing can also affect the equity of the judgement in the course of the competition. The teams do not know how the results of the animal testing may affect the assessment but the outstanding character of animal testing during the (bachelor-)student based iGEM competition could impress the judges in a way that

will undermine the normal assessment standard. The fact that Slovenia won the competition in 2008 with animal testings strengthens such concerns.

Furthermore, the differences according animal testing legislation between the participating teams is enormous. Even the akin nations Germany, Austria and Switzerland differ in crucial points.³¹ About 130 teams from five continents participate at this year's competition. In case of the establishment of animal testing within the iGEM competition, the difference between the nations will lead to favouring the nations, that have a slack legislation. Moreover, the organizers should be conscious about their responsibility at this point. As an organizer they have to take responsibility as well as the teams because they have to provide the framework within the teams shall work and research. The current framework sets no limit so that the teams are only constrained by their national legislations.³² However, these differ in a broad way. Some examples shall clear this situation:

In *South Africa*, the rights and protection of experimentally used animals are on a rudimentary level. The first serious law dates back to the 90s and the deficits have to be estimated so high, that it is not possible to speak about protection in any way. The situation has not changed yet.³³

China lacks still behind in the practice of the 3Rs and has not reached essential standards³⁴ – just like the situation of animal welfare in general.³⁵ KRISHNA draws the same conclusion for *India*.³⁶

In *Latin America* Animal Welfare Acts persist only to an insufficient extent. This applies especially for animal testing or experimentation. Brazil, for instance, passed the first law, which deals with the protection of experimentally used animals in July 2010. However, the Law 11794/08 does not fit the standards of the »western hemisphere«.³⁷ Afore, no norms existed, which protected animals from the extensive access of research.³⁸

These examples show the huge gaps between the participating nations. Teams from Latin America, China or South Africa would have location-specific advantages which prevent equal competition.³⁹ Moreover, the organizers would be complicit in the cases where animal testing would be conducted which do not fit the 3Rs at all and are, therefore, ethically unjustified.⁴⁰

³¹See BINDER: *Rahmenbedingungen*, 55-60.

³²The problems which arise from animal testing are not even part of the safety issue of the iGEM competition: see <http://2010.igem.org/Safety>.

³³PICKOVER: *Committies*, passim.

³⁴KONG/QIN: *Laboratory Animal*, 53-59.

³⁵For examples see LI: *Animal Rights*, 111.

³⁶“These rules [the passed indian laws about animal welfare and testing] are in line with, but less stringent than, those in force in the UK and the USA.” KRISHNA: *Animal testing*, 885.

³⁷See detailed TREZ: *Regulation*, passim.

³⁸REZENDE/PELUZIO/SABARENSE: *Experimentation*, 238-240.

³⁹One has to consider, of course, that research institutes have ethical standards of their choice which may fit the 3Rs, but no law commits them to do so.

⁴⁰There are no international standards which might help the organizers. The only worldwide accepted standard of biomedical research, the Declaration of Helsinki, does not deal with animals at all and thus not with animal experimentation. They come just at one point in focus of the Declaration and this as a cant: “The welfare of animals used for research must be respected.” See DECLARATION OF HELSINKI, §12.

5 Conclusion and Catalog of Measures

Let us recapitulate what has been said. The Heidelberg iGEM team conducts animal testing with 40 mice to test a genetherapeutical regulator. According to the current German legislation these tests are ethically justified. But the students based research teams at the iGEM competition differ from »normal« research teams in several points. The research takes place in a shorter time. The participants have no experience with *in vivo* experiments. The results will not be published. The iGEM competition deals rather with interesting and »funny« ideas than research of a type which has to be done with notably high responsibility.

These differences affect the quality of the research and the decisions which have to be taken. Research involving animal testing has to be necessary enough that the experimentation is justified. But there are legitimate doubts concerning this necessity: (A) Research, which is in this case necessary, could unlikely be done within the short time of three months; (B) To be ethically justified, research has to be published to avoid that the data gained from the testing passes away unheard by the scientific community, but the effort to publish results is not the case so far within the competition. This point is important. If the data can not be made accessible to the scientific community, the testing would just be conducted for winning a competition which is not compatible neither with the AWA nor with the principles of 3Rs and had to be judged in the harshest of terms. (C) The not existing experience of the participants with *in vivo* experimentations could have, moreover, a negative influence on the treatment of the used animals, especially in those countries, where no or less restrictions for animal protection are in force.

Furthermore, there exist several serious endangerments. These are:

1. The equity of judgement by the judges could be threatened by the outstanding character of animal testing.
2. The differences in the national legislations concerning animal testing could constrict the equality of opportunity in research.
3. The lack of standards and restrictions could result in a joint guilt of the organizers in ethically unjustified animal experiments.
4. The rivalry and pressure at the competition may lead to a vicious circle which could raise the number of animal testing without warrantable existing reason.

The endangerments call the current treatment of iGEM teams dealing with animal testing into question. All three points underline the problem of privilege.

The problematic issues could be solved in elaborating an obligatory catalog for animal testing within the competition by the organizers. Such a catalog must contain several points: (1) To adhere the restriction of animal testing equating the 3Rs not less than in the American version. This shall guarantee a minimum of equal assessment and inure to the benefit of the competition as well as the benefit of the animals. (2) To constitute an office which the teams have to address when they wish to execute animal testing. Advisors at that office will introduce the teams interested in animal testing to the elaborated restrictions and be contact

persons for any questions. (3) Moreover, they will support the teams in publishing their data in an adequate journal, wherefore they should be settled between PR and advocacy.

These were just a few possibilities and are recommended as a suggestion how to deal with the occurring problems of animal testing within the competition. All in all, the organizers have four choices, but just three could be seen as ethical. First, they do not care about any ethical considerations and organise the competition as always. This will be the worst and also ethically reprehensible case. Second, they take matters into their own hands and elaborate a private approach as outlined above. Third, they can ensure that the national legislation of the team or at least the instructions at the specific research institute match basically with acceptable standards. This has to be verified somehow by checking, for instance, the application for an animal testing licence or an official ratification. Fourth and last, if the organizers of the iGEM competition are not able to guarantee minimal standards for animal treatment, than they are be bound to disqualify those teams which conduct animal testing.

Online Sources and Pledges

- BMLE: *Versuchstierzahlen* — Number of used animals within experimentations in 2009, published by the Bundesministerium für Ernährung, Landwirtschaft und Verbraucherschutz (BMLE), (URL: http://www.bmelv.de/cln_181/SharedDocs/Standardartikel/Landwirtschaft/Tier/Tierschutz/Versuchstierzahlen.html), retrieved on 28 Sep 2010.
- DECLARATION — Declaration of the World Congress for Freedom of Scientific Research (held in Rome 16-18 Feb 2006), (URL: <http://ieet.org/index.php/IEET/more/489/>), retrieved on 30 Sep 2010.
- DECLARATION OF HELSINKI — The World Medical Association's Declaration of Helsinki, published by the World Medical Association, (URL: <http://www.wma.net/en/30publications/10policies/b3/index.html>), retrieved on 10 Oct 2010.
- DFG: *Forschungsfreiheit* — Forschungsfreiheit. Ein Plädoyer für bessere Rahmenbedingungen der Forschung in Deutschland, published by Deutsche Forschungsgemeinschaft (DFG), Weinheim Basel New York: VCH 1996.
- DFG: *Staatsziel* — Staatsziel Tierschutz: Auswirkungen auf die Forschung, published by DFG at 16 Dec 1999, (URL: http://www.dfg.de/download/pdf/dfg_im_profil/reden_stellungnahmen/download/stellungnahme_010600.pdf), retrieved on 25 Sep 2010.
- DFG: *Stellungnahme* — Gemeinsame Stellungnahme der Deutschen Forschungsgemeinschaft, der Max Planck Gesellschaft und der Leibniz Gemeinschaft zum Vorschlag der EU Kommission für eine Richtlinie des Europäischen Parlaments und des Rates zum Schutz der für wissenschaftliche Zwecke verwendeten Tiere (873/08), published by DFG at 18 Dec 2008, (URL: http://www.dfg.de/download/pdf/dfg_im_profil/gremien/senat/tierexperimentelle_forschung/stellungnahme_dfg_mpg_lb.pdf), retrieved on 25 Sep 2010.

References

- BINDER, Regina: *Rechtliche Rahmenbedingungen für die Prüfung der ethischen Vertretbarkeit tierexperimenteller Vorhaben in Deutschland, Österreich und der Schweiz*, In: *Der ethisch vertretbare Tierversuch: Kriterien und Grenzen*, ed. by Dagmar Borchers and Jörg Luy, Paderborn: mentis 2009, 53–76.
- KOLAR, R.: *Die Abwägung der ethischen Vertretbarkeit von Tierversuchen: Theorie und Praxis*, In: *Altex* Vol. 17 2000, No. 4, 227–234.
- KONG, Qi/QIN, Chuan: *Laboratory Animal Science in China: Current Status and Potential for the Adoption of Three R Alternatives*, In: *ALTA* Vol. 38 2010, No. 1, 53–69.
- KRISHNA, Chinny: *Animal testing in India*, In: *Lancet* Vol. 357 2001, No. 9259, 885.

- LI, Peter J.: *The Evolving Animal Rights and Welfare Debate in China: Political and Social Impact Analysis*, In: *Animals, Ethics and Trade. The Challenge of Animal Sentience*, ed. by Jacky Turner and Joyce D'Silva, London Sterling: Earthscan 2006, 111–128.
- PICKOVER, Michele: *South African "Ethics Committies": Rubber Stamping Vivisection*, 2010 (URL: <http://animalrightsafrica.org/VivisectionEthicsCommittees.php>) – visited on 09 Sep 2010.
- REZENDE, Angélica Heringer de/PELUZIO, Maria do Carmo Gouveia/SABARENSE, Céphora Maria: *Animal experimentation: ethics and the Brazilian legislation*, In: *Revista de Nutrição* Vol. 21 2008, No. 2, 237 – 242.
- RUSSELL, William M. S./BURCH, Rex L.: *The Principles of Humane Experimental Technique*, London: Methuen 1959 (URL: http://altweb.jhsph.edu/pubs/books/humane_exp/het-toc) – visited on 30 Aug 2010.
- TREZ, Thales de A. e: *Refining Animal Experiments: The First Brazilian Regulation on Animal Experimentation*, In: *ATLA - Alternatives to Laboratory Animals* Vol. 38 2010, No. 3, 239–244.
- WEDDERBURN, Pete: *Experiments on animals: did the EU cave in to lobbyists?* In: *Telegraph* 2010 (URL: <http://blogs.telegraph.co.uk/news/peterwedderburn/100053008/experiments-on-animals-did-the-eu-cave-in-to-lobbyists/>) – visited on 27 Sep 2010.